

**Supplementary table 1 Gene ontology enrichment analysis of predicted target genes of differentially expressed microRNAs which were up-regulated in cholangiocarcinoma**

<b>Gene ontology category</b>	<b>P-value</b>	<b>Number of predicted miRNA target genes</b>	<b>Number of miRNAs</b>
Cellular nitrogen compound metabolic process	1.29E-92	2542	39
Biosynthetic process	7.06E-65	2013	34
Cellular protein modification process	4.70E-50	1207	29
Gene expression	1.24E-37	341	29
Neurotrophin TRK receptor signaling pathway	2.58E-23	170	22
Symbiosis, encompassing mutualism through parasitism	8.75E-17	225	12
Transcription, DNA-templated	6.51E-16	632	7
Viral process	2.24E-15	192	11
Fc-epsilon receptor signaling pathway	8.69E-15	92	16
Epidermal growth factor receptor signaling pathway	7.28E-14	106	14
Biological_process	3.33E-13	4407	9
Homophilic cell adhesion via plasma membrane adhesion molecules	1.18E-10	54	5
Blood coagulation	2.68E-10	201	11
Mitotic cell cycle	7.97E-10	170	10
TLR 10 signaling pathway	9.28E-10	28	5
Positive regulation of transcription, DNA-templated	9.28E-10	222	5
TLR6: TLR2 signaling pathway	2.49E-09	29	5
TLR1: TLR2 signaling pathway	2.49E-09	29	5
Response to stress	2.53E-09	652	10
Cellular component assembly	3.00E-09	501	14
Transcription initiation from RNA polymerase II promoter	3.00E-09	82	6

TLR 9 signaling pathway	4.37E-09	29	5
Small molecule metabolic process	4.76E-09	757	9
Regulation of transcription from RNA polymerase II promoter in response to hypoxia	6.83E-09	13	1
TLR 5 signaling pathway	7.00E-09	28	5
Catabolic process	1.28E-08	651	10
Cell death	2.04E-08	285	9
Cell adhesion	2.13E-08	189	4
Fibroblast growth factor receptor signaling pathway	5.73E-08	69	6
Nucleobase-containing compound catabolic process	9.49E-08	252	6
Macromolecular complex assembly	1.07E-07	366	14
Nervous system development	3.06E-07	116	6
Chromatin organization	3.12E-07	41	3
mRNA metabolic process	3.18E-07	47	3
TLR 2 signaling pathway	3.31E-07	25	3
TRIF-dependent TLR signaling pathway	6.84E-07	25	3
TLR 4 signaling pathway	7.86E-07	25	2
Positive regulation of transcription from RNA polymerase II promoter	9.87E-07	282	4
Transcription from RNA polymerase II promoter	1.91E-06	149	3
Fc-gamma receptor signaling pathway involved in phagocytosis	2.52E-06	28	5
TLR signaling pathway	3.07E-06	26	2
MyD88-independent TLR signaling pathway	3.07E-06	20	2
Negative regulation of transcription from RNA polymerase II promoter	4.03E-06	228	5
Membrane organization	5.36E-06	150	4
MyD88-dependent TLR signaling pathway	6.77E-06	23	2

Stress-activated MAPK cascade	6.83E-06	16	2
RNA metabolic process	8.24E-06	39	1
mRNA 3'-end processing	8.73E-06	15	2
Phosphatidylinositol-mediated signaling	1.14E-05	44	6
Cellular lipid metabolic process	1.39E-05	48	5
mRNA processing	1.68E-05	105	2
TLR 3 signaling pathway	1.82E-05	20	2
RNA splicing	2.08E-05	75	2
Transforming growth factor beta receptor signaling pathway	2.27E-05	45	2
Axon guidance	2.33E-05	121	4
Termination of RNA polymerase II transcription	2.93E-05	20	3
Protein complex assembly	4.15E-05	246	8
Glycosaminoglycan metabolic process	9.61E-05	34	3
Post-embryonic development	1.24E-04	41	3
DNA metabolic process	1.76E-04	174	5
Energy reserve metabolic process	1.91E-04	14	2
Apoptotic signaling pathway	2.04E-04	31	2
Synaptic transmission	2.32E-04	173	14
Cell junction assembly	2.51E-04	23	3
Cellular component disassembly involved in execution phase of apoptosis	2.69E-04	18	3
Negative regulation of transcription, DNA-templated	4.19E-04	170	4
In utero embryonic development	4.23E-04	84	4
Cellular protein metabolic process	4.63E-04	88	4
Insulin receptor signaling pathway	4.77E-04	45	3
Notch signaling pathway	4.99E-04	39	2
Nuclear-transcribed mRNA catabolic process, deadenylation-dependent decay	7.03E-04	18	3
Cell-cell signaling	9.06E-04	187	9

The differentially expressed microRNAs obtained from meta-analysis were input to DIANA miRPath version 3.0. *P*-value thresholds were 0.01. miRNA: MicroRNA; TRK: Tropomyosin receptor kinase; TLR: Toll-like receptor.

**Supplementary table 2 Gene Ontology enrichment analysis of predicted target genes of differentially expressed microRNAs which were down-regulated in cholangiocarcinoma**

<b>Gene ontology category</b>	<b>P-value</b>	<b>Number of predicted miRNA target genes</b>	<b>Number of miRNAs</b>
Cellular nitrogen compound metabolic process	3.08E-175	2429	48
Biosynthetic process	1.47E-108	1996	48
Cellular protein modification process	2.95E-83	1216	45
Gene expression	4.24E-60	335	42
Small molecule metabolic process	2.16E-58	1137	46
Neurotrophin TRK receptor signaling pathway	7.16E-57	178	44
Catabolic process	6.82E-43	935	45
Fc-epsilon receptor signaling pathway	2.79E-42	114	39
Symbiosis, encompassing mutualism through parasitism	3.02E-38	281	41
Viral process	4.03E-37	251	40
Cellular component assembly	5.86E-33	639	46
Macromolecular complex assembly	2.72E-25	433	46
Cellular protein metabolic process	7.51E-25	223	40
Nucleobase-containing compound catabolic process	8.44E-25	435	43
Blood coagulation	8.44E-25	230	44
Response to stress	1.20E-24	1019	46
Mitotic cell cycle	1.74E-24	198	42
Membrane organization	6.99E-23	293	44
Post-translational protein modification	4.46E-22	98	34
Epidermal growth factor receptor signaling pathway	1.07E-19	124	41
Protein complex assembly	5.11E-18	368	45
Cell death	2.49E-17	429	45

Biological_process	1.08E-14	7236	48
Cell-cell signaling	1.09E-14	314	43
Synaptic transmission	6.17E-14	206	41
Fibroblast growth factor receptor signaling pathway	1.74E-13	109	40
DNA metabolic process	3.75E-13	357	42
TLR 10 signaling pathway	7.13E-13	39	33
Phosphatidylinositol-mediated signaling	8.84E-13	83	37
Fc-gamma receptor signaling pathway involved in phagocytosis	1.65E-12	43	34
Glycosaminoglycan metabolic process	8.70E-12	60	27
TLR1: TLR2 signaling pathway	1.63E-11	39	33
TLR6: TLR2 signaling pathway	1.63E-11	39	33
Cellular lipid metabolic process	2.23E-11	74	36
Platelet activation	4.91E-11	100	36
TLR 9 signaling pathway	1.23E-10	42	33
TLR 5 signaling pathway	2.56E-10	39	33
TRIF-dependent TLR signaling pathway	7.12E-10	39	36
Hexose transport	9.23E-10	27	28
Activation of signaling protein activity involved in unfolded protein response	3.36E-09	38	26
MyD88-independent TLR signaling pathway	3.47E-09	41	36
Cellular component disassembly involved in execution phase of apoptosis	8.75E-09	28	27
Immune system process	1.03E-08	664	46
Extracellular matrix organization	1.68E-08	179	35
Protein N-linked glycosylation via asparagine	1.77E-08	54	30
Extracellular matrix disassembly	4.80E-08	56	26
Positive regulation of protein insertion into mitochondrial membrane involved in apoptotic signaling pathway	5.84E-08	22	21

Axon guidance	7.64E-08	221	39
Termination of RNA polymerase II transcription	8.25E-08	29	28
Vitamin metabolic process	9.36E-08	40	29
TLR 4 signaling pathway	1.04E-07	50	36
Platelet degranulation	1.62E-07	39	26
Insulin receptor signaling pathway	2.15E-07	89	39
mRNA metabolic process	2.71E-07	88	36
Energy reserve metabolic process	3.30E-07	51	37
TLR 2 signaling pathway	3.64E-07	40	33
Mitotic nuclear envelope disassembly	4.11E-07	22	25
mRNA 3'-end processing	4.11E-07	26	27
Glycerophospholipid biosynthetic process	4.11E-07	45	29
Transcription initiation from RNA polymerase II promoter	4.11E-07	107	40
Transcription, DNA-templated	4.11E-07	1082	48
Intrinsic apoptotic signaling pathway	4.15E-07	42	30
Phospholipid metabolic process	6.78E-07	83	33
Apoptotic signaling pathway	7.88E-07	71	35
Water-soluble vitamin metabolic process	9.18E-07	35	27
TLR 3 signaling pathway	1.20E-06	40	36
Regulation of transcription from RNA polymerase II promoter in response to hypoxia	1.36E-06	20	27
TLR signaling pathway	1.75E-06	54	36
G2/M transition of mitotic cell cycle	2.58E-06	73	34
RNA metabolic process	4.97E-06	99	36
Cell motility	1.26E-05	243	44
Regulation of small GTPase mediated signal transduction	1.39E-05	104	34
Stress-activated MAPK cascade	1.88E-05	29	33
Anatomical structure morphogenesis	1.88E-05	55	38

Cell junction organization	2.32E-05	71	36
Nucleobase-containing small molecule metabolic process	2.59E-05	32	29
Innate immune response	2.73E-05	298	43
Phosphatidylinositol biosynthetic process	3.06E-05	35	25
Cell junction assembly	3.16E-05	31	31
Nucleotide-binding oligomerization domain containing signaling pathway	3.83E-05	15	16
Cellular component movement	3.83E-05	55	36
Regulation of nitric-oxide synthase activity	4.23E-05	17	24
Chondroitin sulfate metabolic process	5.67E-05	25	24
Sulfur compound metabolic process	7.26E-05	120	40
Inositol phosphate metabolic process	1.10E-04	25	26
Nucleotide-binding domain, leucine rich repeat containing receptor signaling pathway	1.20E-04	21	22
Nitric oxide metabolic process	1.37E-04	15	20
Vesicle-mediated transport	3.11E-04	429	42
Chromatin organization	4.09E-04	58	31
Post-Golgi vesicle-mediated transport	4.64E-04	26	26
MyD88-dependent TLR signaling pathway	6.60E-04	42	34
Long-chain fatty-acyl-CoA biosynthetic process	7.44E-04	11	17
O-glycan processing	7.81E-04	25	22
Homeostatic process	8.74E-04	328	44
Regulation of rhodopsin mediated signaling pathway	9.52E-04	16	21

The differentially expressed microRNAs obtained from meta-analysis were input to DIANA miRPath version 3.0. *P*-value thresholds were 0.01. miRNA: MicroRNA; TRK: Tropomyosin receptor kinase; TLR: Toll-like receptor.



**Supplementary table 3 Pathway enrichment analysis of predicted target genes of differentially expressed microRNAs which were up-regulated in cholangiocarcinoma**

<b>KEGG pathway</b>	<b><i>P</i>-value</b>	<b>Number of predicted miRNA target genes</b>	<b>Number of miRNAs</b>
PI3K-Akt signaling pathway	4.24E-03	215	57
MAPK signaling pathway	3.44E-04	169	55
Ras signaling pathway	2.34E-06	159	58
Endocytosis	2.81E-06	150	55
Rap1 signaling pathway	3.96E-05	146	54
Proteoglycans in cancer	8.32E-10	145	55
Focal adhesion	7.78E-05	144	50
Regulation of actin cytoskeleton	1.69E-03	141	55
cAMP signaling pathway	4.69E-03	131	53
Oxytocin signaling pathway	1.14E-04	112	54
cGMP-PKG signaling pathway	5.87E-03	110	55
Hippo signaling pathway	1.01E-06	109	49
Wnt signaling pathway	8.12E-05	101	56
Axon guidance	4.05E-10	99	48
Adrenergic signaling in cardiomyocytes	3.86E-04	97	52
Dopaminergic synapse	1.78E-03	94	50
Thyroid hormone signaling pathway	2.25E-07	89	49
FoxO signaling pathway	9.78E-03	89	50
Glutamatergic synapse	7.34E-07	86	47
Neurotrophin signaling pathway	2.10E-03	83	50
Cholinergic synapse	9.81E-05	81	48
Circadian entrainment	4.62E-08	77	49
Estrogen signaling pathway	1.40E-05	69	46
Retrograde endocannabinoid signaling	9.78E-03	69	46
Melanogenesis	9.36E-03	68	52
Prostate cancer	2.89E-04	66	45

ErbB signaling pathway	2.43E-05	65	50
Adherens junction	1.34E-08	63	45
Insulin secretion	8.49E-04	63	49
Morphine addiction	4.07E-03	63	47
TGF-beta signaling pathway	4.74E-06	60	47
Chronic myeloid leukemia	4.32E-05	59	44
Bacterial invasion of epithelial cells	5.79E-05	59	44
Renal cell carcinoma	5.57E-06	54	47
ECM-receptor interaction	2.89E-04	54	39
Prolactin signaling pathway	2.58E-04	52	42
Long-term potentiation	4.79E-04	52	43
Amphetamine addiction	8.75E-05	51	45
Pancreatic cancer	1.34E-04	51	43
Colorectal cancer	7.78E-05	49	41
Long-term depression	1.55E-06	48	39
Glioma	2.89E-04	47	41
Shigellosis	2.67E-03	47	41
Acute myeloid leukemia	9.76E-03	42	40
Endometrial cancer	2.67E-03	40	39
Lysine degradation	2.00E-03	35	42
Circadian rhythm	3.19E-05	28	43
Prion diseases	1.94E-04	20	21

The differentially expressed microRNAs obtained from meta-analysis were input to DIANA miRPath version 3.0. P-value thresholds were 0.01. KEGG: Kyoto Encyclopedia of Genes and Genomes; miRNA: MicroRNA; PI3K: Phosphatidylinositol-3 kinases; MAPK: Mitogen-activated protein kinase; PKG: cGMP-dependent protein kinase G; TGF: Transforming growth factor; ECM: Extracellular matrix.

**Supplementary table 4 Pathway enrichment analysis of predicted target genes of differentially expressed microRNAs which were down-regulated in cholangiocarcinoma**

KEGG pathway	<i>P</i> -value	Number of predicted miRNA target genes	Number of miRNAs
PI3K-Akt signaling pathway	1.91E-05	209	42
Ras signaling pathway	2.03E-06	147	39
MAPK signaling pathway	7.90E-03	147	42
Proteoglycans in cancer	1.05E-13	134	41
Focal adhesion	1.27E-04	131	42
Rap1 signaling pathway	1.22E-03	127	40
Endocytosis	3.15E-03	121	40
Hippo signaling pathway	7.73E-09	101	37
Wnt signaling pathway	2.96E-06	92	36
FoxO signaling pathway	8.42E-06	89	32
Axon guidance	8.40E-05	83	35
Neurotrophin signaling pathway	9.45E-04	80	39
Choline metabolism in cancer	7.20E-03	64	34
ErbB signaling pathway	1.28E-05	62	39
Prostate cancer	6.08E-04	61	37
TGF-beta signaling pathway	3.49E-08	57	33
Melanoma	5.22E-05	53	34
ECM-receptor interaction	1.67E-12	52	28
Renal cell carcinoma	9.58E-07	50	34
Chronic myeloid leukemia	9.45E-04	50	33
Glioma	1.09E-06	47	34
Pancreatic cancer	5.15E-04	46	31
mTOR signaling pathway	3.18E-04	45	33
Prolactin signaling pathway	2.95E-03	45	32
Colorectal cancer	5.29E-04	44	35

Long-term depression	2.95E-03	41	31
Acute myeloid leukemia	3.15E-03	39	32
Basal cell carcinoma	4.67E-03	39	30
Endometrial cancer	4.19E-04	38	30
Lysine degradation	2.69E-04	29	32
Prion diseases	5.91E-03	12	19
Fatty acid biosynthesis	9.22E-07	7	12

The differentially expressed microRNAs obtained from meta-analysis were input to DIANA miRPath version 3.0. P-value thresholds were 0.01. KEGG: Kyoto Encyclopedia of Genes and Genomes; miRNA: MicroRNA; PI3K: Phosphatidylinositol-3 kinases; MAPK: Mitogen-activated protein kinase; PKG: cGMP-dependent protein kinase G; TGF: Transforming growth factor; ECM: Extracellular matrix.