

Supplemental Material 3. Results from bioinformatic analyses. The results from

I: DIANA miRPath v. 3.0 – with TarBase, TargetScan and micro-T CDS-

II: KEGG Pathway summary report in miRSystem v.2016

III: miRNAs and predicted target genes in PI3k / Akt and fatty acid metabolism in KEGG and Reactome.

miRSystem v.2016

I: DIANA miRPath v. 3.0 – with TarBase, TargetScan and micro-T CDS-

a) DIANA miRPath. KEGG pathways, overexpressed miRNAs. Tarbase. FDR p 0.05, conservative stats.

KEGG pathway	p-value	#genes	#miRNAs
MicroRNAs in cancer	6.0800430848E-053	139	24
Proteoglycans in cancer	4.47238028384E-013	163	23
Renal cell carcinoma	9.4444158425E-009	61	23
Hepatitis B	1.43239063324E-008	117	23
Pancreatic cancer	5.69057185952E-008	61	22
Protein processing in endoplasmic reticulum	7.0057960447E-008	137	23
Cell cycle	2.46101467727E-007	107	23
Fatty acid metabolism	2.55419793394E-006	37	21
Ubiquitin mediated proteolysis	2.55419793394E-006	114	24
Pathways in cancer	0.000006714	295	24
TGF-beta signaling pathway	1.31397551801E-005	66	21
Endocytosis	1.80587561185E-005	162	24
Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate	2.02571096558E-005	17	12
Prostate cancer	2.48763679999E-005	77	22
p53 signaling pathway	2.5241332282E-005	63	23
Transcriptional misregulation in cancer	2.74535181528E-005	135	23
FoxO signaling pathway	4.78834978898E-005	113	23
Chronic myeloid leukemia	4.78834978898E-005	66	23
Small cell lung cancer	8.45151241523E-005	74	22
Adherens junction	9.67690752731E-005	62	22
Non-small cell lung cancer	9.67690752731E-005	48	22
Colorectal cancer	0.0001300855	54	23
Glycosaminoglycan biosynthesis - keratan sulfate	0.0001857917	14	12
Hippo signaling pathway	0.0004545794	110	22
Other types of O-glycan biosynthesis	0.0005215505	23	18
Prion diseases	0.0005215505	25	21
Epstein-Barr virus infection	0.0007014133	156	22
Viral carcinogenesis	0.0008359908	165	23
Glioma	0.0009771701	52	22
Endometrial cancer	0.0015250984	45	22
ErbB signaling pathway	0.0015250984	68	23
MAPK signaling pathway	0.0021346344	188	23

RNA transport	0.0022359145	129	23
mTOR signaling pathway	0.0023013499	54	22
Fatty acid degradation	0.0033484053	28	16
Oocyte meiosis	0.0033484053	84	22
Neurotrophin signaling pathway	0.0034569619	93	23
Phosphatidylinositol signaling system	0.0041427146	63	22
Acute myeloid leukemia	0.0046756119	48	22
Spliceosome	0.0047303608	95	22
Thyroid hormone signaling pathway	0.0047303608	92	22
Bacterial invasion of epithelial cells	0.0047303608	61	23
N-Glycan biosynthesis	0.0048857356	38	18
Central carbon metabolism in cancer	0.006128675	54	22
Fatty acid elongation	0.0064130254	18	16
Lysine degradation	0.0064163531	39	21
Focal adhesion	0.0092435769	155	23
Signaling pathways regulating pluripotency of stem cells	0.0096360024	104	23
Inositol phosphate metabolism	0.0115070838	51	22
Shigellosis	0.0115070838	52	23
Glycosylphosphatidylinositol(GPI)-anchor biosynthesis	0.0117354742	22	16
Thyroid cancer	0.0155024708	25	22
Insulin signaling pathway	0.0170152572	106	23
Melanoma	0.0209452615	55	23
Apoptosis	0.0209554027	69	22
Progesterone-mediated oocyte maturation	0.0224035802	69	22
Sphingolipid signaling pathway	0.0299312683	87	23
Axon guidance	0.0329859637	93	22
TNF signaling pathway	0.0329859637	84	24
Pyrimidine metabolism	0.0331857043	76	22
Lysosome	0.0331857043	88	22
PI3K-Akt signaling pathway	0.0343396695	229	23
DNA replication	0.0343836113	29	15
Chagas disease (American trypanosomiasis)	0.0443312449	77	22

b) DIANA + TargetScan. Overexpressed miRNAs. Context score -0.4, FDR, conservative stats and p 0.05

KEGG pathway	p-value	#genes	#miRNAs
Fatty acid biosynthesis	3.55093059276E-030	3	4
Prion diseases	2.51619786355E-022	4	6
Fatty acid metabolism	3.07474808279E-015	7	8
Glycosphingolipid biosynthesis - lacto and neolacto series	0.0131221549	3	3
Mucin type O-Glycan biosynthesis	0.0181820424	6	7
Cytokine-cytokine receptor interaction	0.0181833996	31	17
PI3K-Akt signaling pathway	0.0181833996	47	22
Glycosaminoglycan biosynthesis - heparan sulfate / heparin	0.0446098753	3	6

c) DIANA + microT-CDS. Overexpressed miRNAs. MicroT Threshold 0.8

KEGG pathway	p-value	#genes	#miRNAs
Fatty acid biosynthesis	1.11889144973E-009	8	8

Mucin type O-Glycan biosynthesis	2.84293839002E-008	17	15
Pathways in cancer	1.15223904047E-006	199	23
Proteoglycans in cancer	1.16457575633E-006	103	23
MAPK signaling pathway	1.70916043456E-005	137	24
Signaling pathways regulating pluripotency of stem cells	1.96231012205E-005	79	24
Axon guidance	2.13652796158E-005	75	22
Thyroid hormone signaling pathway	3.212068906E-005	65	23
Rap1 signaling pathway	4.56119262949E-005	114	23
Prion diseases	0.000058103	12	14
Renal cell carcinoma	6.35216735341E-005	42	22
Ras signaling pathway	0.0001178121	114	22
Long-term depression	0.0001399584	37	20
ErbB signaling pathway	0.000297166	52	22
PI3K-Akt signaling pathway	0.000297166	169	23
Prostate cancer	0.0004776205	53	23
Glioma	0.0005583944	37	22
Hippo signaling pathway	0.0007176661	77	22
Melanoma	0.0007176661	44	22
Glutamatergic synapse	0.0007283007	60	22
Non-small cell lung cancer	0.0010426908	34	19
TGF-beta signaling pathway	0.0010426908	45	21
FoxO signaling pathway	0.0014185679	73	22
Colorectal cancer	0.0014283738	35	20
Gap junction	0.0014283738	49	22
Adherens junction	0.0014659518	44	21
Oxytocin signaling pathway	0.0017371508	83	23
Focal adhesion	0.0023912746	106	23
Neurotrophin signaling pathway	0.0026911488	66	23
Regulation of actin cytoskeleton	0.0029738217	111	22
Choline metabolism in cancer	0.0029738217	57	22
N-Glycan biosynthesis	0.0036893768	24	16
Endometrial cancer	0.0050747077	32	20
Tight junction	0.0061730605	72	23
Adrenergic signaling in cardiomyocytes	0.0070711804	71	23
p53 signaling pathway	0.0081876308	39	20
Pancreatic cancer	0.009425463	38	20
Chronic myeloid leukemia	0.0096394863	41	23
Prolactin signaling pathway	0.0110343244	39	20
Ubiquitin mediated proteolysis	0.0168482958	71	24
Sphingolipid signaling pathway	0.0257373139	61	22
Wnt signaling pathway	0.0335578825	69	22
ECM-receptor interaction	0.0377411885	38	20
Endocytosis	0.0377411885	98	22
mTOR signaling pathway	0.0395918749	35	20

d) Diana + Tarbase. KEGG. Downregulated miRNAs.

KEGG pathway	p-value	#genes	#miRNAs
MicroRNAs in cancer	1.04218336742E-061	104	11
Proteoglycans in cancer	1.91745701273E-011	104	11

Fatty acid metabolism	3.64806861495E-008	22	10
Lysine degradation	1.36782648056E-007	29	11
Protein processing in endoplasmic reticulum	4.37410913424E-007	88	11
Colorectal cancer	7.22137750536E-007	39	11
Cell cycle	1.15136074135E-006	67	11
Adherens junction	1.25206305599E-006	41	11
Fatty acid biosynthesis	1.95739861294E-006	6	8
Hepatitis B	2.78125145325E-006	72	11
Hippo signaling pathway	2.93793121997E-006	65	11
FoxO signaling pathway	9.30614264531E-006	73	11
Pancreatic cancer	1.02678918883E-005	41	11
Glioma	1.17652567901E-005	36	11
Prostate cancer	2.93598021567E-005	52	11
Endometrial cancer	3.67443525449E-005	32	11
Central carbon metabolism in cancer	3.67443525449E-005	36	11
Viral carcinogenesis	5.12394914699E-005	93	11
Spliceosome	9.19036992581E-005	64	11
Thyroid hormone signaling pathway	9.19036992581E-005	58	11
Neurotrophin signaling pathway	0.000101363	63	11
Ubiquitin mediated proteolysis	0.0001119049	72	11
Estrogen signaling pathway	0.0001120435	50	11
Chronic myeloid leukemia	0.0001462347	41	11
Non-small cell lung cancer	0.0001472632	32	11
p53 signaling pathway	0.0001850886	41	11
Renal cell carcinoma	0.0006005235	37	11
Biosynthesis of unsaturated fatty acids	0.0009605068	12	9
TGF-beta signaling pathway	0.0011070787	39	11
ErbB signaling pathway	0.001211141	42	11
RNA transport	0.001548655	78	11
Pathways in cancer	0.001548655	163	11
Regulation of actin cytoskeleton	0.0030158197	91	11
Oocyte meiosis	0.0034169746	52	11
Phosphatidylinositol signaling system	0.0034169746	41	11
Focal adhesion	0.0034169746	94	11
Small cell lung cancer	0.0050852206	43	11
Thyroid cancer	0.0065945316	16	11
mRNA surveillance pathway	0.0080242407	44	11
TNF signaling pathway	0.0080242407	54	11
Epstein-Barr virus infection	0.0087088388	93	11
Bladder cancer	0.0096383971	23	11
Progesterone-mediated oocyte maturation	0.0106482898	43	11
Bacterial invasion of epithelial cells	0.0106482898	36	11
mTOR signaling pathway	0.0108534042	34	11
Prolactin signaling pathway	0.0134001283	34	11
AMPK signaling pathway	0.0135419823	57	11
Fatty acid elongation	0.0160639187	11	8
HIF-1 signaling pathway	0.0226623394	49	11
Choline metabolism in cancer	0.025074804	46	11
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0.0345817991	24	11
PI3K-Akt signaling pathway	0.0368458226	127	11

Endocytosis	0.0410506425	84	11
Wnt signaling pathway	0.0410506425	59	11
HTLV-I infection	0.0423373556	106	11
MAPK signaling pathway	0.0437025212	101	11
Insulin signaling pathway	0.0450318224	61	11
Signaling pathways regulating pluripotency of stem cells	0.0478400082	59	11
Melanoma	0.0478400082	32	11

e) DIANA + Targetscan. Downregulated microRNAs. Context score -0.4

KEGG pathway	p-value	#genes	#miRNAs
Fatty acid biosynthesis	<1E-325	2	2
ECM-receptor interaction	<1E-325	19	5
Mucin type O-Glycan biosynthesis	3.109805E-006	1	2
Fatty acid metabolism	4.098023E-005	6	2
Glycosphingolipid biosynthesis - lacto and neolacto series	0.008277265	1	1
Proteoglycans in cancer	0.008487167	38	2
Steroid hormone biosynthesis	0.01982273	1	2
Adherens junction	0.03674103	14	3

f) DIANA + microT-CDS. Downregulated microRNAs. MicroT Threshold 0.8

KEGG pathway	p-value	#genes	#miRNAs
Mucin type O-Glycan biosynthesis	2.07137645133E-005	8	6
FoxO signaling pathway	0.0005386679	38	8
Neurotrophin signaling pathway	0.0005386679	37	10
MAPK signaling pathway	0.0005386679	64	11
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	0.0331443028	21	5
Axon guidance	0.0331443028	33	7
Long-term depression	0.0331443028	17	7
Amphetamine addiction	0.0331443028	16	7
N-Glycan biosynthesis	0.0331443028	12	8
B cell receptor signaling pathway	0.0331443028	22	9
Non-small cell lung cancer	0.0392900667	16	8
Ras signaling pathway	0.0392900667	46	10
Hippo signaling pathway	0.0408059962	25	7
Ubiquitin mediated proteolysis	0.0408059962	35	8
Glioma	0.0408059962	16	8
Prostate cancer	0.0408059962	22	8
Signaling pathways regulating pluripotency of stem cells	0.0408059962	33	10
Regulation of actin cytoskeleton	0.0412588654	47	8

II: KEGG Pathway summary report in miRSystem v.2016

a) MiRSystem. Overexpressed miRNAs. KEGG Pathway ranking summary report.

KEGG pathway	Total Genes Of The Term	Union Targets In The Term	Mirs In The Term	Score
Pathways_In_Cancer	325	145	22	3.487
Axon_Guidance	129	68	20	2.682
MAPK_Signaling_Pathway	272	114	21	2.636
Focal_Adhesion	199	78	20	2.196
Prostate_Cancer	89	45	20	2.166
Neurotrophin_Signaling_Pathway	127	66	20	2.105
Melanoma	71	38	21	2.036
Wnt_Signaling_Pathway	150	73	21	2.033
Pancreatic_Cancer	70	39	21	1.923
Renal_Cell_Carcinoma	70	38	17	1.908
Glioma	65	33	21	1.884
TGF-Beta_Signaling_Pathway	84	44	19	1.873
Chronic_Myeloid_Leukemia	73	40	22	1.868
Regulation_Of_Actin_Cytoskeleton	213	89	21	1.849
Endocytosis	201	83	20	1.832
Ubiquitin_Mediated_Proteolysis	135	53	19	1.632
ErbB_Signaling_Pathway	87	43	19	1.628
T_Cell_Receptor_Signaling_Pathway	108	48	20	1.569
Insulin_Signaling_Pathway	137	52	19	1.567
Small_Cell_Lung_Cancer	84	36	20	1.531
Adherens_Junction	73	36	18	1.443
Non-Small_Cell_Lung_Cancer	54	29	21	1.39
mTOR_Signaling_Pathway	52	23	18	1.349
Colorectal_Cancer	62	33	18	1.33
P53_Signaling_Pathway	68	33	18	1.324
Cell_Cycle	124	47	21	1.316
Progesterone-Mediated_Oocyte_Maturation	86	34	20	1.308
Oocyte_Meiosis	112	45	19	1.305
Long-Term_Potentialiation	70	33	17	1.253
Fc_Gamma_R-Mediated_Phagocytosis	94	40	19	1.22
Chagas_Disease	104	43	18	1.185
Vegf_Signaling_Pathway	76	29	17	1.173
Aldosterone-Regulated_Sodium_Reabsorption	42	21	17	1.168
Melanogenesis	101	45	18	1.16
Cytokine-Cytokine_Receptor_Interaction	275	61	21	1.114
Jak-Stat_Signaling_Pathway	155	45	21	1.105
Acute_Myeloid_Leukemia	57	27	18	1.104
Chemokine_Signaling_Pathway	189	63	19	1.09
Protein_Processing_In_Endoplasmic_Reticulum	166	46	17	1.069
Gap_Junction	90	35	16	1.048

B_Cell_Receptor_Signaling_Pathway	75	27	17	1.035
Calcium_Signaling_Pathway	177	46	20	0.993
Adipocytokine_Signaling_Pathway	68	23	15	0.974
Bladder_Cancer	42	21	16	0.973
Phosphatidylinositol_Signaling_System	78	29	17	0.97
Tight_Junction	132	51	18	0.968
Amyotrophic_Lateral_Sclerosis_(Als)	54	23	16	0.939
Bacterial_Invasion_Of_Epithelial_Cells	70	24	19	0.931
Dilated_Cardiomyopathy	90	36	16	0.928
Gastric_Acid_Secretion	74	30	16	0.922
Type_Ii_Diabetes_Mellitus	47	19	17	0.92
Endometrial_Cancer	52	22	15	0.91
Apoptosis	88	31	20	0.906
Shigellosis	61	26	17	0.89
Toxoplasmosis	132	38	18	0.89
Hypertrophic_Cardiomyopathy_(Hcm)	87	31	17	0.851
Vascular_Smooth_Muscle_Contraction	126	39	18	0.827
Leukocyte_Transendothelial_Migration	116	34	19	0.825
Notch_Signaling_Pathway	47	20	15	0.815
Gnrh_Signaling_Pathway	101	37	16	0.805
Fc_Epsilon_Ri_Signaling_Pathway	79	29	16	0.803
Hepatitis_C	134	39	19	0.794
Salivary_Secretion	89	28	14	0.79
Toll-Like_Receptor_Signaling_Pathway	102	28	16	0.78
Pancreatic_Secretion	103	27	15	0.763
Long-Term_Depression	70	25	15	0.755
Olfactory_Transduction	388	7	8	0.753
Arrhythmogenic_Right_Ventricular_Cardiomyopathy_(A rvc)	74	27	14	0.731
Huntington's_Disease	183	37	20	0.729
Hedgehog_Signaling_Pathway	56	22	12	0.722
Cell_Adhesion_Molecules_(Cams)	133	30	17	0.69
Natural_Killer_Cell_Mediated_Cytotoxicity	140	28	16	0.667
Amoebiasis	105	30	17	0.666
Inositol_Phosphate_Metabolism	57	19	12	0.654
Neuroactive_Ligand-Receptor_Interaction	318	46	16	0.644
Ecm-Receptor_Interaction	84	25	15	0.633
Snare_Interactions_In_Vesicular_Transport	36	16	11	0.632
Epithelial_Cell_Signaling_In_Helicobacter_Pylori_Infect ion	68	22	16	0.6
Thyroid_Cancer	29	12	11	0.599
Viral_Myocarditis	70	19	11	0.586
Vasopressin-Regulated_Water_Reabsorption	44	17	12	0.582
Basal_Cell_Carcinoma	55	21	16	0.58
Rna_Transport	144	30	17	0.551
Spliceosome	127	22	15	0.537
Nod-Like_Receptor_Signaling_Pathway	62	16	16	0.524
Carbohydrate_Digestion_And_Absorption	43	11	15	0.522
Protein_Digestion_And_Absorption	80	20	15	0.494
Rna_Degradation	57	12	12	0.487

Lysosome	121	24	14	0.482
Alzheimer's_Disease	168	34	15	0.481
Basal_Transcription_Factors	35	12	13	0.468
Phagosome	154	29	15	0.45
Cardiac_Muscle_Contraction	77	19	15	0.449
Purine_Metabolism	161	23	15	0.448
Rig-I-Like_Receptor_Signaling_Pathway	71	19	14	0.444
N-Glycan_Biosynthesis	49	14	10	0.429
Prion_Diseases	36	11	10	0.414
O-Glycan_Biosynthesis	30	10	9	0.412
Glycosaminoglycan_Biosynthesis_Heparan_Sulfate	26	7	6	0.404
Leishmaniasis	72	17	12	0.396
Glycosphingolipid_Biosynthesis_Lacto_And_Neolacto_Series	26	8	7	0.366
Hematopoietic_Cell_Lineage	88	18	12	0.356
PPAR_Signaling_Pathway	70	13	11	0.353
Parkinson's_Disease	130	14	13	0.349
Peroxisome	79	13	12	0.349
Vibrio_Cholerae_Infection	54	14	9	0.339
Nucleotide_Excision_Repair	44	9	9	0.302
Pathogenic_Escherichia_Coli_Infection	56	12	10	0.301
Type_I_Diabetes_Mellitus	43	9	7	0.3
Sphingolipid_Metabolism	40	12	10	0.299
Regulation_Of_Autophagy	34	7	8	0.293
Cysteine_And_Methionine_Metabolism	36	7	11	0.288
Abc_Transporters	44	7	9	0.265
Allograft_Rejection	37	8	6	0.265
Systemic_Lupus_Erythematosus	136	9	8	0.264
Maturity_Onset_Diabetes_Of_The_Young	25	7	6	0.257
Malaria	51	8	9	0.255
Lysine_Degradation	44	10	10	0.251
Graft-Versus-Host_Disease	41	7	6	0.25
Intestinal_Immune_Network_For_Iga_Production	48	7	7	0.244
Pyrimidine_Metabolism	99	9	8	0.224
Antigen_Processing_And_Presentation	76	11	8	0.214
Glycerophospholipid_Metabolism	79	14	6	0.214
Citrate_Cycle_(Tca_Cycle)	31	5	7	0.205
Galactose_Metabolism	26	4	7	0.205
Fructose_And_Mannose_Metabolism	34	7	8	0.202
Selenoamino_Acid_Metabolism	26	3	9	0.195
Fatty_Acid_Metabolism	43	6	6	0.19
Collecting_Duct_Acid_Secretion	27	5	4	0.171
Autoimmune_Thyroid_Disease	52	5	4	0.164
Glycerolipid_Metabolism	49	7	6	0.16
Oxidative_Phosphorylation	132	9	6	0.16
Starch_And_Sucrose_Metabolism	53	4	7	0.153
Amino_Sugar_And_Nucleotide_Sugar_Metabolism	47	7	6	0.149
Complement_And_Coagulation_Cascades	69	5	6	0.139
Taste_Transduction	52	5	6	0.139
Dna_Replication	36	5	5	0.133

Pentose_Phosphate_Pathway	26	3	4	0.133
Homologous_Recombination	28	4	3	0.125
Arginine_And_Proline_Metabolism	54	8	5	0.123
Base_Excision_Repair	33	4	4	0.119
Glycolysis_Gluconeogenesis	65	4	5	0.116
Retinol_Metabolism	65	5	4	0.107
Cytosolic_Dna-Sensing_Pathway	56	4	5	0.096
Proteasome	44	4	4	0.096
Ether_Lipid_Metabolism	35	4	2	0.087
Alanine_Aspartate_And_Glutamate_Metabolism	32	5	3	0.085
Valine_Leucine_And_Isoleucine_Degradation	44	3	3	0.075
Phototransduction	29	2	3	0.073
Glutathione_Metabolism	50	3	3	0.067
Pyruvate_Metabolism	41	3	3	0.062
Propanoate_Metabolism	32	2	2	0.059
Staphylococcus_Aureus_Infection	55	2	2	0.047
RNA_Polymerase	29	2	2	0.04
Glycosylphosphatidylinositol(Gpi)-Anchor_Biosynthesis	25	1	2	0.037
Asthma	30	2	2	0.036
Butanoate_Metabolism	30	1	1	0.032
Glycine_Serine_And_Threonine_Metabolism	32	2	1	0.029
Drug_Metabolism_Other_Enzymes	52	2	1	0.026
Primary_Immunodeficiency	35	1	1	0.025
Aminoacyl-Trna_Biosynthesis	63	1	1	0.019
Steroid_Hormone_Biosynthesis	56	1	1	0.019
Arachidonic_Acid_Metabolism	57	1	1	0.018

b) MiRSystem. Infraexpressed miRNAs. KEGG Pathway ranking summary report.

KEGG Pathways	Total_genes_of_the_term	Union_target_s_in_the_term	Mirs_in_the_term	Score
Axon_guidance	129	39	8	3.215
Neurotrophin_signaling_pathway	127	32	9	2.002
Ubiquitin_mediated_proteolysis	135	29	8	1.972
TGF-beta_signaling_pathway	84	27	7	1.956
MAPK_signaling_pathway	272	54	9	1.946
Pathways_in_cancer	325	62	9	1.89
Endocytosis	201	43	8	1.758
Protein_processing_in_endoplasmic_reticulum	166	30	9	1.691
Pancreatic_cancer	70	21	8	1.647
Cytokine-cytokine_receptor_interaction	275	36	7	1.597
Amyotrophic_lateral_sclerosis_(als)	54	19	7	1.587
Chronic_myeloid_leukemia	73	21	9	1.581
ErbB_signaling_pathway	87	25	10	1.553
Regulation_of_actin_cytoskeleton	213	39	9	1.525
Jak-stat_signaling_pathway	155	22	9	1.403
Bacterial_invasion_of_epithelial_cells	70	19	8	1.388

Prostate_cancer	89	22	8	1.354
Glioma	65	19	8	1.315
Colorectal_cancer	62	16	7	1.225
Melanoma	71	18	7	1.196
Long-term_potentiation	70	19	6	1.194
Insulin_signaling_pathway	137	28	10	1.192
Focal_adhesion	199	33	10	1.162
Adherens_junction	73	19	8	1.144
Shigellosis	61	15	7	1.118
Olfactory_transduction	388	3	3	1.117
T_cell_receptor_signaling_pathway	108	21	7	1.105
Non-small_cell_lung_cancer	54	14	8	1.086
Chemokine_signaling_pathway	189	26	10	1.048
Chagas_disease	104	20	7	1.045
Renal_cell_carcinoma	70	18	8	1.041
Small_cell_lung_cancer	84	14	7	1.03
Toxoplasmosis	132	22	8	1.014
Oocyte_meiosis	112	24	6	1.01
Wnt_signaling_pathway	150	29	7	1.009
Apoptosis	88	17	7	1.001
p53_signaling_pathway	68	17	5	0.996
Dilated_cardiomyopathy	90	19	8	0.989
Calcium_signaling_pathway	177	26	8	0.954
Notch_signaling_pathway	47	12	7	0.941
Type_II_diabetes_mellitus	47	11	8	0.921
Progesterone-mediated_oocyte_maturation	86	17	7	0.914
B_cell_receptor_signaling_pathway	75	11	6	0.91
Cell_cycle	124	21	7	0.909
Arrhythmogenic_right_ventricular_cardiomyopathy_(arvc)	74	12	7	0.882
O-glycan_biosynthesis	30	8	6	0.853
VEGF_signaling_pathway	76	12	7	0.849
Phosphatidylinositol_signaling_system	78	16	7	0.843
Hypertrophic_cardiomyopathy_(hcm)	87	16	8	0.827
N-glycan_biosynthesis	49	10	6	0.813
mTOR_signaling_pathway	52	13	7	0.808
Aldosterone-regulated_sodium_reabsorption	42	11	7	0.789
Natural_killer_cell_mediated_cytotoxicity	140	15	7	0.773
Adipocytokine_signaling_pathway	68	14	7	0.768
Amoebiasis	105	14	8	0.752
Fc_gamma_r-mediated_phagocytosis	94	14	7	0.711
Bladder_cancer	42	9	7	0.694
Hepatitis_c	134	20	7	0.672
Inositol_phosphate_metabolism	57	11	6	0.636
Endometrial_cancer	52	9	8	0.632
Melanogenesis	101	17	5	0.621
Rig-i-like_receptor_signaling_pathway	71	10	7	0.616
Spliceosome	127	11	7	0.592
Gap_junction	90	14	4	0.591
Vasopressin-regulated_water_reabsorption	44	8	7	0.573

Glycosphingolipid_biosynthesis_lacto_and_neolacto_s eries	26	5	5	0.564
Neuroactive_ligand-receptor_interaction	318	22	7	0.559
Viral_myocarditis	70	9	5	0.551
GNRH_signaling_pathway	101	13	6	0.544
Huntington's_disease	183	21	6	0.543
Toll-like_receptor_signaling_pathway	102	9	7	0.54
Vascular_smooth_muscle_contraction	126	14	7	0.533
Hedgehog_signaling_pathway	56	11	5	0.529
Prion_diseases	36	7	5	0.529
Leukocyte_transendothelial_migration	116	11	7	0.514
Acute_myeloid_leukemia	57	8	7	0.5
RNA_degradation	57	8	6	0.499
RNA_transport	144	12	6	0.497
Fc_epsilon_RI_signaling_pathway	79	11	7	0.495
Pancreatic_secretion	103	12	6	0.492
Tight_junction	132	15	6	0.46
Basal_cell_carcinoma	55	9	5	0.452
ECM-receptor_interaction	84	8	5	0.448
Long-term_depression	70	11	4	0.442
Alzheimer's_disease	168	17	7	0.44
Maturity_onset_diabetes_of_the_young	25	4	3	0.418
Salivary_secretion	89	9	4	0.416
ABC_transporters	44	5	5	0.414
Cell_adhesion_molecules_(cams)	133	12	5	0.405
Lysosome	121	11	5	0.404
Phagosome	154	14	6	0.403
Nod-like_receptor_signaling_pathway	62	7	7	0.394
Type_I_diabetes_mellitus	43	5	5	0.377
Purine_metabolism	161	13	5	0.373
Epithelial_cell_signaling_in_helicobacter_pylori_infectio n	68	7	6	0.358
Basal_transcription_factors	35	4	5	0.342
Starch_and_sucrose_metabolism	53	7	4	0.341
Galactose_metabolism	26	3	5	0.336
Gastric_acid_secretion	74	8	4	0.335
Cardiac_muscle_contraction	77	6	6	0.328
Leishmaniasis	72	7	6	0.328
Lysine_degradation	44	6	4	0.325
Thyroid_cancer	29	5	4	0.317
Allograft_rejection	37	4	3	0.312
Hematopoietic_cell_lineage	88	9	5	0.312
Malaria	51	5	5	0.31
Parkinson's_disease	130	7	5	0.306
Antigen_processing_and_presentation	76	8	5	0.304
Carbohydrate_digestion_and_absorption	43	3	5	0.274
Pyrimidine_metabolism	99	4	4	0.274
Retinol_metabolism	65	5	2	0.271
Peroxisome	79	5	5	0.27
Cysteine_and_methionine_metabolism	36	5	5	0.254

Graft-versus-host_disease	41	4	4	0.237
Regulation_of_autophagy	34	5	4	0.237
PPAR_signaling_pathway	70	5	4	0.235
Protein_digestion_and_absorption	80	4	4	0.235
Glycerophospholipid_metabolism	79	6	4	0.226
Nucleotide_excision_repair	44	3	4	0.222
Pentose_phosphate_pathway	26	2	4	0.219
Glycosaminoglycan_biosynthesis_heparan_sulfate	26	3	3	0.21
Glycolysis_gluconeogenesis	65	2	4	0.208
Amino_sugar_and_nucleotide_sugar_metabolism	47	4	3	0.194
Ascorbate_and_aldarate_metabolism	26	3	1	0.19
Snare_interactions_in_vesicular_transport	36	4	3	0.187
Drug_metabolism_other_enzymes	52	5	2	0.179
Pathogenic_escherichia_coli_infection	56	4	3	0.179
Glutathione_metabolism	50	4	3	0.177
Steroid_hormone_biosynthesis	56	4	1	0.175
Pentose_and_glucuronate_interconversions	31	3	1	0.171
Selenoamino_acid_metabolism	26	3	4	0.169
Fructose_and_mannose_metabolism	34	2	3	0.165
Sphingolipid_metabolism	40	3	4	0.163
Complement_and_coagulation_cascades	69	2	3	0.16
Arginine_and_proline_metabolism	54	3	3	0.151
Systemic_lupus_erythematosus	136	4	2	0.151
Metabolism_of_xenobiotics_by_cytochrome_p450	71	4	1	0.147
Glycerolipid_metabolism	49	2	3	0.144
Porphyrin_and_chlorophyll_metabolism	43	3	1	0.139
Intestinal_immune_network_for_iga_production	48	3	3	0.127
Glycine_serine_and_threonine_metabolism	32	2	2	0.125
Alanine_aspartate_and_glutamate_metabolism	32	2	3	0.123
Glycosylphosphatidylinositol(gpi)-anchor_biosynthesis	25	1	3	0.12
Oxidative_phosphorylation	132	4	2	0.115
Proteasome	44	2	2	0.107
Homologous_recombination	28	2	2	0.102
Autoimmune_thyroid_disease	52	2	1	0.1
Drug_metabolism_cytochrome_p450	73	3	1	0.095
<i>Vibrio_cholerae</i> _infection	54	3	1	0.087
Collecting_duct_acid_secretion	27	2	1	0.084
Ether_lipid_metabolism	35	1	2	0.083
Pyruvate_metabolism	41	1	2	0.083
Taste_transduction	52	2	2	0.08
Base_excision_repair	33	1	2	0.078
Citrate_cycle_(tca_cycle)	31	1	2	0.078
Fatty_acid_metabolism	43	2	1	0.063
Primary_immunodeficiency	35	1	1	0.044
Tryptophan_metabolism	42	1	1	0.041
Tyrosine_metabolism	41	1	1	0.041
Asthma	30	1	1	0.04
Phototransduction	29	1	1	0.04
Arachidonic_acid_metabolism	57	1	1	0.039
DNA_replication	36	1	1	0.039

<i>Staphylococcus aureus</i> infection	55	1	1	0.039
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III: miRNAs and predicted target genes in pi3k / Akt and fatty acid metabolism in KEGG and Reactome.

MiRSystem v.2016

REACTOME. PI3K-AKT ACTIVATION. 19 miRNAs TARGET 19 GENES FROM 37 TOTAL GENES IN THE PATHWAY. SCORE 1.371

Target Gene	Gene Description	Observed miRNA
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<i>PTEN</i>	phosphatase and tensin homolog	130b-3p, 142-5p, 148a-3p, 21-5p, 23a-3p, 26b-5p, 320a, 486-5p
<i>IRS1</i>	insulin receptor substrate 1	126-3p, 142-5p, 148a-3p, 15b-5p, 223-3p, 30d-5p
<i>RICTOR</i>	RPTOR independent companion of MTOR, complex 2	142-5p, 148a-3p, 15b-5p, 192-5p, 342-3p, 636
<i>CHUK</i>	conserved helix-loop-helix ubiquitous kinase	130b-3p, 148a-3p, 15b-5p, 223-3p, 23a-3p
<i>AKT3</i>	v-akt murine thymoma viral oncogene homolog 3	122-5p, 15b-5p, 320a, 34a-5p
<i>CDKN1B</i>	cyclin-dependent kinase inhibitor 1B (p27, Kip1)	148a-3p, 222-3p, 24-3p, 34a-5p
<i>FOXO1</i>	forkhead box O1	15b-5p, 223-3p, 320a, 486-5p
<i>FOXO3</i>	forkhead box O3	122-5p, 223-3p, 23a-3p, 30d-5p
<i>IRS2</i>	insulin receptor substrate 2	142-5p, 15b-5p, 23a-3p, 30d-5p
<i>PIK3R1</i>	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	15b-5p, 21-5p, 222-3p, 486-5p
<i>CREB1</i>	cAMP responsive element binding protein 1	122-5p, 223-3p, 30d-5p
<i>CDKN1A</i>	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	130b-3p, 21-5p
<i>FOXO4</i>	forkhead box O4	23a-3p, 24-3p
<i>PDPK1</i>	3-phosphoinositide dependent protein kinase-1	223-3p, 23a-3p
<i>PIK3R2</i>	phosphoinositide-3-kinase, regulatory subunit 2 (beta)	126-3p, 30d-5p
<i>GSK3B</i>	glycogen synthase kinase 3 beta	26b-5p
<i>PIK3CA</i>	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha	148a-3p
<i>RHOA</i>	ras homolog family member A	142-5p
<i>TRIB3</i>	tribbles pseudokinase 3	24-3p

KEGG:INOSITOL_PHOSPHATE_METABOLISM. 18 miRNAs target 25 genes of 57 total in the pathway. Score 0.893

Target Gene	Gene Description	Observed miRNA
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<i>PTEN</i>	phosphatase and tensin homolog	130b-3p, 142-5p, 148a-3p, 21-5p, 23a-3p, 26b-5p, 320a, 486-5p
<i>PLCB1</i>	phospholipase C, beta 1 (phosphoinositide-specific)	122-5p, 130b-3p, 148a-3p, 21-5p, 26b-5p, 34a-5p, 636
<i>SYNJ1</i>	synaptojanin 1	142-5p, 146a-5p, 148a-3p, 15b-5p, 23a-3p, 34a-5p
<i>PIP5K3</i>	Phosphatidylinositol 4-phosphate 5-kinase 3	130b-3p, 15b-5p, 21-5p, 23a-3p, 26b-5p
<i>INPP5B</i>	inositol polyphosphate-5-phosphatase, 75kDa	223-3p, 24-3p, 26b-5p
<i>ITPK1</i>	inositol-tetrakisphosphate 1-kinase	130b-3p, 148a-3p, 30d-5p
<i>OCRL</i>	oculocerebrorenal syndrome of Lowe	122-5p, 130b-3p, 15b-5p
<i>PIP4K2B</i>	phosphatidylinositol-5-phosphate 4-kinase, type II, beta	146a-5p, 23a-3p, 30d-5p
<i>PIP5K1B</i>	phosphatidylinositol-4-phosphate 5-kinase, type I, beta	142-5p, 146a-5p, 30d-5p
<i>INPP5A</i>	inositol polyphosphate-5-phosphatase, 40kDa	197-3p, 23a-3p
<i>PI4KB</i>	phosphatidylinositol 4-kinase, catalytic, beta	15b-5p, 34a-5p
<i>PIP5K1A</i>	phosphatidylinositol-4-phosphate 5-kinase, type I, alpha	23a-3p, 34a-5p
<i>PLCB4</i>	phospholipase C, beta 4	23a-3p, 636
<i>PLCG1</i>	phospholipase C, gamma 1	30d-5p, 34a-5p
<i>INPP5J</i>	inositol polyphosphate-5-phosphatase J	15b-5p
<i>IPPK</i>	inositol 1,3,4,5,6-pentakisphosphate 2-kinase	23a-3p
<i>ITPKB</i>	inositol-trisphosphate 3-kinase B	130b-3p
<i>PI4KA</i>	phosphatidylinositol 4-kinase, catalytic, alpha	148a-3p
<i>PIK3C2B</i>	phosphatidylinositol-4-phosphate 3-kinase, catalytic subunit type 2 beta	30d-5p
<i>PIK3CA</i>	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha	148a-3p
<i>PIK3CD</i>	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit delta	30d-5p
<i>PIK3CG</i>	phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit gamma	122-5p
<i>PIP4K2A</i>	phosphatidylinositol-5-phosphate 4-kinase, type II, alpha	30d-5p
<i>PIP4K2C</i>	phosphatidylinositol-5-phosphate 4-kinase, type II, gamma	142-5p
<i>PLCD1</i>	phospholipase C, delta 1	191-5p

KEGG Fatty acid metabolism. 8 miRNAs target 8 genes from 43 genes total in the pathway. Score 0.229

Target Gene	Gene Description	Observed miRNA
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<i>ACSL1</i>	acyl-CoA synthetase long-chain family member 1	130b-3p, 15b-5p, 26b-5p, 34a-5p, 636
<i>ACSL3</i>	acyl-CoA synthetase long-chain family member 3	15b-5p, 223-3p, 26b-5p
<i>ACSL4</i>	acyl-CoA synthetase long-chain family member 4	130b-3p, 15b-5p, 34a-5p
<i>ACADSB</i>	acyl-CoA dehydrogenase, short/branched chain	26b-5p
<i>ACOX1</i>	acyl-CoA oxidase 1, palmitoyl	15b-5p
<i>ACSL5</i>	acyl-CoA synthetase long-chain family member 5	15b-5p

<i>ACSL6</i>	acyl-CoA synthetase long-chain family member 6	24-3p
<i>ADH4</i>	alcohol dehydrogenase 4 (class II), pi polypeptide	23a-3p

INFRAEXPRESSED>REACTOME. PI3K-AKT ACTIVATION. 9 miRNAs TARGET 14 GENES FROM 37 TOTAL GENES IN THE PATHWAY. SCORE 0.91

Target Gene	Gene Description	Observed miRNA
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<i>PIK3R1</i>	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	21-5p, 324-3p, 590-5p
<i>CDKN1A</i>	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	130b-3p, 21-5p
<i>CREB1</i>	cAMP responsive element binding protein 1	30b-5p, 30c-5p
<i>FOXO3</i>	forkhead box O3	30b-5p, 30c-5p
<i>IRS1</i>	insulin receptor substrate 1	30b-5p, 30c-5p
<i>IRS2</i>	insulin receptor substrate 2	30b-5p, 30c-5p
<i>PIK3R2</i>	phosphoinositide-3-kinase, regulatory subunit 2 (beta)	30b-5p, 30c-5p
<i>PTEN</i>	phosphatase and tensin homolog	130b-3p, 21-5p
<i>AKT3</i>	v-akt murine thymoma viral oncogene homolog 3	151a-3p
<i>CHUK</i>	conserved helix-loop-helix ubiquitous kinase	130b-3p
<i>FOXO1</i>	forkhead box O1	590-5p
<i>GSK3B</i>	glycogen synthase kinase 3 beta	199a-5p
<i>PHLPP</i>	pleckstrin homology domain leucine-rich repeat protein p	331-3p
<i>RICTOR</i>	RPTOR independent companion of MTOR, complex 2	324-3p

INFRAEXPRESSED REACTOME:FATTY_ACID_TRIACYLGLYCEROL_AND_KETONE_BODY_METABOLISM. 9 mir regulates 22 genes from 112 total genes in the pathway.

Target Gene	Gene Description	Observed miRNA
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<i>CHD9</i>	chromodomain helicase DNA binding protein 9	130b-3p, 30b-5p, 30c-5p
<i>GRHL1</i>	grainyhead-like 1 (Drosophila)	125b-5p, 30b-5p, 30c-5p
<i>NCOR2</i>	nuclear receptor corepressor 2	125b-5p, 30b-5p, 30c-5p
<i>TBL1XR1</i>	transducin (beta)-like 1 X-linked receptor 1	130b-3p, 21-5p, 590-5p
<i>ABCA1</i>	ATP-binding cassette, sub-family A (ABC1), member 1	130b-3p, 324-3p
<i>ELOVL5</i>	ELOVL fatty acid elongase 5	30b-5p, 30c-5p
<i>ME1</i>	malic enzyme 1, NADP(+)-dependent, cytosolic	30b-5p, 30c-5p
<i>NCOA2</i>	nuclear receptor coactivator 2	151a-3p, 199a-5p
<i>PPARA</i>	peroxisome proliferator-activated receptor alpha	21-5p, 590-5p
<i>RGL1</i>	ral guanine nucleotide dissociation stimulator-like 1	30b-5p, 30c-5p
<i>TBL1X</i>	transducin (beta)-like 1X-linked	30b-5p, 30c-5p
<i>ACSL1</i>	acyl-CoA synthetase long-chain family member 1	130b-3p
<i>ACSL4</i>	acyl-CoA synthetase long-chain family member 4	130b-3p
<i>CTGF</i>	connective tissue growth factor	199a-5p
<i>CYP1A1</i>	cytochrome P450, family 1, subfamily A, polypeptide 1	125b-5p
<i>ELOVL1</i>	ELOVL fatty acid elongase 1	125b-5p
<i>ELOVL6</i>	ELOVL fatty acid elongase 6	125b-5p
<i>GP1D</i>	glycerol-3-phosphate dehydrogenase 1 (soluble)	199a-5p
<i>LPIN2</i>	lipin 2	21-5p

<i>NCOA1</i>	nuclear receptor coactivator 1	130b-3p
<i>PRKAA2</i>	protein kinase, AMP-activated, alpha 2 catalytic subunit	130b-3p
<i>PRKAG2</i>	protein kinase, AMP-activated, gamma 2 non-catalytic subunit	199a-5p

KEGG. Fatty acid metabolism: mir-130b-3p targets ACSL1 and ACSL4, acyl-CoA synthetase long-chain family member 1 and 4, 2/43 genes of the pathway.