SUPPLEMENTARY TABLES

Table S1: Meta-Analysis of Commonly Implicated Pathways by the Target Genes of Circulatory microRNAs

miRNA	REGULATION	PATHWAY	COUNT	%	p-VALUE	Fold ENRICHMENT	BENFERRONI	BENJAMINI	FDR	TARGET GENES
Let-7e	Downregulated	PCa signalling	16	1.62	0.0004	2.85	0.06	0.01	0.45	CREB1, RB1, PDGFD, CHUK, TP53, CREB5, CREB3L1, E2F3, IGF1R, CCND1, NRAS, CDKN1A, AKT2, BCL2,AKT3, RELA
Let-7c	Downregulated	MAPK signalling	26	3.76	0.0002	2.21	0.03	0.02	0.27	PPP5C, FAS, ACVR1B, DUSP6, MAP4K4, CDC25B, PPP3CA, CHUK, RPS6KA3, MAP4K3, TP53, DUSP4,DUSP1, MAP3K1, NRAS, MAP3K7IP2, CASP3, NLK, DUSP3, AKT3
mir-181	Downregulated	PCa	16	1.53	0.0005	2.8	0.07	0.04	0.55	PTEN, HSP90B1, KRAS, CREB3, MAP2K1, PIK3R3, CREB5, PDGFRA, CDKN1B, MAPK1, CREB1, NRAS, E2F1, SOS1, BCL2, AKT3
miR-223	Downregulated	PCa	11	1.92	0.0011	3.47	0.013	0.04	1.26	IGF1R, KRAS, HSP90B1, PTEN, CREB1, FOXO1A, NRAS, RB1, PIK3R1, CHUK, BCL2
mir-640	Upregulated	Arginine and proline metabolism	6	1.66	0.0059	5.09	0.5	0.5	6.52	GLUL, ALDH1B1, AMD1, ARG2, GOT1, GOT2
mir-766	Upregulated	PCa	10	1.72	0.0044	3.11	0.43	0.11	5.01	IGF2, AR, LEF1, FGFR2, IKBKG, NKX3-1,BCL2, CREB5, AKT3, IGF1
mir-885	Upregulated	ABC transporters	4	2.38	0.0134	7.84	0.61	0.38	13.03	TAP2, ABCC9, ABCB9, ABCG4
mir-940	Upregulated	PCa	10	1.5	0.0126	2.63	0.83	0.09	13.93	CREB1, EP300, PDGFRB, MAPK3, MAP2K1, PIK3R3, BCL2, AKT2, AKT3, RELA

(Table A1). Continued.

miR-9	Upregulated	Focal adhesion	25	2.51	0.0016	1.98	0.22	0.05	1.86	PPP1R12A, PIK3R3, PARVA, CAV2, IGF1R, ITGA6, VCL, CRK, TLN1, DIAPH1, SHC1, SOS1, ACTN1, PRKCA, PAK2, ITGAV, ARHGAP5, PDGFC, JUN, MET, TNC, PPP1CB, RAP1B, BCL2, FN1
miR-200b	Upregulated	Notch signalling	9	0.87	0.0085	3.01	0.75	0.07	9.8	EP300, PSEN1, NOTCH2, CTBP2, NUMB, NOTCH1, NCOR2, PCAF, CREBBP
mir-516	Upregulated	Pathways in cancer	19	4.14	0.0097	1.9	0.69	0.15	10.56	PML, DAPK2, COL4A6, IKBKG, CCNA1, SMO, CSF1R, EGLN2, CBL, VHL, CDKN1A, TGFB3, DVL2, FN1
mir-143	Upregulated	PCa	12	1.78	0.0013	3.13	0.18	0.18	1.58	IGF1R, LEF1, KRAS, PTEN, MAPK1, FOXO1A, PDGFA, RB1, BCL2, CREB5, PDGFRA, RELA
mir-141	Upregulated	p53 signalling	11	1.37	0.0036	2.92	0.41	0.12	4.17	CCND2
mir-26b	Downregulated	Wnt signalling	19	1.98	0.0013	2.29	0.18	0.05	1.59	EP300, LEF1, PPP2R5A, WNT5A, CTNNBIP1, GSK3B, SENP2, PPP3CA, PPP2R5C, FRAT2, NFAT5, CCND2, MAP3K7, PLCB1, APC, PPP3CB, NLK, SMAD4, CREBBP
mir-93	Upregulated	mTOR signalling	10	1.07	0.0025	3.34	0.32	0.03	2.94	RPS6KA2, HIF1A, CAB39, MAPK1, RPS6KB1, VEGFA, EIF4B, RPS6KA3, EIF4B, RPS6KA3, EIF4E2, AKT3
mir-874	Upregulated	Apoptosis	10	2.23	0.0011	3.8	0.14	0.14	1.29	BIRC4, IL1RAP, IL1B,CHP, IL1R1, PPP3CB, CFLAR, BCL2, MAP3K14, RELA

(Table A1). Continued.

miR-1285	Upregulated	Cytokine-cytokine receptor interaction	20	3.15	0.0142	1.8	0.88	0.65	15.66	CXCL9, CD40,TGFBR1, IL9R, LEP, VEGFA, EDA2R, IL25, ACVR2A, IL26, TNFSF12, EDA, PDGFRB, CCL22, PLEKHQ1, IL22RA1, LTA, TNSFSF16, RTEL1. BMPR2
miR-346	Upregulated	Hedgehog signalling	5	1.66	0.018	4.88	0.82	0.35	18.11	IHH, WNT11, WNT10B, CSNK1G1, SMO
miR-375	Upregulated	Maturity onset diabetes of the young	3	2.7	0.0132	16.49	0.47	0.47	11.91	TCF2, PAX6, NR5A2
miR-21	Upregulated	Spliceosome	12	2.45	0.001	3.25	0.11	0.11	1.15	RBM22. SFRS2B, RBM8A, PCBP1, SFRS5, SR140, HNRPA1, PTPRUM HNRPA3, SFRS3, HNRPU, HNRPK, PPIE
miR-221	Upregulated	Cell adhesion molecules	9	2.36	0.0135	2.82	0.79	0.4	14.28	PTPRM, NCAM1, CD6, NLGN4X, HLA-DQA1, ITGB8, NRXN3, CD4, PVRL1
miR-20a	Upregulated	Endocytosis	24	2.52	0.0002	2.3	0.04	0.01	0.29	RAB11FIP2, TGFBR2, ACVR1B, PIP5K3, CENTD1, VPS24, SSEF2, AP2B1, RAB11FIP1, MET, RABEP1, IGF1R, RAB22A, EPS15, PSD3, HSPA8, F2R, PDCD6IP, SMURF1, IQSEC1, EEA1, RAB5B, CENTB2, NEDD4L
miR-298	Upregulated	Phosphatidylinositol signalling system	9	1.21	0.0119	2.88	0.83	0.18	13.33	PIP5K2C, OCRL, PTEN, PRKCA, PLCB1, CALM2, PIK3R3, ITPR2, SYNJ1
miR-24	Downregulated	T cell receptor signalling	12	2.21	0.0042	2.72	0.47	0.19	4.89	TEC, CD28, VAV1, CD40LG, TNF, CD247, GRAP2,MAP2K7, PTPRC, MAPK14, CD3E, IFNG
miR-30c	Upregulated	Inositol phosphate metabolism	7	1.12	0.0184	3.28	0.88	0.21	19.03	PIK3CD, PIP5K2B, ITPK1, PIK3C2B, PIP5K2A, SKIP, PIP5K1B

(Table A1). Continued.

miR-1207	Upregulated	T cell receptor signalling	13	1.59	0.0096	2.31	0.76	0.3	10.91	NFATC4, CD28, CD40LG, VAV3, MAP2K7, CD3E, NFAT5, LAT, NFATC1, TNF, GRAP2,CBL
miR-106a	Upregulated	mTOR signalling	11	1.07	0.0013	3.34	0.18	0.01	1.52	RPS6KA2, HIF1A, CAB39, MAPK1, VEGFA, PIK3R1, PIK3R3, EIF4B, RPS6KA3, EIF4E2, AKT3
miR-296	Upregulated	ECM-receptor interaction	9	1.53	0.015	2.77	0.87	0.17	16.2	ITGA10, THBS1, SV2A, COL4A6, ITGB8, COL5A3, ITGA9, ITGB3, COL4A4
miR-125b	Upregulated	Calcium signalling	17	3.62	0.0001	3.05	0.01	0.01	0.13	ADCY1, RYR1, GRIN2A, ERBB3, SLC8A2, RYR2, ATP2B3, PDGFRA, CAMK2G, CACNA1C, CD38, ERBB4, HTR4, PDE1B, PLCB1, CHRM5, MYLK
miR-107	Upregulated	PCa	17	1.83	0	3.31	0.01	0	0.11	PTEN, CREB3L2, CREB1, CREB3, PIK31, MAP2K1, CHUKM E2F3, PDGFRA, RAF1, CDKN1AM SOS1, CCNE1, BCL2, AKT3, TGFA, CRECCP
miR-574	Upregulated	Cell cycle	11	2.47	0.0022	3.17	0.23	0.04	2.46	ANAPC13, RAD21, ATR, YWHAB, CCNE2, SMC1A, SMAD2, SMAD4, E2F3, CREBBP, HDAC2
miR-328	Upregulated	Cell adhesion molecules	10	2.42	0.0028	3.32	0.27	0.15	3.13	CLDN4, CNTNAP2, CD34, NCAM1, CD40LG, HLA-DQA1, NRXN3, NFASC, SIGLEC1, CLDN11
miR-485	Upregulated	VEGF signalling	9	1.84	0.0018	3.94	0.19	0.02	2.02	KRAS, PRKCA, NRAS, RAC1, PIK3R1, MAP2K1, PIK3R3, PLA2G4A, AKT3

(Table A1). Continued.

miR-16	Upregulated	GnRH signalling pathway	18	1.8	0.0001	2.96	0.01	0	0.1	GRB2, KRAS, ITPR1, PRKCA, CAMK2G, PRKACB, MAP2K1, PLD1, ITPR2, MAP2K3, NCLN, CALM1, RAF1, PLCB1, SOS1, MAPK9, MAP3K4, MAP2K4
miR-92a	Upregulated	Calcium signalling pathway	9	2.7	0.0121	2.21	0.73	0.28	12.89	VDAC2, ATP2A2, SPHK2, ITPR1, EDNRB, PDGFRA, CALM3, CHP, PLCB1, PPP3CB, ADCY3, ATP2B4, MYLB
miR-103	Upregulated	Pathways in cancer	11	4.78	0.01	2.51	0.57	0.19	10.24	LAMC1, CRKL, PTCH1, RAF1, CUL2, FGF2, MAP2K1, BCL2,PIAS1, E2F3, AKT3
miR-636	Upregulated	Endocytosis	16	3.65	0.0001	3.3	0.01	0.01	0.09	FAM125B, TGFBR2, PIP5K3, RNF41, KIT, AP2M1, PDGFRA, STAM2, RABEP1, CENTG2M PSD3, SNF8, IQSEC1, HLA-G, ZNF289, SH3GL1
miR-197	Upregulated	Regulation of actin cytoskeleton	12	2.76	0.0189	2.2	0.91	0.26	19.81	TMSB4X, PAP5K2C, MAPK1, PPP1CC, ITGAV, MYH9, TIAM1, MAP2K1, ARPC5, ARPC4, PDGFC, PDGFRA
miR-34b	Upregulated	Focal adhesion	12	3.4	0.0039	2.73	0.37	0.2	4.33	GRB2, CDC42, BIRC4, ITGA10, ITGA2, ACTIN2, PDGFB, PDPK1, RELN, ELK1, BCL2, IGF1
miR-486	Upregulated	ECM receptor interaction	11	1.68	0.0026	3.08	0.3	0.07	3.05	ITGA2B, ITGA10, COL2A1, SV2A, HSPG2, VWF, COL6A3, ITGA5, THBS1, ITGA7, COL4A4

Table S2: Examples of Molecular Functions Regulated by Predicted miRNA Target Genes

Genes	Corrected hypergeometric p-Value	Annotations
2854	<0.001	GO:0005515 : Protein binding
1768	3.60525e-289	GO:0046872 : metal ion binding
1328	2.84346e-223	GO:0000166 : nucleotide binding
1217	3.95061e-204	GO:0008270 : zinc ion binding
1134	5.90336e-189	GO:0046872: metal ion binding GO:0008270: zinc ion binding
1066	1.92387e-154	GO:0003677 : DNA binding
930	1.31983e-151	GO:0005524 : ATP binding
863	2.62977e-144	GO:0005524: ATP binding GO:0000166: nucleotide binding
601	2.25195e-115	GO:0003700: sequence-specific DNA binding transcription factor activity
541	7.13587e-112	GO:0005515: protein binding GO:0000166: nucleotide binding

Table S3: Examples of Biological Functions Regulated by Predicted miRNA Target Genes

Genes	Corrected hypergeometric p-Value	Annotations
1003	6.1765e-162	GO:0006355: regulation of transcription, DNA-dependent
747	7.39835e-125	GO:0006355: Signal transduction
585	6.98189e-90	GO:0006355: Organismal development
408	1.92832e-87	GO:0045944: positive regulation of transcription from RNA polymerase II promoter
399	2.33308e-64	GO:0055085: transmembrane transport
365	5.73351e-54	GO:0006915: apoptotic process
348	5.02177e-56	GO:0006811: ion transport
338	1.88227e-48	GO:0007155: cell adhesion
338	1.27622e-37	GO:0006810: transport
325	2.68881e-66	GO:0045893: positive regulation of transcription, DNA-dependent
324	9.75669e-50	GO:0030154: cell differentiation
296	2.99634e-66	GO:0007399: nervous system development
288	3.63491e-59	GO:0015031: protein transport
280	8.29811e-59	GO:0006468: protein phosphorylation

Table S4: Examples of Pathways Regulated by Predicted miRNA Target Genes Using PANTHER Analysis

Genes	Corrected hypergeometric p-Value	Annotations
175	5.78827e-27	P00057: Wnt signaling pathway
120	6.13224e-17	P00031: Inflammation mediated by chemokine and cytokine signaling pathway
118	3.30659e-30	P00005: Angiogenesis
114	9.50443e-26	P00034: Integrin signalling pathway
103	2.59615e-29	P00047: PDGF signaling pathway
95	2.96435e-15	P00026: Heterotrimeric G-protein signaling pathway-Gi alpha and Gs alpha mediated pathway
95	1.83569e-29	P00018: EGF receptor signaling pathway
91	1.24029e-15	P00012: Cadherin signaling pathway
83	6.28028e-21	P00021: FGF signaling pathway
76	2.93304e-16	P00006: Apoptosis signaling pathway
67	1.25437e-15	P00052: TGF-beta signaling pathway
59	2.22092e-19	P04393: Ras Pathway

Table S5: Examples of Pathways Regulated by Predicted miRNA Target Genes Using KEGG Analysis

Genes	Corrected hypergeometric p-Value	Annotations
236	1.84759e-53	05200 : Pathways in cancer
197	3.85769e-48	04010 : MAPK signalling
150	1.90989e-37	04510 : Focal adhesion
149	9.63291e-32	04810 : Regulation of actin cytoskeleton
144	3.10908e-34	04144 : Endocytosis
133	3.36959e-11	04060: Cytokine-cytokine receptor interaction
121	2.47362e-20	04062: Chemokine signaling pathway
114	1.7081e-24	04141: Protein processing in endoplasmic reticulum
112	4.56714e-18	04020: Calcium signaling pathway
108	7.23651e-24	04310: Wnt signaling pathway
105	4.34504e-31	04360: Axon guidance
102	1.03042e-25	04910: Insulin signaling pathway
101	4.99225e-24	04120: Ubiquitin mediated proteolysis
100	2.1178e-28	04722: Neurotrophin signaling pathway