

Table S2. DIANA-mirPath pathway analysis - Second Approach: interaction between selected miRNAs and several molecular and signaling pathways involved in cancer development.

miRNAs		p Value	N° of Targets	Gene Targets
Proteoglycans in cancer (hsa05205)				
	hsa-miR-133b	0.0129	6	MET, PPP1CC, IGF1R, EGFR, DDX5, FGFR1
	hsa-miR-143-3p	0.0039	13	THBS1, KRAS, TFAP4, MMP2, AKT1, IGF2, FZD2, PTPN11, HRAS, MAPK1, PLAU, MDM2, CD44
	hsa-miR-145-5p	≤ 0.001	40	FZD7, ESR1, ACTB, PRKCA, STAT3, ITGB1, SMAD2, NRAS, THBS1, CAV1, WNT5A, MAPK14, ACTG1, ITGA5, IFGR1, EGFR, WNT5B, CAV2, ERBB3, TGFB1, MSN, PAK1, PTK2, ITGAV, MMP2, CCND1, CTNNB1, AKT1, MYC, MMP9, RAC1, WNT11, TGFB2, NANOG, FN1, CDKN1A, TWIST1, VEGFA, MDM2, PRKACB
	hsa-miR-183-5p	≤ 0.001	26	BRAF, ACTB, PDCD4, ITGB1, EZR, CBL, NRAS, CAV1, PPP1CC, ROCK2, RDX, IQGAP1, ITGA5, IGF1R, KRAS, PAK1, TP53, PPP1R12A, CCND1, HIF1A, MYC, ITPR1, PTPN11, RAC1, FGF2, MAPK1
	hsa-miR-18b-5p	0.0324	14	ESR1, BRAF, ACTB, STAT3, SMAD2, MAPK14, CTTN, CCND1, CTNNB1, TIMP3, ITGA2, CDKN1A, MDM2, PPP1CB
	hsa-miR-195-5p	≤ 0.001	36	ACTB, STAT3, PDCD4, SMAD2, PPP1CC, MAPK14, ACTG1, FRS2, FZD6, IGF1R, RRAS2, MSN, HSPG2, CCND1, CTNNB1, MYC, MMP9, CBL, PRKACA, DDX5, FGF2, CDC42, AKT3, WNT3A, PIK3CA, CDKN1A, SDC4, VMP1, HGF, VEGFA, ITPR2, PLAU, GRB2, MDM2, WNT9A, CD44
	hsa-miR-223-3p	0.0179	7	STAT3, IGF1R, MMP2, PIK3CD, MMP9, MTOR, VEGFA
	hsa-miR-375	≤ 0.001	23	PRKCA, ERBB2, ITGB1, SDC1, IQGAP1, RAF1, IGF1R, RHOA, FZD8, RPS6, ANK2, FZD4, CASP3, HIF1A, MYC, FLBN, PRKX, DDX5, CDC42, TGFB2, PLCE1, CDKN1A, MDM2
	hsa-miR-378a-3p	0.0015	20	ESR1, ACTB, MET, CBL, SDC1, ARHGEF12, ROCK2, IGF1R, TLR4, MSN, PIK3R3, CCND1, MYC, FLNA, PIK3R1, VEGFA, MAPK1, GRB2, MDM2, ELK1
	hsa-miR-497-5p	≤ 0.001	43	BRAF, ACTB, PDCD4, SOS2, SMAD2, PTCH1, WNT5A, PIK3R2, PPP1CC, ACTG1, ROCK2, FRS2, FZD6, IQGAP1, IGF1R, RPS6, HSPG2, AKT2, TFAP4, MMP2, CCND1, MYC, MMP9, IGF2, ITPR1, FGF2, CDC42, AKT3, PIK3CA, FN1, CDKN1A, MAP2K1, SDC4, SMO, HGF, MTOR, VEGFA, MAPK1, GRB2, CD63, MDM2, WNT9A, CD44
Hippo signaling pathway (hsa04390)				
	hsa-miR-135b-5p	0.0177	10	APC, YWHAG, PPP1CC, CCND2, FZD6, BIRC5, MYC, TEAD1, LATS1, LATS2

hsa-miR-145-5p	≤ 0.001	25	FZD7, ACTB, GSK3B, SAMD2, NF2, WNT5A, ACTG1, SNAI2, WNT5B, TGFB1, CDH1, CCND1, CTNNB1, MYC, STK3, BMP2, WNT11, TGFB2, BBC3, PARD3, SOX2, BPM7, SERPINE1, CTGF, TGFB3
hsa-miR-183-5p	≤ 0.001	18	ACTB, YAP1, PPP2CA, TCF7L2, YWHAG, PPP1CC, MOB1B, PPP2R2D, CDH1, CCND1, SMAD4, MYC, LLGL1, FRMD6, SMAD7, LATS1, LATS2, AJUBA
hsa-miR-195-5p	≤ 0.001	28	ACTB, DVL3, YAP1, SMAD2, BTRC, PPP2CA, YWHAG, PPP1CC, CCND2, ACTG1, GLI2, FZD6, BIRC5, YWHAB, AMOT, CDH1, CCND1, CTNNB1, MYC, PPP2R1A, PP2CB, WNT3A, SMAD7, LATS1, PPP2R1B, PARD6B, WNT9A, CCND3
hsa-miR-21-5p	0.0065	25	ACTB, TGFB1, YAP1, BTRC, APC, NF2, WNT5A, DLG1, CCND2, BIRC5, AXIN1, TP53BP2, TGFB1, MPP5, CCND1, CTNNB1, MYC, SAV1, TGFB2, SMAD7, LATS1, SOX2, PPP2R1B, TGFB2, BMPR2
hsa-miR-224-5p	0.0012	18	ACTB, GSK3B, PRKCI, DLG1, YWHAG, PPP1CC, GLI2, FZD6, MPP5, CDH1, CCND1, SMAD4, YWHAZ, LATS1, SERPINE1, PARD6B, BMPR2, TGFB3
hsa-miR-375	≤ 0.001	19	YAP1, YWHAG, CCND2, MOB1B, YWHAB, WWC1, AMOT, FZD8, MPP5, FZD4, DLG4, CTNNA1, MYC, YWHAZ, TGFB2, PARD3, PARD6B, BMPR2, CTGF
hsa-miR-378a-3p	0.0082	16	ACTB, ID2, YAP1, BTRC, YWHAG, CCND2, MOB1B, MPP5, CCND1, DVL1, CTNNA1, MYC, PPP2R1A, YWHAZ, SERPINE1, DVL2
hsa-miR-497-5p	≤ 0.001	27	ACTB, DVL3, YAP1, SMAD2, BTRC, PPP2CA, WNT5A, PPP1CC, CCND2, ACTG1, GLI2, FZD6, SMAD3, BIRC5, AMOT, WWTR1, TP53BP2, CSNK1D, CCND1, MYC, FRMD6, SMAD7, LATS1, LATS2, WNT9A, CCND3, SCRIB
Viral carcinogenesis (hsa05203)			
hsa-miR-1246	≤ 0.001	6	PIK3CB, BAX, CDK6, TP53, KAT2B, CCNE1
hsa-miR-143-3p	0.0235	17	CDK4, DLG1, HLA-E, YWHAB, KRAS, CDK6, HIST1H2BD, YWHAQ, EIF2AK2, CCR5, REL, HRAS, EP300, CREB3L2, MPAK1, LYN, MDM2
hsa-miR-150-5p	≤ 0.001	9	BAX, PKM, CDKN1B, TP53, EGR2, KIST1H2BG, EP300, HLA-A, HIST1H2BM
hsa-miR-183-5p	≤ 0.001	28	CDK4, ATF2, NRAS, ATF6B, YWHAG, HIST1H2BC, PKM, HIST1H4C, HLA-C, KRAS, DDX3X, CHD4, TP53, HNRNPK, EIF2AK2, CCND1, CCNE2, KAT2A, RAC1, RBPJ, GTF2H3, CREB3L2, GTF2A1, MAPK1, HLA-A, HIST1H4J, HIST1H2BO, HIST1H4E

	hsa-miR-195-5p	≤ 0.001	39	RBL2, STAT3, CDK4, ATF2, CCNA2, YWHAG, CCND2, PKM, HIST1H4C, YWHAB, TRAF5, CDK6, CHD4, CREB1, EIF2AK2, CCND1, CCNE2, UBE3A, PRKACA, DDB1, RBL1, HIST1H2BG, CDC42, EP300, CCNE1, PIK3CA, IL6ST, CDKN1A, TBP, CREBBP, TBPL1, GRB2, MDM2, CCND3, UBR4, VDAC3, HIST1H2BH, HIST1H2BE
	hsa-miR-375	0.0022	26	CCNA2, GTF2H1, YWHAG, CCND2, HIST1H4C, CDKN2B, YWHAB, RHOA, CREB3, CHD4, EGR3, EIF2AK2, CASP3, JUN, UBE3A, REL, YWHAZ, PRKX, CDC42, RBPJ, BAK1, USP7, CDKN1A, SRF, JAK1, MDM2
	hsa-miR-378a-3p	0.0201	21	YWHAG, CCND2, PKM, CDK1, CDK6, DDX3X, HIST1H2BD, CHEK1, SND1, JUN, PIK3R3, YWHAZ, HDAC2, EP300, IL6ST, MAPK1, GRB2, TRAF1, MDM2
p53 signaling pathway (hsa04115)				
	hsa-miR-1246	0.0437	6	BAX, CDK6, TP53, TP53I3, CCNE1, CCNG2
	hsa-miR-143-3p	0.0063	11	CDK4, THBS1, PERP, CDK6, APAF1, SESN2, TNFRSF10B, BBC3, PTEN, SERPINE1, MDM2
	hsa-miR-145-5p	0.0150	11	CCNG1, CDK4, THBS1, ATM, CCND1, SESN3, SERPINE1, PPM1D, MDM2
	hsa-miR-18a-5p	0.0023	13	CCNG1, ZMAT3, CCNB1, CDK4, CCND2, ATM, CCND1, SHISA5, CDKN1A, RRM2, PTEN, PPM1D, MDM2
	hsa-miR-378a-3p	0.0201	12	ZMAT3, CCNB1, CCND2, CDK1, CDK6, CHEK1, CCND1, TNFRSF10B, MDM4, PTEN, SERPINE1, MDM2
	hsa-miR-497-5p	≤ 0.001	18	ZMAT3, CCNB1, CDK4, CCND2, PERP, RRM2B, CDK6, CCND1, SHISA5, SESN1, TNFRSF10B, CCNE1, IGF1BP3, CDKN1A, SESN3, PIDD1, MDM2, CCND3
Pathways in cancer (hsa05200)				
	hsa-miR-145-5p	≤ 0.001	41	FZD7, GSK3B, PRKCA, STAT3, ITGB1, CDK4, GNG11, SMAD2, NRAS, WNT5A, ITGA3, IGF1R, EGFR, WNT5B, TGFB1, TPM3, PTK2, ITGAV, CDH1, MMP2, CCND1, CTNNA1, MMP1, AKT1, MYC, MMP9, HSP90AB1, HDAC2, RAC1, WNT11, TGFB2, FN1, CDKN1A, BIRC3, STAT1, VEGFA, MDM2, PDGFRB, PRKACB, TGFB3
	hsa-miR-150-5p	0.0188	14	MET, GNG11, CXCR4, BAX, SMAD3, CDKN1B, TP53, TCEB2, BMP2, FLT3, EP300, SLC2A1, VEGFA, FGFR1
	hsa-miR-183-5p	0.0094	37	BRAF, FOS, ITGB1, CDK4, CBL, NRAS, CRKL, STK4, TCF7L2, GNA13, HSP90AA1, ROCK2, TRAF4, IGF1R, GNB1, KRAS, TPM3, TP53, CDH1, AR, CCND1, SMAD4, MSH6, CCNE2, HIF1A, MYC, MSH2, RAC1, FGF2, RALGDS, PTEN, FOXO1, MAPK1, GNG5, PLCB4, CCDC6, RASSF5

hsa-miR-195-5p	≤ 0.001	62	DVL3, STAT3, GNA12, CDK4, CXCL8, SMAD2, CRKL, CRK, COL4A5, GNA13, HSP90AA1, GLI2, BDKRB2, FZD6, CHUK, BCL2, TRAF4, BIRC5, IGF1R, GNAI3, PTCH2, TRAF5, CDK6, PML, VHL, IKBKB, ARHGEF11, CDH1, MAPK9, GNB2, CCND1, CTNNB1, CCNE2, E2F3, MAPK8, MYC, MMP9, CBLC, PRKACA, HSP90AB1, FGF2, CDC42, EP300, GNAQ, NKX3-1, AKT3, PIAS2, WNT3A, CCNE1, PIK3CA, CDKN1A, LAMC2, HGF, VEGFA, CREBBP, GRB2, TGF, MDM2, WNT9A, XIAP, PDGFA, ADCY6
hsa-miR-378a-3p	0.0157	37	MET, CBL, CRKL, GNAS, TGFA, ARHGEF12, GNA13, HSP90AA1, ROCK2, ARNT, GNG12, BCL2, CXCL12, IGF1R, CDK6, PML, JUN, PIK3R3, CCND1, DVL1, CTNNA1, E2F3, MYC, PIK3R1, HDAC2, EP300, RBX1, SUFU, VEGFA, PTEN, MAPK1, GNG5, GRB2, DVL2, TRAF, MDM2, GNAI1
hsa-miR-497-5p	0.0025	56	BRAF, DVL3, SOS2, CDK4, SMAD2, PTCH1, WNT5A, PIK2R2, HSP90AA1, GLI2, ROCK2, FZD6, SMAD3, CHUK, RARB, BIRC5, IGF1R, PTCH2, CDK6, TCEB1, PML, IKBKB, AKT2, MMP2, GNB2, CCND1, LPAR1, MMP1, E2F3, MAPK8, MYC, MMP9, HSP90AB1, NOS2, FGF2, CDC42, LAMC1, AKT3, CCNE1, PIK3CA, FN1, CDKN1A, MAP2K1, SMO, LAMC2, HGF, MTOR, VEGFA, MAPK1, GRB2, MDM2, WNT9A, ADCY6
Central carbon metabolism in cancer (hsa05230)			
hsa-miR-1246	0.0206	3	PIK3CB, TP53, PDK1
hsa-miR-133b	≤ 0.001	4	MET, PKM, EGFR, FGFR1
hsa-miR-150-5p	≤ 0.001	6	MET, PKM, TP53, FLT3, SLC2A1, FGFR1
hsa-miR-375	0.0080	9	PDGFRA, ERBB2, FGFR3, RAF1, GLS, HK2, HIF1A, MYC, PDK1
hsa-miR-378a-3p	0.0266	10	MET, PKM, GLS, SLC7A5, PIK3R3, MYC, PIK3R1, LDHA, PTEN, MAPK1
FoxO signaling pathway (hsa04068)			
hsa-miR-145-5p	0.0331	17	IRS2, STAT3, SMAD2, BNIP3, NRAS, MAPK14, IGF1R, EGFR, TGFB1, ATM, CCND1, AKT1, IRS1, TGFB2, CDKN1A, MDM2, TGFB3
hsa-miR-183-5p	0.0316	17	BRAF, FBXO32, CCNB1, NRAS, STK4, PCK2, IGF1R, KRAS, CCND1, SMAD4, IRS4, SOD2, PTEN, SGK3, FOXO1, MAPK1, BCL2L11
hsa-miR-224-5p	0.0249	18	NRAS, SETD7, CDKN1B, IGF1R, EGFR, PIK3R3, CCND1, SMAD4, MAPK8, INSR, PRKAA1, MAPK12, SOD2, CDKN1A, PLK3, CCNG2, BCL2L11, TGFB3
hsa-miR-375	0.0080	17	PRKAA2, SETD7, CCND2, RAF1, CDKN2B, IGF1R, GADD45A, HOMER2, PLK2, IRS1, TGFB2, SOD2, FOXO3, USP7, CDKN1A, MDM2, BCL2L11

	hsa-miR-497-5p	0.0025	28	BRAF, CCNB1, SOS2, SMAD2, PRKAA2, PIK3R2, CCND2, STK11, SMAD3, CHUK, IGF1R, IKBKB, AKT2, NLK, CCND1, S1PR1, MAPK8, IRS4, PRKAB2, AKT3, PIK3CA, CDKN1A, MAP2K1, MAPK1, GRB2, SGK1, MDM2, BCL2L11
TGF-beta signaling pathway (hsa04350)				
	hsa-miR-145-5p	0.0010	12	FST, SMAD2, NODAL, THBS1, ID4, TGFB1, ACVR1, MYC, BPM7, TGFB3
	hsa-miR-150-5p	≤ 0.001	5	SMAD3, BPM2, SP1, EP300, PPP2CB
	hsa-miR-18b-5p	0.0281	4	SMAD2, ACVR2B, ACVR2A, PPP2R1B
	hsa-miR-195-5p	0.0022	16	SMAD2, PPP2CA, SMURF2, CUL1, MYC, PPP2R1A, RBL1, ACVR2A, SP1, EP300, PPP2CB, BAMBI, LTBP1, SMAD7, CREBBP, PPP2R1B
	hsa-miR-497-5p	≤ 0.001	13	FST, SMAD2, PPP2CA, ACVR1B, SMURF2, SMAD3, ID4, ACVR2B, MYC, RBL1, SP1, SMAD7, MAPK1
Colorectal cancer (hsa05210)				
	hsa-miR-145-5p	0.0022	10	GSK3B, SMAD2, TGFB1, CCND1, CTNNB1, AKT1, MYC, RAC1, TGFB2, TGFB3
	hsa-miR-183-5p	0.0030	13	BRAF, FOS, TCF7L2, KRAS, TP53, CCND1, SMAD4, MSH6, MYC, MSH2, RAC1, RALGDS, MAPK1
	hsa-miR-21-5p	≤ 0.001	17	TGFBR1, APC, BCL2, BIRC5, AXIN1, APPL1, TGFB1, AKT2, CCND1, CTNNB1, MSH6, MYC, MSH2, PIK3R1, TGFB2, MAPK1, TGFB2
	hsa-miR-497-5p	0.0194	14	BRAF, SMAD2, PIK3R2, SMAD3, BCL2, BIRC5, AKT2, CCND1, MAPK8, MYC, AKT3, PIK3CA, MAP2K1, MAPK1
Cell cycle (hsa04110)				
	hsa-miR-143-3p	0.0382	13	SMC1A, CDK4, DBF4, YWHAB, WEE1, CDK6, YWHAQ, TFDP2, MCM2, CDC7, EP300, MDM2, MCM3
	hsa-miR-195-5p	0.0047	29	RBL2, CDK4, SMAD2, CDC14A, CCNA2, YWHAG, CCND2, SMC3, CUL1, YWHAB, WEE1, CDK6, CCND1, CCNE2, E2F3, MYC, RBL1, TTK, CDC7, EP300, CCNE1, CDC27, CDKN1A, PRKDC, ANAPC13, CREBBP, MDM2, CCND3, CDC25A
	hsa-miR-21-5p	0.0012	25	E2F1, SMC1A, E2F2, MDM6, CCND2, BUB1, MCM4, STAG2, WEE1, CDK6, TGFB1, TFDP2, CCND1, SKP2, E2F3, MYC, RB1, HDAC2, ANAPC5, TGFB2, PRKDC, PLK1, MDM2, MCM3, CDC25A
	hsa-miR-378a-3p	0.0119	20	CCNB1, YWHAG, CCND2, MCM4, CDK1, CDK6, BUB3, CHEK1, SMC1B, CCND1, E2F5, E2F3, MYC, YWHAZ, HDAC2, EP300, RBX1, PLK1, RAD21, MDM2
ErbB signaling pathway (hsa04012)				
	hsa-miR-145-5p	0.0061	12	GSK3B, PRKCA, NRAS, EGFR, ERBB3, PAK1, PTK2, AKT1, MYC, PAK4, CDKN1A, ABL2

	hsa-miR-21-5p	0.0275	14	ERBB2, SOS2, NRAS, CRKL, PAK2, MAP2K7, EGFR, AKT2, PTK2, MYC, PIK3R1, GAB1, MAP2K4, MAPK1
	hsa-miR-378a-3p	0.0201	14	CBL, CRKL, MAP2K7, TGFA, JUN, PIK3R3, MYC, PIK3R1, PAK4, NRG1, MAPK1, ABL2, GRB2, ELK1
HIF-1 signaling pathway (hsa04066)				
	hsa-miR-150-5p	0.0296	6	CDKN1B, TCEB2, EP300, EIF4E2, SLC2A1, VEGFA
	hsa-miR-21-5p	0.0090	22	STAT3, ERBB2, NFKB1, CUL2, GAPDH, BCL2, IGF1R, EGFR, TRL4, HK2, AKT2, PDHA2, TFRC, PIK3R1, LDHA, PFKFB2, MKNK2, ALDOA, VEGFA, MAPK1, TEK, PGK1
	hsa-miR-378a-3p	0.0201	16	IFNGR2, ARNT, BCL2, IGF1R, TLR4, ENO1, PIK3R3, TFRC, PIK3R1, LDHA, EP300, RBX1, ALDOA, VEGFA, MAPK1, SERPINE1
mTOR signaling pathway (hsa04150)				
	hsa-miR-223-3p	0.0258	4	DDIT4, PIK3CD, MTOR, VEGFA
	hsa-miR-497-5p	≤ 0.001	18	BRAF, RRAGD, PRKAA2, PIK3R2, STK11, RPS6, RICTOR, IKBKB, AKT2, EIF4E, RRAGA, RPS6KA3, AKT3, PIK3CA, MTOR, ULK1, VEGFA, MAPK1
MicroRNAs in cancer (hsa05206)				
	hsa-miR-143-3p	0.0380	23	THBS1, MAPK7, BCL2, GLS, KRAS, CDK6, KIF23, PRKCE, SLC7A1, RPTOR, PIM1, PTGS2, IRS1, DNMT3A, FSCN1, HRAS, EP300, CYP1B1, PTEN, MAPK1, PLAU, MDM2, CD44
	hsa-miR-150-5p	≤ 0.001	8	MET, CDKN1B, ZEB1, TP53, MDM4, EP300, NOTCH3, VEGFA
PI3K-Akt signaling pathway (hsa04151)				
	hsa-miR-145-5p	0.0061	38	GSK3B, PRKCA, ITGB1, ITGB8, CDK4, GNG11, NRAS, THBS1, IFNB1, ANGPT2, ITGA5, ITGA3, EGFR, COL3A1, COL6A1, PTK2, ITGAV, ITGA11, DDIT4, CCND1, EIF4E, AKT1, MYC, COL5A1, COL1A1, HSP90AB1, IRS1, RAC1, COL1A2, FN1, TNC, CDKN1A, VEGFA, COL5A2, SPP1, MDM2, PDGFRB
	hsa-miR-497-5p	0.0308	48	SOS2, CDK4, ATF2, PRKAA2, PPP2CA, PIK3R2, IL2RB, MCL1, CCND2, HSP90AA1, STK11, CHUK, BCL2, IGF1R, RPS6, CDK6, IKBKB, COL6A1, AKT2, CRTC2, GNB2, CCND1, EIF4E, LPAR1, MYC, HSP90AB1, HSP90B1, FGF2, COL1A2, LAMC1, AKT3, CCNE1, PIK3CA, FN1, TNC, CDKN1A, MAP2K1, LAMC2, HGF, MTOR, COL5A3, VEGFA, MAPK1, GRB2, SGK1, MDM2, BCL2L11, CCND3