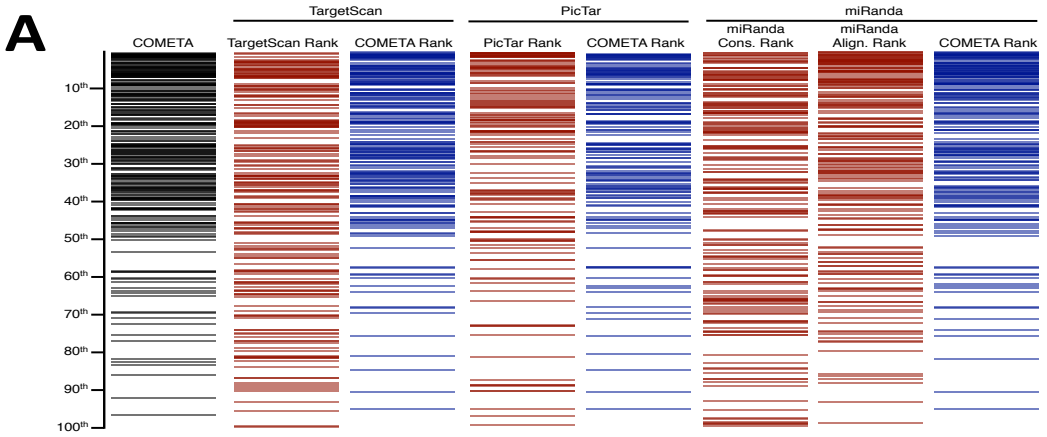
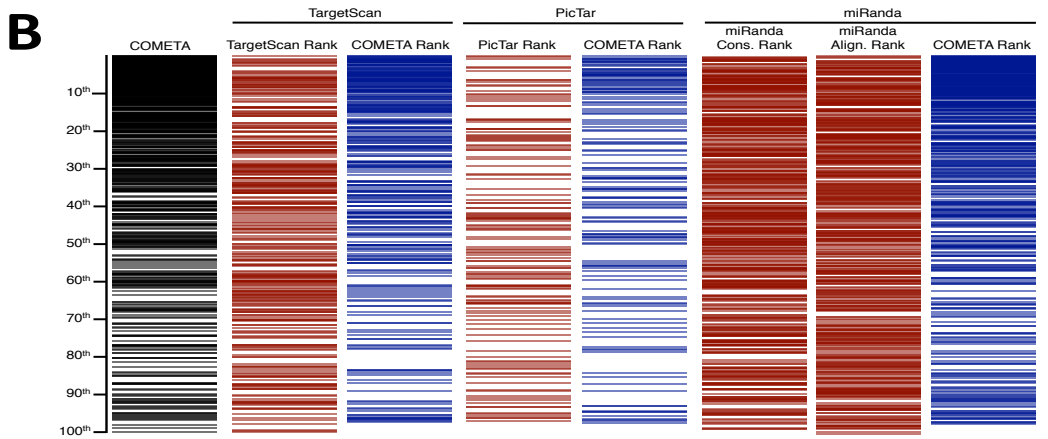
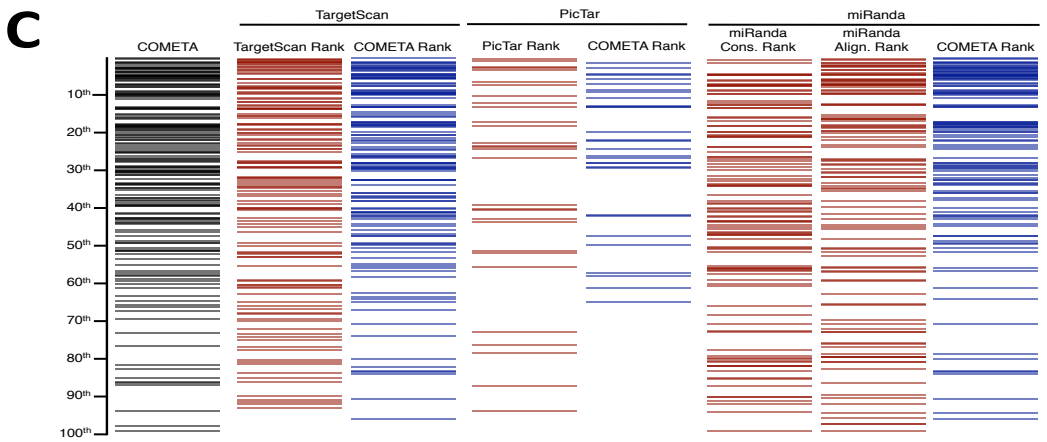


Percentile DS1	COMETA	TargetScan Rank	COMETA Rank	PicTar Rank	COMETA Rank	miRanda Cons. Rank	miRanda Align. Rank	COMETA Rank
30th	183 (68%)***	83 (44%)*	121 (64%)***	88 (62%)**	87 (62%)**	85 (47%)*	103 (57%) **	120 (67%)***
50th	247 (91%) ***	126 (67%)*	172 (91%)***	115 (80%) **	125 (89%)**	117 (65%)*	140 (77%) **	163 (91%)***



Percentile DS2	COMETA	TargetScan Rank	COMETA Rank	PicTar Rank	COMETA Rank	miRanda Cons. Rank	miRanda Align. Rank	COMETA Rank
30th	439 (65%)***	100 (32%)*	179 (57%)**	42 (31%)#	66 (46%)*	183 (37%)*	179 (36%)*	310 (62%)***
50th	547 (82%)***	171 (56%)*	239 (77%)***	69 (51%)#	99 (70%)**	301 (61%)*	281 (57%)**	383 (76%)***



Percentile DS3	COMETA	TargetScan Rank	COMETA Rank	PicTar Rank	COMETA Rank	miRanda Cons. Rank	miRanda Align. Rank	COMETA Rank
30th	94 (58%)***	64 (51%)*	73 (58%)**	17 (57%)#	22 (73%)*	44 (40%)*	56 (50%)*	70 (63%)***
50th	131 (81%)***	88 (70%)*	101 (80%)***	22 (73%)#	25 (84%)*	73 (66%)*	73 (66%)**	94 (85%)***

Figure S1. Distribution of validated miRNA targets within CoMeTa, TargetScan, PicTar and miRanda lists of putative targets. Analysis of DS1 *(A)*, DS2 *(B)*, and DS3 *(C)* are reported. Counts within the first 30th and 50th percentiles are provided for each software in the tables below the graphs. Horizontal lines indicate the positions of validated targets along the prediction lists ranked according to the scoring systems of each method. miRanda lists have been ranked by either the conservation (Cons.) or the alignment (Align.) score. The lists of predicted targets have been ranked by using either the scoring systems provided by each specific software (red columns) or the CoMeTa scoring system (blue columns). The analysis shows that the validated miRNA targets analyzed show an increased tendency to be localized in the top positions when using the CoMeTa ranking system as compared with the other scoring systems. *P value<10^{-2}, *P value<10^{-8}, ***P value<10^{-20}.

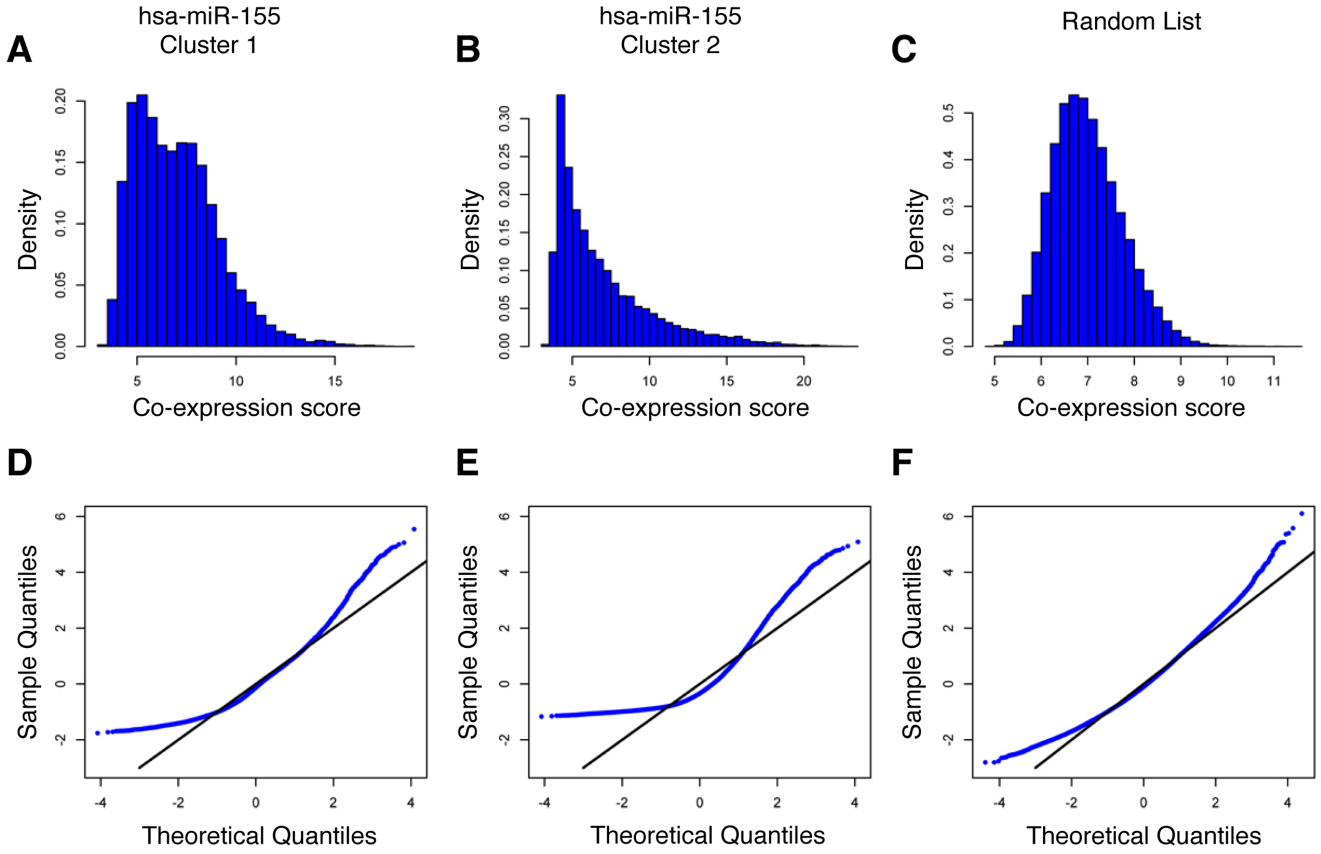


Figure S2. Q-Q Plot distribution analysis. *(A-C)* Co-expression score distributions of the two clusters generated by hierarchical clustering of co-expression data of hsa-miR-155 predicted targets *(A,B)* and of a size-matched list of co-expression scores for randomly selected genes *(C)*. *(D-F)* Normal probability plots of the two clusters *(D,E)* and the randomly selected genes *(F)*, where the black line represents the case of perfect normality. Histograms and normal probability plots show how departure from normality is higher in COOL clusters *(A,B,D,E)* than in random lists *(C,F)*.

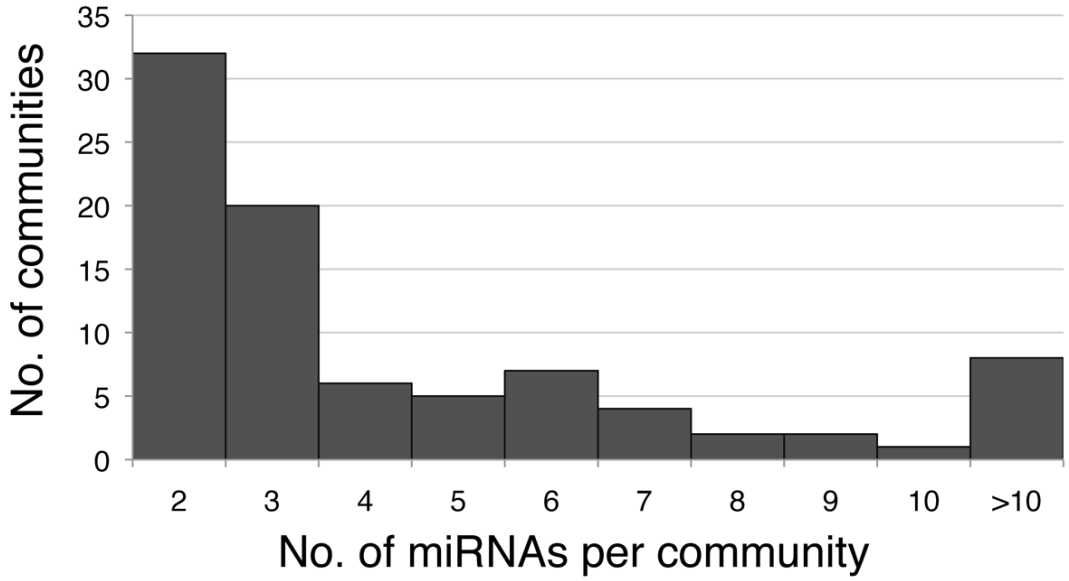


Figure S3. Histogram summarizing the miRNA distributions within the miRCos identified.

Table S1. The experimentally validated miRNA–target pairs used to build dataset 1 (DS1).

miRNA	Validated target	Validation procedure	Predicted by sequence-based tools	Reference
hsa-let-7a	*NF2*	Translational	Yes	(Meng et al. 2007)
hsa-let-7b	*LIN28*	Translational	Yes	(Kiriakidou et al. 2004)
hsa-let-7b	*CCND1*	Translational	Yes	(Schultz et al. 2008)
hsa-let-7f	*KLK6*	Transcriptional	Yes	(Chow et al. 2008)
hsa-let-7f	*KLK10*	Transcriptional	No	(Chow et al. 2008)
hsa-let-7g	*HMGA2*	Translational	Yes	(Boyerinas et al. 2008)
hsa-miR-1	*BDNF*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-1	*G6PD*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-1	*HAND2*	Translational	Yes	(Zhao et al. 2005)
hsa-miR-1	*KCNJ2*	Translational	Yes	(Yang et al. 2007)
hsa-miR-1	*GJA1*	Translational	Yes	(Anderson et al. 2006; Yang et al. 2007)
hsa-miR-101	*MYCN*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-101	*ATXN1*	Translational Transcriptional	Yes	(Lee et al. 2008)
hsa-miR-101	*EZH2*	Translational	Yes	(Lewis et al. 2003; Friedman et al. 2009)
hsa-miR-106a	*RB1*	Translational	Yes	(Volinia et al. 2006)
hsa-miR-106a	*ARID4B*	Translational	Yes	(Landais et al. 2007)
hsa-miR-106a	*MYLIP*	Translational	Yes	(Landais et al. 2007)
hsa-miR-106a	*CDKN1A (p21)*	Translational	Yes	(Ivanovska et al. 2008)
hsa-miR-106b	*CDKN1A (p21)*	Translational Transcriptional	Yes	(Ivanovska et al. 2008)
hsa-miR-10a	*HOXA1*	Translational Transcriptional	Yes	(Garzon et al. 2006)
hsa-miR-10b	*HOXD10*	Translational Transcriptional	Yes	(Ma et al. 2007)
hsa-miR-122	*CCNG1*	Translational	Yes	(Gramantieri et al. 2007)

hsa-miR-122	*BCL2L2*	Translational Transcriptional	Yes	(Lin et al. 2008)
hsa-miR-124	*MAPK14*	Translational	Yes	(Krek et al. 2005)
hsa-miR-124	*ACAA2*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*ATP6V0E1*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*CD164*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*ELOVL5*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*GAS2L1*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*LAMC1*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*RAVER2*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*SERP1*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*SLC16A1*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*SUCLG2*	Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*VAMP3*	Translational Transcriptional	Yes	(Wang 2006)
hsa-miR-124	*CTDSP1*	Translational	Yes	(Karginov et al. 2007)
hsa-miR-125a-5p	*ERBB3*	Translational	Yes	(Scott et al. 2007)
hsa-miR-125a-5p	*ERBB2*	Translational	No	(Scott et al. 2007)
hsa-miR-125b	*BMPR1B*	Translational Transcriptional	Yes	(Saetrom et al. 2009)
hsa-miR-125b	*ERBB2*	Translational	No	(Scott et al. 2007)
hsa-miR-126	*VCAM1*	Translational	Yes	(Harris et al. 2008)
hsa-miR-126	*HOXA9*	Translational	Yes	(Shen et al. 2008)
hsa-miR-126	*IRS-1*	Translational	Yes	(Zhang et al. 2008)
hsa-miR-126	*VEGF-A*	Translational	Yes	(Liu et al. 2009a)
hsa-miR-128	*SNAP25*	Translational	Yes	(Eletto et al. 2008)
hsa-miR-128	*TFEB*	Translational Transcriptional	Yes	(Sardiello et al. 2009)
hsa-miR-129-5p	*CAMTA1*	Translational	Yes	(Liao et al. 2008)
hsa-miR-129-5p	*EIF2C3*	Translational	Yes	(Liao et al. 2008)
hsa-miR-130a	*CSF1 (MCSF)*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-130a	*MAFB*	Transcriptional	Yes	(Garzon et al. 2006)

hsa-miR-130a	*HOXA5*	Translational Transcriptional	Yes	(Chen and Gorski 2008)
hsa-miR-130a	*MEOX2 (GAX)*	Translational Transcriptional	Yes	(Chen and Gorski 2008)
hsa-miR-130a	*ATXN1*	Translational	Yes	(Lee et al. 2008)
hsa-miR-130a	*ZFPM2 (FOG2)*	Translational	Yes	(Kim et al. 2009a)
hsa-miR-130a	*TAC1*	Translational	No	(Greco and Rameshwar 2007)
hsa-miR-130b	*CSF1 (MCSF)*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-130b	*MAFB*	Transcriptional	Yes	(Garzon et al. 2006)
hsa-miR-130b	*ATXN1*	Translational	Yes	(Lee et al. 2008)
hsa-miR-132	*RICS (PPGC)*	Translational	Yes	(Vo et al. 2005)
hsa-miR-133a	*PTBP2*	Translational	Yes	(Boutz et al. 2007)
hsa-miR-133a	*SRF*	Translational	No	(Chen et al. 2006)
hsa-miR-133b	*PTBP2*	Translational	Yes	(Boutz et al. 2007)
hsa-miR-133b	*PITX3*	Translational	Yes	(Kim et al. 2007)
hsa-miR-133b	*BCL2L2*	Translational Transcriptional	Yes	(Crawford et al. 2009)
hsa-miR-133b	*MCL1*	Translational Transcriptional	Yes	(Crawford et al. 2009)
hsa-miR-140-5p	*HDAC4*	Translational	Yes	(Tuddenham et al. 2006)
hsa-miR-140-5p	*PDGFRA*	Translational	Yes	(Clouthier 2008)
hsa-miR-141	*CLOCK*	Transcriptional	Yes	(Kiriakidou et al. 2004)
hsa-miR-142-3p	*ADCY9 (AC9)*	Translational	Yes	(Huang et al. 2009a)
hsa-miR-145	*IRS1*	Translational	Yes	(Shi et al. 2007; La Rocca et al. 2009)
hsa-miR-150	*MYB*	Translational	Yes	(Xiao et al. 2007)
hsa-miR-153	*BCL2*	Translational	Yes	(Xu et al.)
hsa-miR-153	*MCL1*	Translational	Yes	(Xu et al.)
hsa-miR-155	*BACH1*	Translational	Yes	(Skalsky et al. 2007)
hsa-miR-155	*MATR3*	Translational	Yes	(Skalsky et al. 2007)

hsa-miR-155	*AGTR1*	Translational	No	(Martin et al. 2006)
hsa-miR-15a	*DMTF1*	Translational	Yes	(Kiriakidou et al. 2004)
hsa-miR-15a	*BCL2*	Translational Transcriptional	Yes	(Cimmino et al. 2005)
hsa-miR-15a	*CREBL2*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15a	*IGSF4*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15a	*PDCD4*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15a	*PDCD6IP*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15a	*RAD51C*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15a	*WT1*	Translational Transcriptional	No	(Calin et al. 2008)
hsa-miR-15b	*DMTF1*	Translational	Yes	(Kiriakidou et al. 2004)
hsa-miR-15b	*BCL2*	Translational Transcriptional	Yes	(Cimmino et al. 2005)
hsa-miR-15b	*CREBL2*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15b	*IGSF4*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15b	*PDCD4*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-15b	*RAD51C*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-16	*CGI-38*	Translational	Yes	(Kiriakidou et al. 2004)
hsa-miR-16	*BCL2*	Translational Transcriptional	Yes	(Cimmino et al. 2005)
hsa-miR-16	*CREBL2*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-16	*IGSF4*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-16	*PDCD4*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-16	*PDCD6IP*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-16	*RAD51C*	Translational Transcriptional	Yes	(Calin et al. 2008)
hsa-miR-16	*GPIAP1*	Translational	Yes	(Kaddar et al. 2009)
hsa-miR-16	*HMGA1*	Translational Transcriptional	Yes	(Kaddar et al. 2009)
hsa-miR-16-1	*WT1*	Translational Transcriptional	No	(Calin et al. 2008)
hsa-miR-17	*E2F1*	Translational	Yes	(O'Donnell et

				al. 2005)
hsa-miR-17	*NCOA3 (AIB1)*	Translational	Yes	(Hossain et al. 2006)
hsa-miR-17	*CDKN1A (p21)*	Translational	Yes	(Ivanovska et al. 2008)
hsa-miR-181b	*GRIA2*	Translational Transcriptional	Yes	(Beveridge et al. 2008)
hsa-miR-183	*EZR (VIL2)*	Translational	Yes	(Wang et al. 2008a)
hsa-miR-196a	*HOXA7*	Translational	Yes	(Yekta et al. 2004)
hsa-miR-196a	*HOXB8*	Translational	Yes	(Yekta et al. 2004)
hsa-miR-196a	*HOXC8*	Translational	Yes	(Yekta et al. 2004)
hsa-miR-19a	*PTEN*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-19a	*ATXN1*	Translational	Yes	(Lee et al. 2008)
hsa-miR-19b	*HIPK3*	Translational	Yes	(Landais et al. 2007)
hsa-miR-19b	*MYLIP*	Translational	Yes	(Landais et al. 2007)
hsa-miR-19b	*ATXN1*	Translational	Yes	(Lee et al. 2008)
hsa-miR-200a	*TCF8 (ZEB1)*	Transcriptional	No	(Park et al. 2008)
hsa-miR-200b	*ZEB1 (TCF8)*	Translational Transcriptional	Yes	(Korpal et al. 2008)
hsa-miR-200c	*ZEB1 (TCF8)*	Transcriptional	Yes	(Park et al. 2008; Lindenblatt et al. 2009)
hsa-miR-206	*GJA1*	Translational	Yes	(Anderson et al. 2006)
hsa-miR-206	*ESR1*	Translational Transcriptional	No	(Adams et al. 2007)
hsa-miR-208a	*THRAP1*	Translational Transcriptional	Yes	(van Rooij et al. 2007)
hsa-miR-208b	*THRAP1*	Translational Transcriptional	Yes	(van Rooij et al. 2007)
hsa-miR-20a	*E2F1*	Translational	Yes	(O'Donnell et al. 2005)
hsa-miR-20a	*TGFBR2*	Translational	Yes	(Volinia et al. 2006)
hsa-miR-20b	*ARID4B*	Translational	Yes	(Landais et al. 2007)
hsa-miR-20b	*MYLIP*	Translational	Yes	(Landais et al. 2007)
hsa-miR-20b	*CDKN1A (p21)*	Translational	Yes	(Ivanovska et al. 2008)

hsa-miR-21	*BCL2*	Translational Transcriptional	Yes	(Si et al. 2007)
hsa-miR-21	*NFIB*	Transcriptional	Yes	(Fujita et al. 2008)
hsa-miR-21	*SPRY2*	Translational	Yes	(Sayed et al. 2008)
hsa-miR-21	*MTAP*	Translational	Yes	(Chen et al. 2008)
hsa-miR-21	*SPRY1*	Translational	Yes	(Thum et al. 2008)
hsa-miR-21	*TIMP3*	Transcriptional	Yes	(Selaru et al. 2009)
hsa-miR-21	*JAG1*	Translational	Yes	(Hashimi et al. 2009)
hsa-miR-21	*BTG2*	Translational	Yes	(Liu et al. 2009b)
hsa-miR-21	*BMPR2*	Translational	Yes	(Qin et al. 2009)
hsa-miR-21	*CDC25A*	Translational Transcriptional	Yes	(Wang et al. 2009b)
hsa-miR-21	*PDCD4*	Translational	Yes	(Asangani et al. 2008; Talotta et al. 2009)
hsa-miR-21	*TPM1*	Translational	No	(Zhu et al. 2007)
hsa-miR-21	*SERPINB5*	Translational	No	(Zhu et al. 2008)
hsa-miR-210	*EFNA3*	Translational	Yes	(Fasanaro et al. 2008)
hsa-miR-210	*MNT*	Translational	Yes	(Zhang et al. 2009b)
hsa-miR-214	*PTEN*	Translational	Yes	(Yang et al. 2008)
hsa-miR-221	*KIT*	Translational	Yes	(Felli et al. 2005)
hsa-miR-221	*CDKN1C (p57)*	Translational	Yes	(Medina et al. 2008)
hsa-miR-221	*CDKN1B (KIP1)*	Translational	Yes	(Galardi et al. 2007; Medina et al. 2008)
hsa-miR-222	*KIT*	Translational	Yes	(Felli et al. 2005)
hsa-miR-222	*CDKN1C (p57)*	Translational	Yes	(Medina et al. 2008)
hsa-miR-222	*CDKN1B (KIP1)*	Translational	Yes	(Galardi et al. 2007; Medina et al. 2008)
hsa-miR-222	*SOD2*	Translational	No	(Liu et al. 2009c)
hsa-miR-222	*MMP1*	Translational	No	(Liu et al. 2009c)

hsa-miR-224	*API5*	Translational Transcriptional	Yes	(Wang et al. 2008f)
hsa-miR-23a	*CXCL12*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-23a	*POU4F2*	Translational	Yes	(Lewis et al. 2003)
hsa-miR-23a	*FLJ13158 (C6orf134)*	Translational	Yes	(Kiriakidou et al. 2004)
hsa-miR-23b	*GLS*	Translational Transcriptional	Yes	(Gao et al. 2009)
hsa-miR-24	*MAPk14*	Translational	Yes	(Kiriakidou et al. 2004)
hsa-miR-24	*ACVR1B (ALK4)*	Translational	Yes	(Wang et al. 2008d)
hsa-miR-24	*DHFR*	Translational Transcriptional	No	(Mishra et al. 2007)
hsa-miR-25	*CCDC131 (MGC23401)*	Translational	Yes	(Grimson et al. 2007)
hsa-miR-25	*CDH10*	Translational	Yes	(Grimson et al. 2007)
hsa-miR-25	*DYRK2*	Translational	Yes	(Grimson et al. 2007)
hsa-miR-25	*NFIB*	Translational	Yes	(Grimson et al. 2007)
hsa-miR-25	*PHTF2*	Translational	Yes	(Grimson et al. 2007)
hsa-miR-26a	*SERBP1*	Translational	Yes	(Beitzinger et al. 2007)
hsa-miR-26a	*SMAD1*	Translational	Yes	(Luzi et al. 2008)
hsa-miR-26a	*EZH2*	Translational Transcriptional	Yes	(Wong and Tellam 2008)
hsa-miR-26b	*SERBP1*	Translational	Yes	(Beitzinger et al. 2007)
hsa-miR-26b	*ACSL3*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*ARFGEF1*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*ARPP-19*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*C20orf24*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*CHORDC1*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*DRAM*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*EIF5*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*FBXO11*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*G3BP2*	Transcriptional	Yes	(Gennarino et

				al. 2009)
hsa-miR-26b	*GGA3*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*GMFB*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*HELZ*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*HMGA2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*KPNA2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*KPNA6*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*LARP4*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*MAPK6*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*MKNK2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*MTDH*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*MTX2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*NLK*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*PHTF2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*PTEN*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*RCN2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*RHOQ*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*RKHD2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*RNF6*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*SACS*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*SAR1B*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*SLC7A11*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*SOCS5*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*SRP19*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*WNT5A*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-26b	*EZH2*	Transcriptional	Yes	(Wong and Tellam 2008;

				Gennarino et al. 2009)
hsa-miR-27a	*MYT1*	Translational Transcriptional	Yes	(Mertens-Talcott et al. 2007)
hsa-miR-27a	*ZBTB10*	Translational Transcriptional	Yes	(Mertens-Talcott et al. 2007)
hsa-miR-27a	*RUNX1*	Translational	Yes	(Ben-Ami et al. 2009)
hsa-miR-27a	*FOXO1 (FOXO1A)*	Translational	Yes	(Guttilla and White 2009)
hsa-miR-27b	*CYP1B1*	Translational	Yes	(Tsuchiya et al. 2006)
hsa-miR-27b	*ST14*	Translational	Yes	(Wang et al. 2009c)
hsa-miR-29a	*BACE1*	Translational	Yes	(Hebert et al. 2008)
hsa-miR-29b	*MCL1*	Translational	Yes	(Mott et al. 2007)
hsa-miR-29b	*BACE1*	Translational	Yes	(Hebert et al. 2008)
hsa-miR-29c	*COL15A1*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*COL1A1*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*COL1A2*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*COL3A1*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*COL4A2*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*FUSIP1*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*LAMC1*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*SPARC*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-29c	*TDG*	Translational	Yes	(Sengupta et al. 2008)
hsa-miR-30a	*BECN1*	Transcriptional	Yes	(Zhu et al. 2009)
hsa-miR-30e	*UBE2I (Ubc9)*	Translational	Yes	(Wu et al. 2009)
hsa-miR-33b	*FOXG1B*	Translational	Yes	(Bredenkamp et al. 2007)
hsa-miR-34a	*E2F3*	Translational	Yes	(Welch et al. 2007)
hsa-miR-34a	*CCND1*	Translational	Yes	(Sun et al. 2008)
hsa-miR-370	*MAP3K8*	Translational	Yes	(Meng et al.

				2008)
hsa-miR-375	*ADIPOR2*	Translational	Yes	(Krek et al. 2005)
hsa-miR-375	*USP1*	Translational	Yes	(Krek et al. 2005)
hsa-miR-375	*C1QBP*	Translational	No	(Krek et al. 2005)
hsa-miR-375	*JAK2*	Translational	No	(Krek et al. 2005)
hsa-miR-378	*TUSC2*	Translational	Yes	(Lee et al. 2007a)
hsa-miR-433	*FGF20*	Translational	No	(Wang et al. 2008b)
hsa-miR-449a	*HDAC1*	Translational	No	(Noonan et al. 2009)
hsa-miR-503	*CCND1*	Translational Transcriptional	Yes	(Jiang et al. 2009)
hsa-miR-520h	*ABCG2*	Translational	No	(Liao et al. 2008)
hsa-miR-559	*ERBB2*	Translational	No	(Chen et al. 2009a)
hsa-miR-7	*EGFR*	Translational Transcriptional	Yes	(Webster et al. 2009)
hsa-miR-7	*SNCA*	Translational	Yes	(Junn et al. 2009)
hsa-miR-7	*PAK1*	Translational Transcriptional	No	(Reddy et al. 2008)
hsa-miR-9	*FOXG1B*	Translational	Yes	(Bredenkamp et al. 2007)
hsa-miR-9	*BACE1*	Translational	Yes	(Hebert et al. 2008)
hsa-miR-92	*HIPK3*	Translational	No	(Landais et al. 2007)
hsa-miR-92a	*HIPK3*	Translational	Yes	(Landais et al. 2007)
hsa-miR-92a	*MYLIP*	Translational	Yes	(Landais et al. 2007)
hsa-miR-92a	*ITGA5*	Translational Transcriptional	Yes	(Bonauer et al. 2009)
hsa-miR-92b	*CDKN1C (p57)*	Translational	Yes	(Sengupta et al. 2009)
hsa-miR-96	*FOXO1 (FOXO1A)*	Translational	Yes	(Guttilla and White 2009)
hsa-miR-98	*HMGA2*	Transcriptional	Yes	(Hebert et al. 2007)
hsa-miR-98	*ARMC8*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*ATP2B1*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*C6orf211*	Translational Transcriptional	Yes	(Gennarino et al. 2009)

hsa-miR-98	*CPEB3*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*E2F6*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*EIF4G2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*EZH2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*GABPA*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*GALNT2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*LRIG1*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*MAPK6*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*NRAS*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*NRBF2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*PAK1*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*POGZ*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*RIOK3*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*SMAD2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*SNAP23*	Translational Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*STAT3*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*THOC2*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*UGCGL1*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*USP47*	Transcriptional	Yes	(Gennarino et al. 2009)
hsa-miR-98	*TBC1D13*	Transcriptional	No	(Gennarino et al. 2009)

Table S2. CoMeTa predictions of human miRNA-regulated biological functions confirmed by experimental studies.

miRNA	COOL cluster	R^2 value	Enriched pathway	DAVID	FDR	Reference
let-7a	1	0.85	Cell cycle	KEGG	1.60	(Zhou et al. 2009; Bueno et al. 2010)
let-7a	1	0.85	Prostate cancer	KEGG	19.42	(Dong et al. 2010)
let-7c	1	0.91	Pancreatic cancer	KEGG	2.47	(Li et al. 2009c)
let-7c	1	0.91	Cell death	BP	3.75	(Ovcharenko et al. 2007; Shimizu et al. 2010)
let-7i	1	0.90	G1-S transition of mitotic cell cycle	BP	1.38	(Bueno et al. 2010)
miR-101	1	0.85	Colorectal cancer	KEGG	4.26	(Strillacci et al. 2009)
miR-101	1	0.85	Response to cytokine stimulus	BP	0.24	(Vilardo et al. 2010)
miR-106a	1	0.85	TGFb signaling pathway	KEGG	0.00	(Petrocca et al. 2008a; Petrocca et al. 2008b)
miR-106a	1	0.85	Pathways in cancer	KEGG	0.01	(Volinia et al. 2006; Landais et al. 2007; Diaz et al. 2008; Uren et al. 2008)
miR-106b	2	0.86	Pathways in cancer	KEGG	0.33	(Petrocca et al. 2008b; Li et al. 2009b; Borgdorff et al. 2010; Poliseno et al. 2010)
miR-106b	2	0.86	TGFb signaling pathway	KEGG	0.06	(Petrocca et al. 2008a; Petrocca et al. 2008b)
miR-106b	2	0.86	G1-S transition of mitotic cell cycle	BP	0.01	(Kim et al. 2009b; Bueno et al. 2010)
miR-106b	2	0.86	Cell-cycle phase	BP	0.98	(Ivanovska et al. 2008)
miR-106b	2	0.86	Haematopoiesis	BP	3.49	(Merkerova et al. 2008)
miR-107	1	0.87	Pancreatic cancer	KEGG	2.88	(Lee et al. 2009)
miR-107	1	0.87	Pathways in cancer	KEGG	0.02	(Takahashi et al. 2009; Yamakuchi et al. 2010)
miR-107	1	0.87	G1/S transition of mitotic cell cycle	BP	0.01	(Takahashi et al. 2009)
miR-10a	1	0.89	Apoptosis	KEGG	15.91	(Ovcharenko et al. 2007; Sirotkin et al. 2010)
miR-124	1	0.86	Glioma	KEGG	4.24	(Silber et al. 2008)
miR-124	1	0.86	Axon guidance	KEGG	0.70	(Yu et al. 2008a)

miR-124	1	0.86	Neurotrophin signaling pathway	KEGG	1.34	(Le et al. 2009)
miR-124	1	0.86	Actin cytoskeleton organisation	BP	0.14	(Yu et al. 2008a)
miR-130a	1	0.85	Angiogenesis	BP	1.22	(Chen and Gorski 2008; Urbich et al. 2008)
miR-130b	2	0.84	Pathways in cancer	KEGG	0.00	(Yeung et al. 2008; Borgdorff et al. 2010; Lai et al. 2010)
miR-130b	2	0.84	Regulation of growth	BP	0.71	(Yeung et al. 2008; Borgdorff et al. 2010)
miR-135a	2	0.86	Colorectal cancer	KEGG	0.00	(Nagel et al. 2008)
miR-135a	2	0.86	Apoptosis	KEGG	1.18	(Navarro et al. 2009)
miR-135b	1	0.87	Prostate cancer	KEGG	9.65	(Wang et al. 2008c)
miR-138	1	0.88	Pathways in cancer	KEGG	3.16	(Mitomo et al. 2008; Jiang et al. ; Nicoloso et al. 2010)
miR-138	1	0.88	Cell migration	BP	0.01	(Jiang et al. 2010a)
miR-143	1	0.89	Prostate cancer	KEGG	1.58	(Clape et al. 2009; Szczyrba et al. 2010)
miR-143	1	0.89	Pathways in cancer	KEGG	1.80	(Akao et al. 2006; Wang et al. 2008e; Chen et al. 2009b; Suzuki et al. 2009; Takagi et al. 2009; Akao et al.)
miR-143	1	0.89	Regulation of actin cytoskeleton	KEGG	11.49	(Xin et al. 2009; Quintavalle et al.)
miR-155	2	0.84	Pathways in cancer	KEGG	0.10	(Tam and Dahlberg 2006; Volinia et al. 2006; Jiang et al. ; Kong et al. ; Valeri et al. ; Volinia et al.)
miR-155	2	0.84	TGFb receptor signaling pathway	BP	1.22	(Pottier et al. 2009; Rai et al.)
miR-155	2	0.84	Regulation of cell proliferation	BP	0.07	(Jiang et al.)
miR-155	2	0.84	B-cell-receptor signaling pathway	KEGG	0.83	(Calame 2007; Vigorito et al. 2007; Yin et al. 2008)
miR-155	2	0.84	Immune system development	BP	4.87	(Rodriguez et al. 2007; Vigorito et al. 2007; Sonkoly et al. 2008)
miR-155	2	0.84	Pancreatic cancer	KEGG	8.44	(Gironella et al. 2007; Habbe et al. 2009; Ryu et al.)

miR-155	2	0.84	T-cell-receptor signaling pathway	KEGG	11.68	(Thai et al. 2007; Banerjee et al.)
miR-155	2	0.84	Acute myeloid leukemia	KEGG	2.24	(Garzon et al. 2008; O'Connell et al. 2008; Cammarata et al.)
miR-155	2	0.84	Haematopoiesis	BP	1.73	(Ramkissoon et al. 2006; Masaki et al. 2007; Merkerova et al. 2008; O'Connell et al. 2009; Hu et al.)
miR-15a	2	0.84	B-cell-receptor signaling pathway	KEGG	6.04	(Klein et al.)
miR-15a	2	0.84	Cell proliferation	BP	3.73	(Bonci et al. 2008; Lerner et al. 2009)
miR-15a	2	0.90	Pathways in cancer	KEGG	0.01	(Calin et al. 2002; Garzon et al. 2007; Bonci et al. 2008; Calin et al. 2008; Bhattacharya et al. 2009; Aqeilan et al.)
miR-15a	2	0.90	Regulation of apoptosis	BP	0.56	(Cimmino et al. 2005; Tarasov et al. 2007; Bonci et al. 2008)
miR-15a	2	0.90	G1/S transition of mitotic cell cycle	BP	3.38	(Linsley et al. 2007; Bandi et al. 2009)
miR-15a	2	0.90	Prostate cancer	KEGG	0.18	(Bonci et al. 2008)
miR-15b	1	0.90	Pathways in cancer	KEGG	0.00	(Wang et al. 2008e; Xia et al. 2009)
miR-15b	1	0.90	G1/S transition of mitotic cell cycle	BP	4.92	(Xia et al. 2009; Bueno et al.)
miR-15b	1	0.90	Glioma	KEGG	0.11	(Xia et al. 2009)
miR-16	1	0.89	Prostate cancer	KEGG	0.11	(Bonci et al. 2008; Schaefer et al.)
miR-16	1	0.89	Pathways in cancer	KEGG	0.00	(Chung et al. 2008; Bhattacharya et al. 2009; Suzuki et al. 2009; Takeshita et al.)
miR-16	1	0.89	G1/S transition of mitotic cell cycle	BP	2.11	(Linsley et al. 2007; Liu et al. 2008; Bandi et al. 2009; Bueno et al.)
miR-16	1	0.89	Regulation of cell proliferation	BP	0.27	(Kaddar et al. 2009)
miR-16	1	0.89	Regulation of apoptosis	BP	2.26	(Cimmino et al. 2005; Guo et al. 2009a)
miR-16	1	0.89	p53 signaling pathway	KEGG	9.69	(Suzuki et al. 2009)
miR-16	1	0.89	B-cell-receptor signaling pathway	KEGG	0.71	(Klein et al.)

miR-17	2	0.87	Glioma	KEGG	0.70	(Malzkorn et al. 2009; Ernst et al.)
miR-17	2	0.87	TGFb signaling pathway	KEGG	0.00	(Petrocca et al. 2008a; Petrocca et al. 2008b)
miR-17	2	0.87	Pathways in cancer	KEGG	0.01	(Tagawa et al. 2007; Aguda et al. 2008; Chang et al. 2008; Yu et al. 2008b; Bonauer and Dimmeler 2009; Uziel et al. 2009; Olive et al. ; van Haaften and Agami ; Yu et al.)
miR-17	2	0.87	MAPK signaling pathway	KEGG	0.51	(Cloonan et al. 2008; Yang et al.)
miR-17	2	0.87	Haematopoietic or lymphoid organ development	BP	0.08	(Shan et al. 2009)
miR-17	2	0.87	G1/S transition of mitotic cell cycle	BP	0.06	(Cloonan et al. 2008; Pickering et al. 2009)
miR-17	2	0.87	p53 signaling pathway	KEGG	1.42	(Yan et al. 2009b)
miR-17	2	0.87	Apoptosis	BP	0.00	(Matsubara et al. 2007; Yan et al. 2009b)
miR-17	2	0.87	Regulation of cell proliferation	BP	2.55	(O'Donnell et al. 2005; Hossain et al. 2006; Lu et al. 2007)
miR-181a	1	0.86	Acute myeloid leukaemia	KEGG	0.06	(Debernardi et al. 2007)
miR-181a	1	0.86	Regulation of apoptosis	BP	0.03	(Galluzzi et al. ; Zhu et al.)
miR-181a	1	0.86	Glioma	KEGG	0.06	(Shi et al. 2008; Chen et al.)
miR-181a	1	0.86	Pathways in cancer	KEGG	0.02	(Pichiorri et al. 2008; Maillot et al. 2009; Galluzzi et al. ; Zhu et al.)
miR-181a	1	0.86	G1/S transition of mitotic cell cycle	BP	0.03	(Galluzzi et al.)
miR-181b	1	0.86	Glioma	KEGG	0.06	(Ciafre et al. 2005; Shi et al. 2008)
miR-181b	1	0.86	Regulation of apoptosis	BP	0.03	(Zhu et al.)
miR-181b	1	0.86	Pathways in cancer	KEGG	0.02	(Cervigne et al. 2009; Conti et al. 2009; Wang et al.)
miR-181b	1	0.86	Colorectal cancer	KEGG	0.09	(Nakajima et al. 2006)
miR-181c	1	0.85	Pathways in cancer	KEGG	0.04	(Hashimoto et al.)
miR-181c	1	0.85	Glioma	KEGG	0.03	(Ciafre et al. 2005; Slaby et al.)

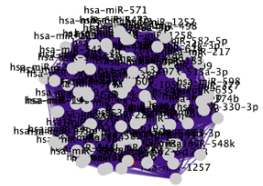
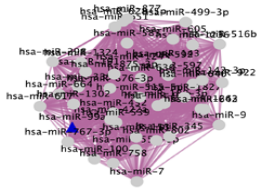
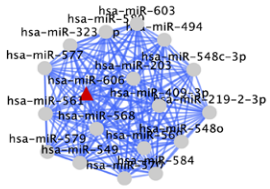
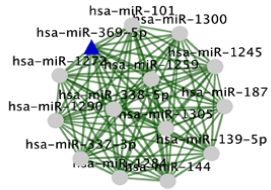
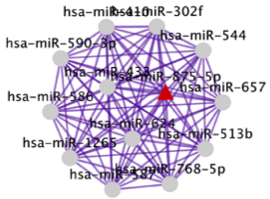
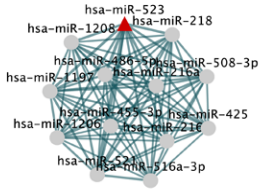
miR-1	2	0.87	Heart development	BP	0.10	(Zhao et al. 2005; Chen et al. 2006; Mishima et al. 2007; Sayed et al. 2007; Zhao et al. 2007; Liu and Olson)
miR-1	2	0.87	Regulation of actin cytoskeleton	KEGG	3.03	(Mishima et al. 2009; Jiang et al.)
miR-1	2	0.87	Regulation of apoptosis	BP	0.19	(Tang et al. 2009)
miR-200a	1	0.83	Wnt signaling pathway	KEGG	0.04	(Saydam et al. 2009)
miR-200a	1	0.83	Pathways in cancer	KEGG	0.10	(Bracken et al. 2008; Gregory et al. 2008; Hu et al. 2009b; Hu et al.)
miR-200b	2	0.85	Pathways in cancer	KEGG	0.02	(Bracken et al. 2008; Gregory et al. 2008; Adam et al. 2009; Li et al. 2009c; Tryndyak et al.)
miR-200b	2	0.85	TGFb signaling pathway	KEGG	9.42	(Christoffersen et al. 2007)
miR-200c	1	0.83	Pathways in cancer	KEGG	0.02	(Hurteau et al. 2007; Burk et al. 2008; Gregory et al. 2008; Adam et al. 2009; Hurteau et al. 2009; Shimono et al. 2009; Wellner et al. 2009; Mees et al.)
miR-200c	1	0.83	Renal cell carcinoma	KEGG	0.01	(Nakada et al. 2008)
miR-206	1	0.83	Regulation of apoptosis	BP	0.01	(Song et al. 2009)
miR-206	1	0.86	Pathways in cancer	KEGG	5.61	(Kondo et al. 2008; Leivonen et al. 2009; O'Day and Lal)
miR-206	1	0.86	Regulation of cell proliferation	BP	0.01	(Yan et al. 2009a)
miR-206	1	0.86	Cell migration	BP	0.01	(Yan et al. 2009a)
miR-20a	1	0.85	TGFb signaling pathway	KEGG	0.01	(Petrocca et al. 2008a; Petrocca et al. 2008b)
miR-20a	1	0.85	Pathways in cancer	KEGG	0.42	(Volinia et al. 2006; Matsubara et al. 2007; Taguchi et al. 2008; Yu et al. 2008b; Ebi et al. 2009)

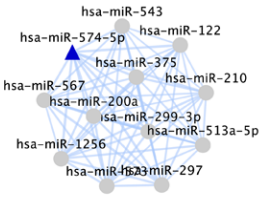
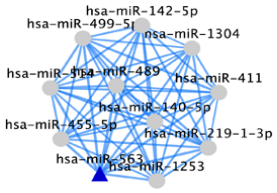
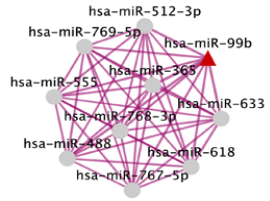
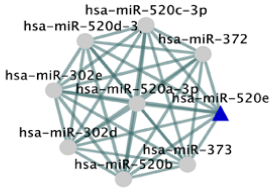
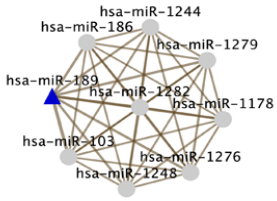
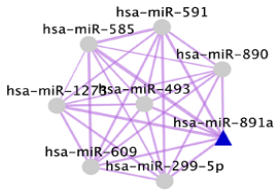
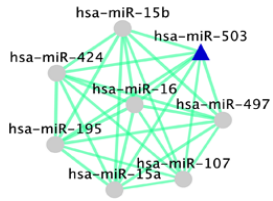
miR-20a	1	0.85	Apoptosis	BP	0.03	(Matsubara et al. 2007; Sylvestre et al. 2007; Yan et al. 2009b)
miR-20a	1	0.85	Cell-cycle process	BP	0.04	(Sylvestre et al. 2007; Yu et al. 2008b; Pickering et al. 2009)
miR-20a	1	0.85	G1-S transition of mitotic cell cycle	BP	0.42	(Pickering et al. 2009)
miR-21	2	0.83	MAPK signaling pathway	KEGG	11.25	(Huang et al. 2009b)
miR-221	1	0.86	Pathways in cancer	KEGG	1.21	(le Sage et al. 2007; Visone et al. 2007; Felicetti et al. 2008; Fornari et al. 2008; Sun et al. 2009; Di Leva et al. ; Pineau et al. ; Fu et al.)
miR-221	1	0.86	Cell cycle	BP	0.41	(le Sage et al. 2007; Visone et al. 2007; Medina et al. 2008; Mayoral et al. 2009; Park et al. 2009a; Zhou et al. 2009)
miR-221	1	0.86	Regulation of cell proliferation	BP	0.56	(le Sage et al. 2007; Fornari et al. 2008; Medina et al. 2008; Mayoral et al. 2009)
miR-221	1	0.86	Regulation of cell-matrix adhesion	BP	4.58	(Hu et al.)
miR-221	1	0.86	Induction of apoptosis	BP	0.04	(Gramantieri et al. 2009; Park et al. 2009a),
miR-222	1	0.86	Pathways in cancer	KEGG	18.81	(le Sage et al. 2007; Felicetti et al. 2008; Hu et al. 2009a; Kim et al. 2009b; Sun et al. 2009; Wong et al.)
miR-222	1	0.86	Cell cycle	BP	1.67	(Galardi et al. 2007; Visone et al. 2007; Medina et al. 2008; Kim et al. 2009b; Zhang et al. 2009a; Forrest et al.)
miR-224	2	0.88	Pathways in cancer	KEGG	0.14	(Li et al. 2009a; Li et al.)
miR-224	2	0.88	TGFb signaling pathway	KEGG	19.48	(Yao et al.)
miR-224	2	0.88	Regulation of apoptosis	BP	2.92	(Wang et al. 2008f)

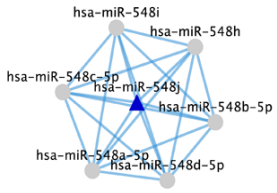
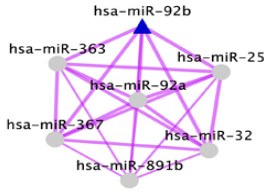
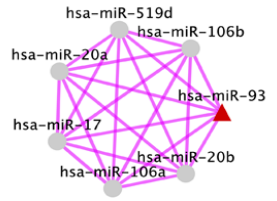
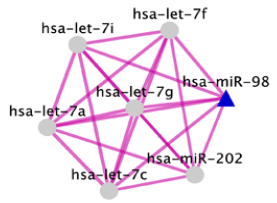
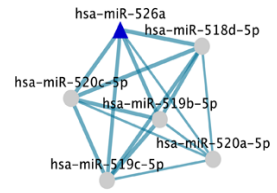
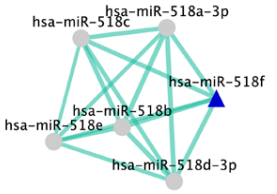
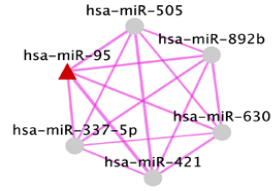
miR-25	1	0.83	Phosphoinositide signaling system	KEGG	4.66	(Poliseno et al.)
miR-25	1	0.83	Cell cycle	KEGG	0.01	(Kim et al. 2009b; Bueno et al.)
miR-26a	2	0.83	Regulation of striated muscle tissue development	BP	4.98	(Wong and Tellam 2008; Ciarapica et al. 2009)
miR-26a	2	0.83	Immune system development	BP	2.16	(Witwer et al.)
miR-26a	2	0.83	Regulation of cyclin-dependent protein kinase activity	BP	2.11	(Kota et al. 2009; Kim et al.)
miR-26a	2	0.83	Cell cycle	BP	0.20	(Sander et al. 2009)
miR-27a	1	0.85	Cell cycle	BP	0.91	(Mertens-Talcott et al. 2007; Chintharlapalli et al. 2009)
miR-27a	1	0.85	Insulin signaling pathway	KEGG	0.08	(Herrera et al.)
miR-27a	1	0.85	Cellular response to insulin stimulus	BP	0.88	(Herrera et al.)
miR-27b	1	0.89	MAPK signaling pathway	KEGG	0.28	(Akhtar et al.)
miR-27b	1	0.89	Muscle cell differentiation	BP	1.01	(Crist et al. 2009)
miR-298	1	0.87	Alzheimer's disease	KEGG	19.99	(Boissonneault et al. 2009; Provost)
miR-373	1	0.88	Pathways in cancer	KEGG	0.02	(Voorhoeve et al. 2006; Voorhoeve et al. 2007; Huang et al. 2008; O'Day and Lal)
miR-7	1	0.88	Axon guidance	KEGG	0.69	(Chen et al.)
miR-7	1	0.88	Insulin signaling pathway	KEGG	0.28	(Bravo-Egana et al. 2008; Correa-Medina et al. 2009; Joglekar et al. 2009)
miR-93	1	0.85	TGFb signaling pathway	KEGG	0.01	(Petrocca et al. 2008a; Petrocca et al. 2008b)
miR-93	1	0.85	Pathways in cancer	KEGG	0.00	(Petrocca et al. 2008b; Yeung et al. 2008; Du et al. 2009; Li et al. 2009b)
miR-93	1	0.85	G1/S transition of mitotic cell cycle	BP	1.55	(Kim et al. 2009b)
miR-9	1	0.87	Pathways in cancer	KEGG	0.33	(Lujambio et al. 2008; Guo et al. 2009b; Khew-Goodall and Goodall ; Ma et al. ; Tan et al.)

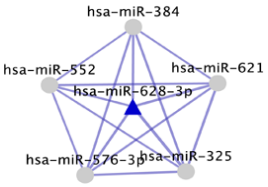
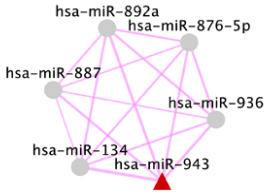
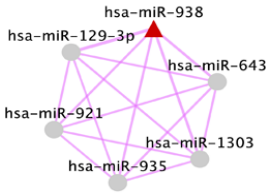
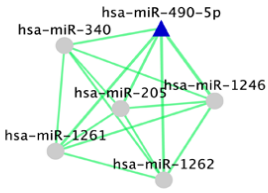
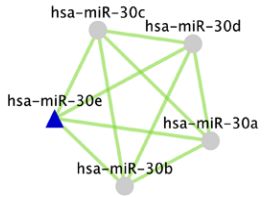
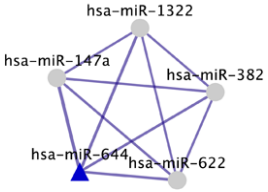
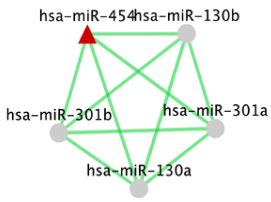
miR-29a	1	0.86	G1/S transition of mitotic cell cycle	BP	3.10	(Han et al.)
miR-29a	1	0.86	Pathways in cancer	KEGG	0.14	(Gebeshuber et al. 2009; Muniyappa et al. 2009; Xiong et al.)
miR-29a	1	0.86	Wnt signaling pathway	KEGG	10.60	(Kapinas et al. 2009)
miR-29a	1	0.86	Apoptosis	KEGG	0.53	(Park et al. 2009b; Xiong et al.)
miR-29b	1	0.86	Apoptosis	KEGG	3.99	(Mott et al. 2007; Park et al. 2009b; Wang and Lee 2009)
miR-29b	1	0.86	Focal adhesion	KEGG	0.11	(Luna et al. 2009)
miR-29c	1	0.90	Wnt signaling pathway	KEGG	11.74	(Kapinas et al. 2009)
miR-29c	1	0.90	Apoptosis	KEGG	14.71	(Park et al. 2009b)
miR-29c	1	0.90	Extracellular matrix organisation	BP	0.08	(Sengupta et al. 2008)

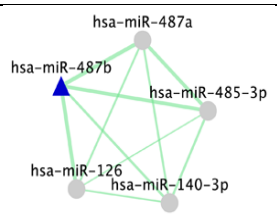
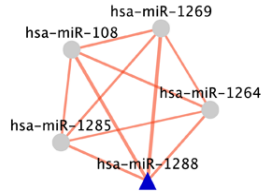
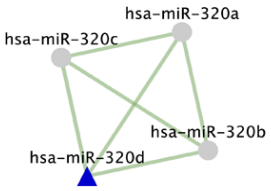
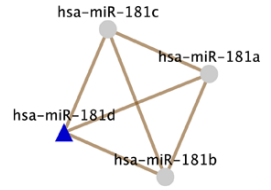
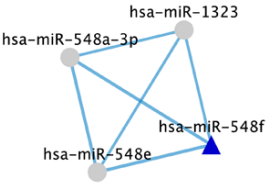
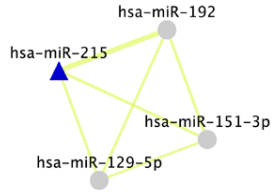
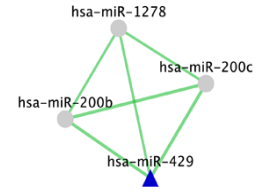
Table S3. Complete summary of miRCo functional predictions.

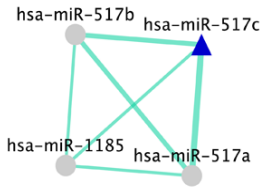
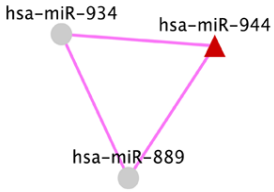
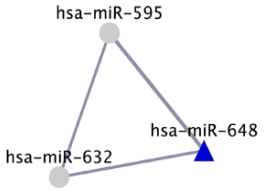
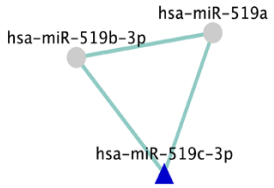
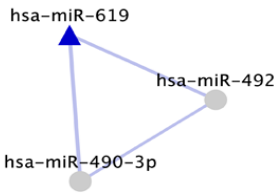
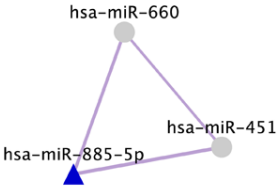
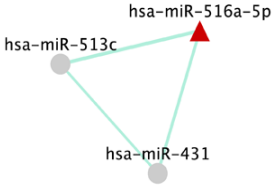
miRCo	miRCo network	Enriched GO terms (FDR ≤ 0.05)
miRCo1		DNA damage stimulus
		Cell division
		Cellular response to stress
miRCo2		TGFb signaling pathway
		Myeloid cell differentiation
		ErbB signaling pathway
		mTOR signaling pathway
miRCo3		Catabolic and metabolism processes
		Insulin signaling pathway
		RNA processing
		Spliceosome
miRCo4		Methylation
		Heart development
		Head development
		Steroid hormone stimulus
miRCo5		Regulation of translation
		Microtubule cytoskeleton
		Induction of apoptosis
		DNA repair
miRCo6		Chromatin organization
		Long-term depression

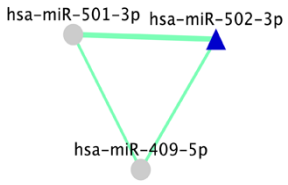
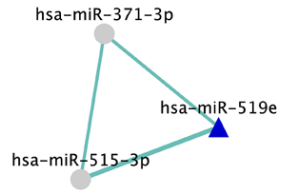
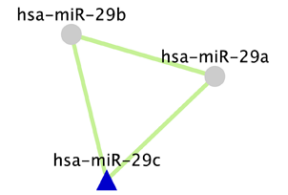
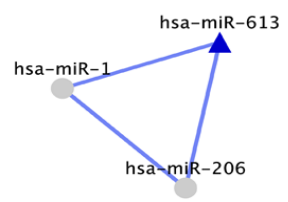
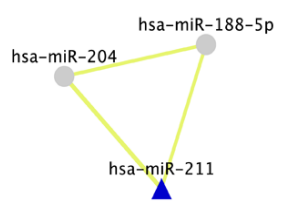
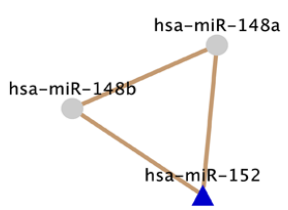
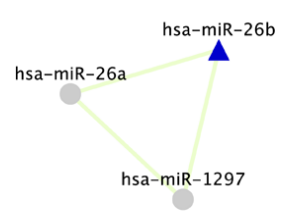
miRCo7		Axon guidance
		Protein localization
miRCo8		Gene silencing by miRNA
miRCo9		Histone deacetylation
		MAPK signaling pathway
		Melanoma
miRCo10		Apoptosis
		Regulation of I-kB kinase - NF-kB
		Pathways in cancer
		Cell cycle
miRCo11		Regulation of cellular component biogenesis
		Protein import into nucleus
miRCo12		Regulation of transcription
		Protein localization
miRCo13		B-cell-receptor signaling pathway
		Metabolism process
		Pathways in cancer
		G1/S transition of mitotic cell-cycle process

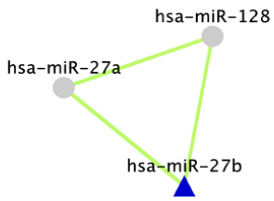
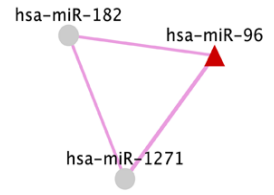
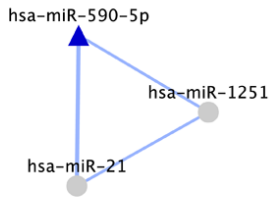
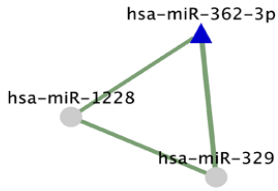
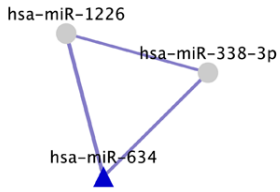
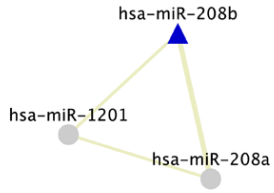
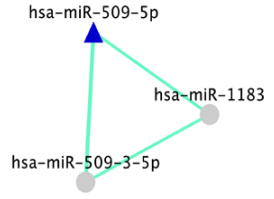
miRCo14		Immune system development
		Haematopoiesis and haematopoietic development
		Metabolism
		Notch signaling pathway
miRCo15		Cell cycle
		Regulation of cell motion and communication
		Inositol phosphate metabolism
		Wnt receptor signaling pathway
miRCo16		TGFb signaling pathway
		Cell-cycle process
		MAPK signaling pathway
		Pathways in cancer
miRCo17		Cell cycle
		Lysosome
		Cytokine stimulus
		P53 signaling pathway
miRCo18		Pathways in cancer
		Regulation of developmental processes
		Phosphoinositide dephosphorylation
		Membrane organization
miRCo19		Protein amino-acid autophosphorylation
miRCo20		No statistically significant categories

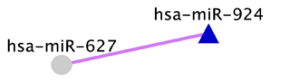
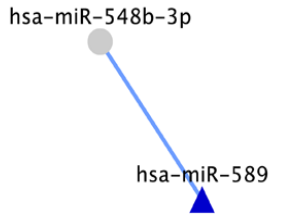
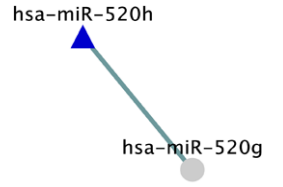
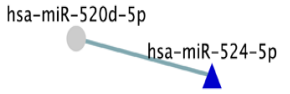
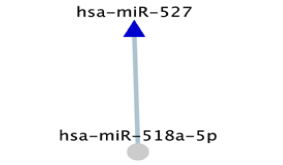
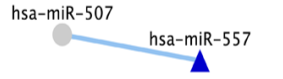
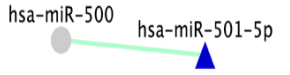
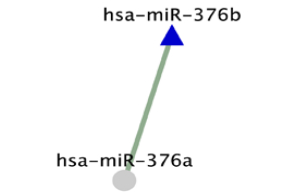
miRCo21		Natural-killer-cell-mediated cytotoxicity
		Organophosphate metabolic processes
miRCo22		No statistically significant categories
miRCo23		No statistically significant categories
miRCo24		No statistically significant categories
miRCo25		Apoptosis
		Muscle development and cell differentiation
		Circadian rhythm
		Heart development
miRCo26		Hormone metabolic processes
miRCo27		Tube development
		Angiogenesis
		Melanogenesis
		Wnt signaling pathway

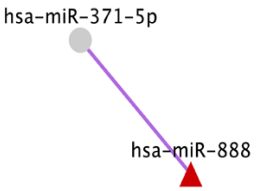
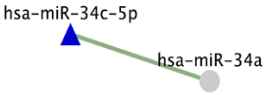
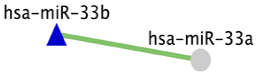
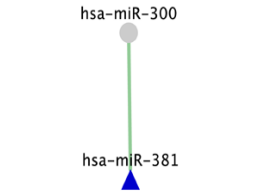
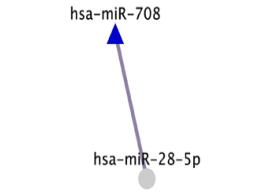
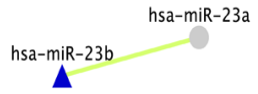
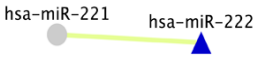
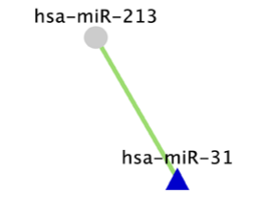
miRCo28		Transcription
miRCo29		Head development
miRCo30		Insulin signaling pathway Vasculogenesis and angiogenesis Metabolic processes Palate development
miRCo31		Acute myeloid leukaemia Aging Response to hypoxia Glioma
miRCo32		Phosphoinositide signaling system Angiogenesis Axon guidance Lung and respiratory tube development
miRCo33		DNA modification
miRCo34		Metabolic processes TGFb signaling pathway Aging MAPKKK cascade

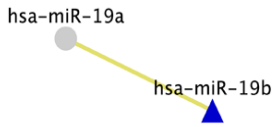
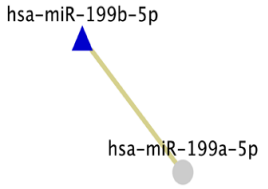
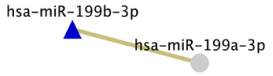
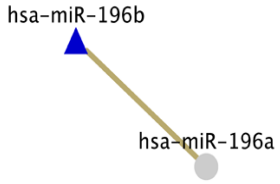
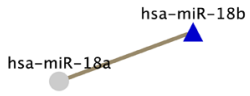
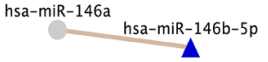
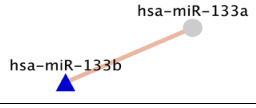
miRCo35		DNA unwinding during replication
miRCo36		Lung and respiratory tube development
		Gap junction
miRCo37		NOD-like receptor signaling pathway
miRCo38		Heart development
		Embryonic development
		Regulation of actin cytoskeleton
		Ras GTPase activity
miRCo39		Centrosome organization
		Microtubule organization
miRCo40		No statistically significant categories
miRCo41		No statistically significant categories

miRCo42		VEGF signaling pathway
		Bladder cancer
miRCo43		No statistically significant categories
miRCo44		Apoptosis
		Regulation of actin cytoskeleton
		Skin development
		PDGF receptor pathway
miRCo45		Cell proliferation and differentiation
		Heart development
		Actin cytoskeleton and polymerization
		Stem cell maintenance
miRCo46		Proteolysis
		Spliceosome
		Nucleotide excision repair
		Chronic myeloid leukaemia
miRCo47		Melanoma
		Inositol phosphate metabolism
		VEGF signaling pathway
		B-cell and T-cell receptor signaling pathway
miRCo48		Cyclin-dependent protein kinase activity
		Muscle cell differentiation
		mTOR signaling pathway
		Erythrocyte homeostasis and differentiation

miRCo49		Methylation
		O-Glycan biosynthesis
		Insulin signaling pathway
		Chemokine signaling pathway
miRCo50		Cell junction organization and assembly
		Actin cytoskeleton organization
		Response to insulin stimulus
		Muscle development
miRCo51		MAPK activity
miRCo52		Metabolic process
		Gap junction
		Anti-apoptosis
miRCo53		Homeostatic processes
		Sexual reproduction
miRCo54		B-cell and T-cell receptor signaling pathway
		Chromatin assembly or disassembly
miRCo55		Leukocyte transendothelial migration
		Germ cell development

miRCo56		No statistically significant categories
miRCo57		Graft-*versus*-host disease
miRCo58		T-cell receptor signaling pathway Apoptosis Extracellular matrix–receptor interaction Response to hypoxia
miRCo59		Gastrulation Cytoskeleton organization Haematopoiesis Glucose transport
miRCo60		Angiogenesis Regulation of I-kB kinase - NF-kB VEGF signaling pathway DNA damage response
miRCo61		Cyclin-dependent protein kinase activity Haematopoiesis
miRCo62		Segmentation Glyoxylate and dicarboxylate metabolism
miRCo63		Alzheimer’s disease Phosphoinositide signaling system Actin filament and cytoskeleton organization Cell size, shape and morphogenesis

miRCo64		Palate development
		Regulation of myeloid cell differentiation
		Phosphoinositide signaling system
		Phosphoinositide signaling system
miRCo65		Regulation of coagulation
		Response to unfolded proteins
miRCo66		Axon guidance
		Actin polymerization and depolymerization
miRCo67		Wnt receptor signaling pathway
		Immune system development
		Auditory receptor cell differentiation
		Haematopoietic or lymphoid organ development
miRCo68		Telencephalon development
		Huntington's disease
		Post-replication repair
miRCo69		Liver development
		SNARE interactions
		DNA damage response
		ER-to-Golgi vesicle-mediated transport
miRCo70		Leukocyte transendothelial migration
		RNA catabolic processes
		Spliceosome
		Insulin receptor signaling pathway
miRCo71		Cerebral cortex development
		Cellular homeostasis

miRCo72		Wnt receptor signaling pathway
		Muscle organ development
		Neural tube development
		Peptidyl-lysine and threonine modifications
miRCo73		Phosphorus metabolic processes
		Lymphoid progenitor cell differentiation
miRCo74		Osteoblast differentiation
		Neuron migration
		TGFb receptor signaling pathway
		Response to oxygen levels
miRCo75		Jak-STAT signaling pathway
miRCo76		Neuron apoptosis
		Muscle tissue development
		Rhythmic processes
		B-cell differentiation and activation
miRCo77		Retinoic acid receptor signaling pathway
		Endosome organization
		mTOR signaling pathway
		Ras protein signal transduction
miRCo78		p53 signaling pathway
		Peptidyl-lysine modification
		Protein import into nucleus
miRCo79		Phosphoinositide metabolic processes
		Apoptosis
		VEGF signaling pathway
		Leukocyte and lymphocyte activation
miRCo80		Selenoamino acid metabolism

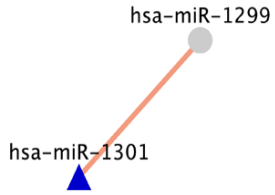
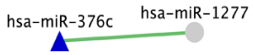
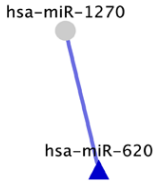
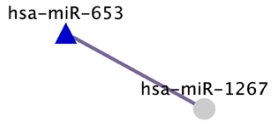
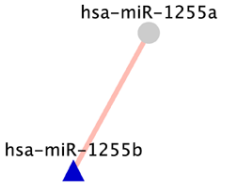
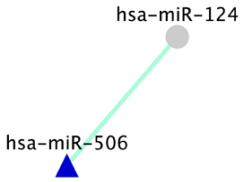
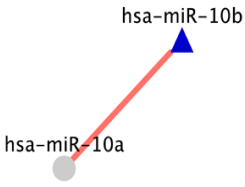
miRCo81		Histone acetylation
		Glycerophospholipid metabolic processes
		Apoptosis and cell death
		Apoptosis and cell death
miRCo82		Cell proliferation
		Epithelium development
		DNA replication
miRCo83		Transcriptional preinitiation complex assembly
		Lipid modification
miRCo84		No statistically significant categories
miRCo85		No statistically significant categories
miRCo86		Axon guidance
		Lymphocyte activation and differentiation
		B-cell and T-cell receptor signaling pathway
		Dorso-ventral axis formation
miRCo87		Apoptosis
		Face development
		Mesoderm morphogenesis and formation

Table S4. Summary of miRCo functional predictions with published support.

miRCo	miRNA	miRCo function	DAVID	FDR	Literature reference
miRCo2	miR-7	ErbB signaling pathway	KEGG	1.87E-01	(Webster et al. 2009; Li et al.)
miRCo4	miR-101	Methylation	BP	3.45E-02	(Varambally et al. 2008; Friedman et al. 2009)
miRCo10	miR-372/373	Colorectal cancer	KEGG	3.45E-03	(Loayza-Puch et al.)
miRCo10	miR-372/373/302d	Induction of apoptosis - induction of apoptosis by extracellular signals	BP	6.15E-06	(Voorhoeve et al. 2007; Cho et al. 2009; Borgdorff et al.)
miRCo10	miR-372	Cell cycle	KEGG	1.22E-02	(Cho et al. 2009; Qi et al. 2009)
miRCo10	miR-520b	Positive regulation of I-kB kinase - NF-kB cascade	BP	3.35E-02	(Yadav et al. 2009)
miRCo10	miR-373/520c	Prostate cancer	KEGG	3.07E-02	(Yang et al. 2009)
miRCo13	miR-107	Pancreatic cancer	KEGG	4.76E-03	(Lee et al. 2009)
miRCo13	miR-107/16/15a/195/497	Pathways in cancer	KEGG	1.03E-01	(Calin et al. 2008; Chung et al. 2008; Bhattacharya et al. 2009; Flavin et al. 2009; Persson et al. 2009; Takahashi et al. 2009; Xu et al. 2009; Aqeilan et al. ; Takeshita et al.)
miRCo13	mir-107/16/15a/15b/195/503/424	G1/S transition of mitotic cell cycle-cell cycle process	BP	4.33E-03	(Linsley et al. 2007; Liu et al. 2008; Bandi et al. 2009; Wang et al. 2009a; Xia et al. 2009; Xu et al. 2009; Sarkar et al.)
miRCo13	miR-16/15b/15a	Glioma	KEGG	2.66E-03	(Malzkorn et al. 2009; Xia et al. 2009)
miRCo13	miR-15a/16	Prostate cancer	KEGG	8.50E-03	(Bonci et al. 2008)
miRCo13	miR-16/15a	Regulation of cell proliferation	BP	3.72E-02	(Bhattacharya et al. 2009; Kaddar et al. 2009; Klein et al. ; Takeshita et al.)
miRCo13	miR-16/15a	B-cell receptor signaling pathway	KEGG	4.76E-06	(Klein et al.)
miRCo13	mir-107/16/15a/15b/195/503	Regulation of cyclin-dependent protein kinase activity	BP	3.48E-02	(Jiang et al. 2009; Lee et al. 2009; Wang et al. 2009a; Xu et al. 2009; Takeshita et al.)
miRCo13	miR-15a/16	Regulation of cell proliferation - cell cycle processes	BP	3.72E-02	(Bonci et al. 2008; Kaddar et al. 2009; Lerner et al. 2009)
miRCo13	miR-15a/15b/16/107/424/195/503/497	Glycerophospholipid metabolism	BP, KEGG	1.12E-03	(Finnerty et al.)
miRCo15	miR-25/92b	Cell cycle	KEGG	1.72E-01	(Kim et al. 2009b; Sengupta et al. 2009; Bueno et al.)

miRCo16	miR-17-92 cluster	Pathways in cancer	KEGG	1.39E-01	(Hossain et al. 2006; Matsubara et al. 2007; Tagawa et al. 2007; Aguda et al. 2008; Chang et al. 2008; Pichiorri et al. 2008; Yu et al. 2008b; Uziel et al. 2009; Yu et al.)
miRCo16	miR-17-92 cluster	TGFb signaling pathway	KEGG	3.15E-03	(Petrocca et al. 2008a; Petrocca et al. 2008b)
miRCo16	miR-106b/20a/93/17	G1/S transition of mitotic cell cycle	BP	1.25E-03	(Cloonan et al. 2008; Kim et al. 2009b; Pickering et al. 2009; Bueno et al.)
miRCo16	miR-106b/20a/93	Cell-cycle processes	BP	3.44E-03	(Ivanovska et al. 2008; Yu et al. 2008b)
miRCo16	miR-106b	Haematopoiesis	BP	2.36E-03	(Merkerova et al. 2008)
miRCo16	miR-106b/20a/93/17	Glioma	KEGG	3.52E-02	(Ernst et al.)
miRCo16	miR-20a/93/17	Apoptosis	KEGG	2.23E-03	(O'Donnell et al. 2005; Matsubara et al. 2007; Petrocca et al. 2008b; Yan et al. 2009b)
miRCo16	miR-17	MAPK signaling pathway	KEGG	4.89E-03	(Cloonan et al. 2008; Yang et al.)
miRCo16	miR-17	p53 signaling pathway	KEGG	1.55E-02	(Yan et al. 2009b)
miRCo17	let-7a/7i	Cell cycle	KEGG	5.38E-02	(Yu et al. 2007; Schultz et al. 2008; Legesse-Miller et al. 2009; Bueno et al.)
miRCo17	let-7c	Pancreatic cancer	KEGG	1.92E-01	(Li et al. 2009c)
miRCo17	miR-98/let-7	Response to cytokine stimulus	BP	1.72E-01	(Hu et al.)
miRCo25	miR-30	Negative regulation of apoptosis	BP	3.76E-03	(Li et al.)
miRCo27	miR-301	Pancreatic cancer	KEGG	1.99E-01	(Lee et al. 2007b)
miRCo30	miR-320	Insulin signaling pathway	KEGG	2.97E-02	(Ling et al. 2009)
miRCo31	miR-181a	Acute myeloid leukaemia	KEGG	7.61E-03	(Debernardi et al. 2007)
miRCo31	miR-181a/181b/181c	Glioma	KEGG	6.83E-02	(Ciafre et al. 2005; Shi et al. 2008; Chen et al.)
miRCo34	miR-200b/200c	TGFb signaling pathway	KEGG	4.72E-02	(Christoffersen et al. 2007; Gregory et al. 2008; Hurteau et al. 2009)
miRCo44	miR-29a/29b/29c	Apoptosis	KEGG	3.24E-02	(Mott et al. 2007; Park et al. 2009b; Wang and Lee 2009)
miRCo45	miR-1	Heart development	BP	3.88E-02	(Zhao et al. 2005; Chen et al. 2006; Sayed et al. 2007; Zhao et al. 2007; Liu and Olson)
miRCo45	miR-1	Regulation of actin cytoskeleton	KEGG	1.51E-01	(Mishima et al. 2009; Jiang et al.)
miRCo45	miR-206	Cell proliferation	BP	4.38E-03	(Yan et al. 2009a)

miRCo47	miR-148	Melanoma	KEGG	3.66E-02	(Haflidadottir et al.)
miRCo48	miR-26a	Regulation of cyclin-dependent protein kinase activity	BP	1.39E-02	(Kota et al. 2009; Kim et al.)
miRCo48	miR-26a	Negative regulation of muscle cell differentiation	BP	1.58E-01	(Wong and Tellam 2008)
miRCo49	miR-27a	Insulin signaling pathway	KEGG	8.80E-02	(Herrera et al.)
miRCo51	miR-21	Negative regulation of MAPK activity	BP	1.87E-01	(Huang et al. 2009b)
miRCo79	miR-135a	Apoptosis	KEGG	1.27E-01	(Navarro et al. 2009)
miRCo86	miR-124	Axon guidance	KEGG	1.31E-01	(Yu et al. 2008a)
miRCo87	miR-10a	Apoptosis	KEGG	1.27E-01	(Ovcharenko et al. 2007; Sirotkin et al.)

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