

Supplementary material S1: List of included studies for selection up-regulated miRNA clusters in CRC.

First author	Year	Ref.	Country/ Region	Tumour type	Control samples	Method of analysis	Upregulated miRNAs	Normalization
Motoyama	2009	[270]	Japan	CRC	PAT	microarray	21	RNU6-6P
Ng	2009	[97]	Hong Kong	CRC	PAT	array	14	RNU6-1
Arndt	2009	[271]	Australia	CRC	NT	array	22	quantile normalization
Wang	2010	[272]	China	CC	PAT	microarray	12	RNU6-1
Huang	2011	[273]	Shangai	CRC	PAT	microarray	26	RNU6-1
Fu	2012	[274]	China	CRC	PAT	microarray	16	quantile scaling algorithm
Hamfjord	2012	[275]	Norway	CAD	PAT	sequencing	24	SNORD48
Chen	2012	[276]	China	CRC	PAT	array	32	RNU6-6P
Li	2012	[277]	China	RC	PAT	miRNA chip	65	RNU6-6P
Mosakhani	2012	[278]	Finland	CRC	NT	microarray	7	RNU6-1
Nishida	2012	[279]	Japan	CRC	NT	microarray	127	LOWESS method
Pizzini	2013	[3]	Italy	CRC	PAT	microarray	29	SNORD44
Chen	2013	[280]	Taiwan	CRC	PAT	array	5	RNU6-1
Ak	2014	[281]	Turkey	CRC	NT	qPCR	1	SNORD 44, SNORD47, SNORD 48
Li	2014	[282]	USA	CRC	PAT	microarray	49	miR-191
Fukushima	2015	[283]	Japan	CRC	PAT	array	5	RNU6-1
Mo	2015	[284]	Korea	CRC	PAT	microarray	29	SNORD48, RNA5-8S5
Peng	2015	[285]	China	CRC	PAT	qPCR	12	RNU6-1
Rotelli	2015	[114]	Italy	CRC	NT	qPCR	11	RNU6-6P, miR-16-3p
Tanoglu	2015	[286]	Turkey	CC	PAT	qPCR	4	RNU6-6P
Vishnubalaji	2015	[2]	Saudi Arabia	CC	PAT	microarray	42	SNORD44, SNORD48
Wu	2015	[287]	China	CRC	PAT	qPCR	3	RNU6-6P, SNORD44, SNORD48, SNORD49A
Neerincx	2015	[288]	Netherlands	CRC	NT	NGS	121	edgeRs TMM method
Meng	2015	[289]	China	CRC	PAT	array	11	NS
Kara	2015	[290]	Turkey	CRC	NT	array	19	SNORD61, SNORD68, SNORD72, SNORD95
Chen	2015	[263]	China	CRC	PAT	qPCR	4	RNU6-6P
Ozcan	2016	[291]	Turkey	CRC	NT	array	20	SNORD61, SNORD68, SNORD96A, RNU6-2
Pelossof	2016	[292]	USA	RC	PAT	sequencing	39	Quantile normalization
Sun	2016	[293]	USA	CRC	PAT	sequencing	12	SNORD47
Zekri	2016	[294]	Egypt	CRC	NT	qPCR	4	SNORD68
Li	2017	[295]	China	CRC	PAT	miRNA microarray	17	RNU-6
Nagy	2017	[296]	Hungary	CRC	NT	microarray	6	Hsa-miR-423-5
Wu	2017	[297]	-	CAD	NT	sequencing	99	Log10

Du	2018	[298]	China	CRC	PAT	miRNA array	182	RMA algorithm
Pellatt	2018	[299]	USA	CRC	PAT	microarray	36	Scaling factor based on median expression
Slattery	2018	[140]	USA	CRC	NT	microarray	22	Scaling factor based on median expression
Wu	2018	[255]	USA	CRC	NT	miRNA sequencing	34	Localized smoothing algorithm
Zhang	2018	[300]	China	CRC	PAT	miRNA microarray	1	NS
Brînzan	2019	[301]	Romania	CAD	PAT	qPCR	5	miR-26b, miR-92N
Li	2019	[302]	China	CRC, CAD	NT	miRNA sequencing	34	NS
Zhang	2019	[303]	China	CRC	NT	qPCR	4	RNU6-6P
Gungormez	2019	[304]	Turkey	CC	PAT	array	3	NS
Hao	2019	[305]	China, Italy, USA	CRC	PAT	miRNA array	8	RNU6-1
Duran-Sanchon	2020	[119]	Spain	CRC	PAT	NGS	21	Cyclic-loess method
Wei	2020	[306]	China	CC, RC	PAT	miRNA microarray	4	RNU6-1
Milanesi	2020	[307]	Romania	CRC	NT	array	1	SNORD61, SNORD95, SNORD96A
Zhou	2020	[308]	China	CRC	NT	qPCR	226	RNU6-1

Tumour type – CRC (colorectal cancer); CAD (colorectal adenocarcinoma); RC (rectal cancer). miRNA expression in tumour in referred studies was compared to paired adjacent tissue (PAT) or to normal tissue (NT). Method of analysis – NGS – next gene sequencing; qPCR - quantitative real-time PCR. Normalization – NS – not specified; RNA5-8S5 - RNA, 5.8S ribosomal 5; RNU6-1 - RNA, U6 small nuclear 1; RNU6-2 - RNA, U6 small nuclear 2; RNU6-6P - RNA, U6 small nuclear 6, pseudogene; SNORD44 - small nucleolar RNA, C/D box 44; SNORD47 - small nucleolar RNA, C/D box 47; SNORD48 - small nucleolar RNA, C/D box 48; SNORD49A - small nucleolar RNA, C/D box 49A; SNORD61 - small nucleolar RNA, C/D box 61; SNORD68 - small nucleolar RNA, C/D box 68; SNORD72 - small nucleolar RNA, C/D box 72; SNORD95 - small nucleolar RNA, C/D box 95; SNORD96A - small nucleolar RNA, C/D box 96A. Ref. – reference.

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Supplementary material S2: Up- or down-regulation of the analysed miRNA clusters levels in tumour tissue and circulation of patients with CRC

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Cluster	miRNA	Expression in tumour tissue	Levels in serum	Levels in plasma
<i>miR-106a/18b/20b/19b-2/92a-2/363</i>	miR-106a	↑ [3,96,277,281,284,286,293,298,308–311,97,312,114, 130,131,134,158,255,271]	↑ [104,312] ↓ [313]	↑ [133]
	miR-18b	↑ [2,3,298,309,314,270,272,273,277,279,282,295,296]		↑ [303] ↓ [314]
	miR-20b	↑ [2,3,140,279,284,299,309] ↓ [208,276,308,315]		↑ [316]
	miR-19b	↑ [114,115,292,299,302,308,317,140,158,255,271,274, 282,284,288] ↓ [318]		
	miR-92a	↑ [97,114,270,277,279,282,288,289,292,298,299,308, 115,319–321,119,138–140,158,202,255] ↓ [318]	↑ [129,136,154,322,323] ↓ [324]	↑ [99,325,326]
	miR-363	↓ [144,275,276,282,308,327]	↓ [328]	
<i>miR-106b/93/25</i>	miR-106b	↑ [2,3,284,288,292,298,299,302,308,329,330,97,119, 255,271,272,274,277,279] ↓ [234,288,308,331,332]	↑ [330]	↑ [325]
	miR-93	↑ [140,202,308,333,271,274,279,282,284,288,289,298] ↓ [81,145,147,222]	↓ [324]	
	miR-25	↑ [3,119,282,284,288,298,299,308,334,335,140,148, 149,202,271,274,277,279] ↓ [336]	↑ [335,337] ↓ [324]	
<i>miR-17/18a/19a/20a/19b-1/92a-1</i>	miR-17	↑ [2,3,270,271,273,274,276,277,279,282,284,288,97, 289,290,292–294,298,299,303,308,309,114,314,334,338, 339,115,119,140,158,202,255,263] ↓ [3,318]	↑ [104,294]	↑ [97,303,326] ↓ [314]
	miR-18a	↑ [2,3,270–273,277,279,280,282,288,292,57,296,298,302, 303,309,323,338,97,114,115,117,119,153,255,305] ↓ [318,340]	↑ [323]	↑ [303,325]
	miR-19a	↑ [2,3,277,279,284,288,291,292,294,302,308,309,114, 341–343,115,132,255,271–274] ↓ [318]	↑ [154,294,322,344–347]	
	miR-20a	↑ [2,3,140,155,158,270,272–274,277,279,282,29,284, 288,289,291,292,299,308,309,314,323,65,338,348–351, 97,114,115,119,130,134,305,263] ↓ [318]	↑ [294,323,344,350] ↓ [352]	↑ [133,185,325,348] ↓ [314]
	miR-19b	↑ [2,114,299,302,308,317,115,140,158,255,274,279, 284,292] ↓ [318]	↑ [104]	

	miR-92a	↑ [3,97,255,270,277,279,282,288,289,292,298,299,114, 308,319–321,115,119,138–140,158,202] ↓ [318]	↑ [129,136,154,322,323, 353] ↓ [324,354]	↑ [97,99,325,326]
<i>miR-181a-1/181b-1</i>	miR-181a	↑ [29,158–160,279,291,308,355] ↓ [42,82]	↑ [104]	↑ [303]
<i>miR-181a-2/181b-2</i>	miR-181b	↑ [134,171,271,279,291,298,308,356] ↓ [357]	↑ [358] ↓ [354]	↑ [97]
<i>miR-181c/181d</i>	miR-181c	↑ [279,282,284,288,289,291]		↑ [97]
	miR-181d	↑ [3,34,298,359,158,161,270,277,279,288,291,292]		↑ [97]
<i>miR-183/ 96/182</i>	miR-183	↑ [2,3,276,277,279,282,288,291,292,301,302,360,158, 361,362,162,164,202,255,270,271,273,305,263]		↑ [97]
	miR-96	↑ [2,119,276,277,280,282,283,287,288,290,292,308,158, 309,323,363,165,220,255,271,273–275]	↑ [323]	
	miR-182	↑ [2,3,271,273,276,277,282,285,287–289,292,29,293, 298,301,308,364,365,100,119,158,168,169,255,270] ↓ [366]	↑ [105]	↑ [100,185,367]
<i>miR-191/ 425</i>	miR-191	↑ [289,298,308,368,369]		
	miR-425	↑ [2,140,279,282,298,299,302,308,346,370]	↑ [337,346]	
<i>miR-200c/ 141</i>	miR-200c	↑ [158,171,373,172,173,177,255,291,308,371,372] ↓ [348,374–376]	↑ [104,373,377] ↓ [378]	↑ [97] ↓ [348]
	miR-141	↑ [114,177,379–381,255,277,282,285,289,301,308,371] ↓ [78,179,382]	↑ [377,383] ↓ [382]	
<i>miR-203a/203b</i>	miR-203	↑ [130,158,271,277,282]	↓ [354]	
	miR-203a	↑ [2,119,140,180,202,255,290,302,308,384] ↓ [58,181,238,385–387]	↑ [180,378]	↑ [97]
	miR-203b	↓ [72,308]	↓ [388]	
<i>miR-222/ 221</i>	miR-222	↑ [288–290,308] ↓ [376]		↑ [97,103]
	miR-221	↑ [2,97,292,299,302,308,117,119,140,198,273,276,279, 282]	↑ [389,390]	↑ [103]
<i>miR-23a/ 27a/ 24-2</i>	miR-23a	↑ [158,279,394,288,295,298,299,308,391–393]	↑ [358] ↓ [391,395]	↑ [103]
	miR-27a	↑ [158,184,298,394,396,186,274,275,277,284,290,292, 295] ↓ [376,397]	↑ [124]	↑ [103]
	miR-24	↑ [119,158,277–279,292,299,308,394] ↓ [188,275,341]	↓ [398]	↓ [399,400]
<i>miR-29b-1/ 29a</i>	miR-29b	↑ [3,29,302,140,158,271,274,277,282,290,295] ↓ [64,101,189,376,401]	↓ [402]	↓ [101]
	miR-29a	↑ [192,271,277,284,290,292,323,403] ↓ [404]	↑ [323,345,405] ↓ [389]	↑ [99,325]
<i>miR-301b/ 130b</i>	miR-301b	↑ [272,275,288,308]		

	miR-130b	↑[2,119,308,406,194,271,279,282,285,292,298,299]	↑ [337]
<i>miR-452/ -224</i>	miR-452	↑ [158,195,255,276,277,279,284,288,308] ↓ [196]	↓ [388]
	miR-224	↑[2,3,273,274,279,282–284,288,292,293,298,97,305,308 ,323,407–409,197,198,233,255,270–272] ↓ [410]	↑ [104] ↓ [388]

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Supplementary material S3: Analysis of miRNA expression with clinicopathological characteristics.

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cluster	miRNA	advanced TNM stage	Presence of metastasis
<i>miR-106a/18b/20b/19b-2/92a-2/363</i>	miR-106a		↑ TU [411]
	miR-18b		↑ TU [295]
	miR-363	↓ S [328]	↓ S [328] ↓ TU [144,327]
<i>miR-106b/93/25</i>	miR-106b	↑ S [330]	↓ TU [74,234,332]
	miR-93		↑ TU [145]
	miR-25	↑ TU [148]	↑ TU [148]; S [335,337]
<i>miR-17/18a/19a/20a/19b-1/92a-1</i>	miR-17		↑ M [412]; P [326]; TU [321] ↓ TU [413]
	miR-18a		↑ S [390]
	miR-19a	↑ S [344]; TU [342]	↑ TU [236,342] S [343,344] ↓ P [414]
	miR-20a	↑ S [344]; TU [415]	↑ S [344]; TU [155,415]
	miR-19b		↑ M [156]; TU [317]
	miR-92a	↑ TU [137,138] ↑ S [353]	↑ TU [137,139,279,319,321,416]; P [326]; S [319,353]
	<i>miR-181a-1/181b-1</i> <i>miR-181a-2/181b-2</i>	miR-181a	↑ TU [159]
<i>miR-181c/181d</i>	miR-181d		↑ TU [34]
<i>miR-183/96/182</i>	miR-183	↑ TU [162,370]; P [360]	↑ TU [162]; P [360]
	miR-96	↑ TU [165]	↑ TU [165]
	miR-182	↑ TU [169,196,301]	↑ TU [168,169,176]
<i>miR-191/425</i>	miR-191	↑ TU [417]	↑ TU [417] ↓ TU [170]
	miR-425		↑ S [337]
<i>miR-200c/141</i>	miR-200c	↑ TU [177,373]; S [173] ↓ TU [418]	↑ TU [173,373,419]; S [173,371] ↓ TU [176,418,420]
	miR-141	↑ TU [177]; P [166,178] ↓ TU [179]	↑ TU [36]; S [371,421] ↓ TU [179]
<i>miR-203a/203b</i>	miR-203a	↑ S [180] ↓ TU [422]	↑ S [180] ↓ TU [181,386]
	miR-221	↓ TU [182]	↓ TU [182]
<i>miR-23a/27a/24-2</i>	miR-23a	↑ BL [391]	
	miR-27a	↑ TU [186]	↑ TU [183,184,423]; P [185]
	miR-24	↓ TU [188,341]	↓ TU [188,341]
<i>miR-29b/ 29a</i>	miR-29b	↓ S [402]	
	miR-29a	↑ S [424] ↓ TU [64]	↑ TU [190,425] ↑ S [190] ↓ TU [64,176,401]

<i>miR-301b/ 130b</i>	miR-130b		↑ TU [194]
	miR-224	↓ TU [182]	↑ LM [407,409]; TU [198,408] ↓ LNM [409]; TU [182]

↑ depicts increased expression/levels associated with advanced TNM stage or metastasis, respectively ↓ decreased expression/levels.
 Source for measurement of miRNA expression is bolded – TU (tumor tissue); P (plasma); S (serum); LM (liver metastasis); BL (blood); LNM (lymph node metastases); M - metastasis

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Supplementary material S4: Alphabetical list of target genes of up-regulated miRNA clusters.

Gene symbol	Gene name	Function	miRNA	Cluster	Reference
ABCA1	ATP binding cassette subfamily A member 1	TS	miR-183-5p	miR-183/96/182	[426]
ABCF1	ATP-binding cassette, subfamily F, member 1	TS	miR-23a-3p	miR-23a/27a/24-2	[427]
ADAM9	ADAM metalloproteinase domain 9	O	miR-20b-5p	miR-106a/363	[208]
AFDN	Afadin, Adherens junction formation factor	TS	miR-183-3p	miR-183/96/182	[428]
AGER	Advanced glycosylation end-product specific receptor	TS	miR-182	miR-183/96/182	[48]
AKAP12	A kinase anchor protein 12	TS	miR-183-5p	miR-183/96/182	[370]
AKT2	AKT serine/threonine kinase 2	O	miR-203a-3p	miR-203a/203b	[429]
AMER1	APC membrane recruitment protein 1	TS	miR-20a	miR-17/92a-1	[310]
			miR-106a-5p	miR-106a/363	[310]
ANGPTL8	Angiopoietin like 8	O	miR-25	miR-106b/25/93	[430]
APAF1	Apoptotic peptidase activating factor 1	TS	miR-23a-3p	miR-23a/27a/24-2	[392]
AQP8	Aquaporin 8	TS	miR-92a-5p	miR-106a/363 miR-17/92a-1	[431]
ARID4B	AT-rich interaction domain 4B	TS	miR-93-3p	miR-106b/25/93	[55]
ATG12	Autophagy related 12	O	miR-93-5p	miR-106b/25/93	[66]
ATG16L1	Autophagy Related 16 Like 1	TS	miR-106b-5p	miR-106b/25/93	[432]
			miR-93-5p		
ATG5	Autophagy related 5	TS	miR-20a-5p	miR-17/92a-1	[433]
			miR-183-5p	miR-183/96/182	[164]
ATG7	Autophagy related 7	TS	miR-106a-5p	miR-106a/363	[131]
ATM	ATM serine/threonine kinase	TS	miR-18a-5p	miR-17/92a-1	[153]
			miR-203a-3p	miR-203a/203b	[232]
ATXN3	Ataxin 3	TS	miR-25-3p	miR-106b/25/93	[149]
BCL2L1	BCL2 like 1	O	miR-203b-3p	miR-203a/203b	[72]
BCL2L11	BCL2 like 11	TS	miR-92a-3p	miR-106a/363	[434]
				miR-17/92a-1	
BCL9L	BCL9 like	O	miR-29b-3p	miR-29b-1/29a	[435]
BID	BH3 interacting domain death agonist	TS	miR-20a-5p	miR-17/92a-1	[350]
BMI1	BMI1 proto-oncogene, polycomb ring finger	O	miR-200c-3p	miR-200c/141	[241]
BNIP2	BCL2 interacting protein 2	TS	miR-20a-5p	miR-17/92a-1	[436]
BTG1	BTG anti-proliferation factor 1	TS	miR-27a-3p	miR-23a/27a/24-2	[437]
BTG3	BTG anti-proliferation factor 3	TS	miR-17-5p	miR-17/92a-1	[68]
CEBPB	CCAAT enhancer binding protein beta	TS	miR-191-5p	miR-191/425	[369]

CALR	Calreticulin	TS	miR-27a-3p	miR-23a/27a/24-2	[438]
			miR-93-5p	miR-106b/25/93	[222]
CCND1	Cyclin D1	O	miR-18a-5p	miR-17/92a-1	[224]
			miR-96-5p	miR-183/96/182	[167]
CCND2	Cyclin D2	O	miR-141-3p	miR-200c/141	[375]
CD274	CD274 molecule	O	miR-93-5p	miR-106b/25/93	[147]
CDC42	Cell division cycle 42	O	miR-18a-5p	miR-17/92a-1	[224]
CDH1	Cadherin 1	TS	miR-224-5p	miR-452/224	[198]
CDK19	Cyclin dependent kinase 19	O	miR-18a-5p	miR-17/92a-1	[439]
CDK2	Cyclin Dependent Kinase 2	O	miR-200c-3p	miR-200c/141	[43]
			miR-106b-5p	miR-106b/25/93	[234]
CDKN1A	Cyclin dependent kinase inhibitor 1A	TS	miR-20a-5p	miR-17/92a-1	[235]
			miR-224-5p	miR-452/224	[233]
CDKN2B	Cyclin dependent kinase inhibitor 2B	TS	miR-18b-5p	miR-106a/363	[295]
CDS2	CDP-diacylglycerol synthase 2	O	miR-224-5p	miR-452/224	[440]
CLU	Clusterin	TS	miR-17	miR-17/92a-1	[33]
CPEB4	Cytoplasmic polyadenylation element-binding 4	O	miR-203a-3p	miR-203a/203b	[226]
CREB1	cAMP responsive element binding protein 1	O	miR-203a-3p	miR-203a/203b	[54]
CRY2	Cryptochrome circadian regulator 2	TS	miR-181d-5p	miR-181c/181d	[34]
CSE1L	Chromosomal segregation 1 like	O	miR-203a-3p	miR-203a/203b	[49]
			miR-93-5p	miR-106b/25/93	[222]
CTNNB1	Catenin Beta 1	O	miR-181a-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[56]
			miR-203a-3p	miR-203a/203b	[67]
			miR-24-5p	miR-23a/27a/24-2	[441]
CTNND1	Catenin delta 1	TS	miR-425-5p	miR-191/425	[442]
CTSA	Cathepsin A	O	miR-106b-5p	miR-106b/25/93	[332]
CXCL8	C-X-C motif chemokine ligand 8	O	miR-20a-5p	miR-17/92a-1	[443]
CYP7B1	Cytochrome P450, family 7, subfamily B, member 1	O	miR-17-5p	miR-17/92a-1	[368]
DAB2IP	DAB2 interacting protein	TS	miR-182-5p	miR-183/96/182	[105]
DHFR	Dihydrofolate reductase	O	miR-24-3p	miR-23a/27a/24-2	[444]
DKK3	Dickkopf WNT signalling pathway inhibitor 3	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[210]
			miR-106b-5p	miR-106b/25/93	[329,330]
DLC1	DLC1 Rho GTPase activating protein	TS	miR-106b-3p	miR-106b/25/93	[329,330]
			miR-141-3p	miR-200c/141	[381]
DND1	DND microRNA-mediated repression inhibitor 1	O	miR-24-3p	miR-23a/27a/24-2	[445]
DNMT3B	DNA methyltransferase 3 beta	O	miR-203a-3p	miR-203a/203b	[385]

DUSP2	Dual-specificity phosphatase 2	TS	miR-106a-5p	miR-106a/363	[311]
E2F5	E2F transcription factor 5	O	miR-181a-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[446]
EGFR	Epidermal growth factor receptor	O	miR-141-3p	miR-200c/141	[447]]
EIF5A2	Eukaryotic initiation factor 5A2	O	miR-203a-3p	miR-203a/203b	[181]
ETS1	ETS proto-oncogene 1, transcription Factor	O	miR-200c-3p	miR-200c/141	[36]
EZH2	Enhancer of zeste 2 polycomb repressive complex 2 subunit	O	miR-363-3p	miR-106a/363	[73]]
F2RL3	F2R like thrombin or trypsin receptor 3	TS	miR-17-3p	miR-17/92a-1	[339]
FAM172A	Family with sequence similarity 172 member A	TS	miR-27a-3p	miR-23a/27a/24-2	[186]
FBXL3	F-box and leucine rich repeat protein 3	TS	miR-181d-5p	miR-181c/181d	[34]
FBXW7	F-Box and WD repeat domain containing 7	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[319]
			miR-182-5p	miR-183/96/182	[448]
FLT1	Fms related receptor tyrosine kinase 1	O	miR-200c-3p	miR-200c/141	[36]
FOXA1	Forkhead box A1	TS	miR-93-5p	miR-106b/25/93	[333]]
FOXF2	Forkhead box F2	TS	miR-19a-3p	miR-17/92a-1	[347]
			miR-182-5p	miR-183/96/182	[449]
FOXJ2	Forkhead Box J2	O	miR-20a-5p	miR-17/92a-1	[450]
FOXO1	Forkhead box protein O1	TS	miR-96-5p miR-182-5p	miR-183/96/182	[220]
FOXO3a	Forkhead box protein O3a	TS	miR-96-5p miR-182-5p	miR-183/96/182	[62,220]
FOXQ1	Forkhead box Q1	O	miR-106a-5p	miR-106a/363	[451]
GABBR1	Gamma-amino-butyric acid type B receptor 1	TS	miR-106a-5p miR-20b-5p	miR-106a/363	[452]
			miR-106b-5p	miR-106b/25/93	[452]
			miR-20a-5p miR-17-5p	miR-17/92a-1	[452]
GATA6	GATA Binding Protein 6	O	mi-363-3p	miR-106a/363	[38]
			miR-203a-3p	miR-203a/203b	[453]
GEMIN2	Gem nuclear organelle associated protein 2	O	miR-141-3p	miR-200c/141	[454]
GPC1	Glypican-1	O	miR-96-5p	miR-183/96/182	[262]
GRN	Granulin precursor	O	miR-29b-3p	miR-29b-1/29a	[64]
GSK3B	Glycogen synthase kinase 3 beta	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[210]
			miR-452-3p miR-224-5p	miR-452/224	[195,221]
HIF1A	Hypoxia inducible factor 1 subunit alpha	O	miR-93-5p	miR-106b/25/93	[81]
			miR-18a-5p	miR-17/92a-1	[230]
HNRNPA1	Heterogeneous nuclear ribonucleoprotein	O	miR-18a-5p	miR-17/92a-1	[455]

A1					
ING4	Inhibitor of growth family member 4	TS	miR-18a-5p	miR-17/92a-1	[60]
ITGA5	Integrin subunit alpha 5	O	miR-130b-3p	miR-301b/130b	[406]
ITGB1	Integrin subunit beta 1	O	miR-130b-3p	miR-301b/130b	[456]
ITGB8	Integrin subunit beta 8	O	miR-106b-5p	miR-106b/25/93	[53]
KIF14	Kinesin family member 14	O	miR-200c-3p	miR-200c/141	[457]
KLF4	Krüppel like factor 4	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[210]
			miR-29a-3p	miR-29b-1/29a	[190]
KLK6	Kallikrein related peptidase 6	O	miR-203a-3p	miR-203a/203b	[458]
KRAS	KRAS proto-oncogene, GTPase	O	miR-19a-3p	miR-17/92a-1	[229]
			miR-96-5p	miR-183/96/182	[167]
LGALS1	Galectin like	O	miR-224-5p	miR-452/224	[440]
MAP2K4	Mitogen-activated protein kinase kinase 4	TS	miR-141-3p	miR-200c/141	[380]
MAP3K5	Mitogen-activated protein kinase kinase 5	TS	miR-20a-5p	miR-17/92a-1	[459]
MAP4K4	Mitogen-activated protein kinase kinase 4	O	miR-141-3p	miR-200c/141	[460]
MARK1	Microtubule affinity regulating kinase 1	TS	miR-23a-3p	miR-23a/27a/24-2	[393]
MBD2	Methyl-CpG binding domain protein 2	O	miR-221-5p	miR-221/222	[182]
			miR-224-5p	miR-452/224	[182]
MCU	Mitochondrial calcium uniporter	TS	miR-25-3p	miR-106b/25/93	[334]
MICA	MHC class I polypeptide-related sequence A	TS	miR-20a-5p	miR-17/92a-1	[461]
MMP14	Matrix metalloproteinase 14	O	miR-181a-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[462]
MMP2	Matrix metalloproteinase 2	O	miR-29a-3p	miR-29b-1/29a	[245]
MOAP1	Modulator of apoptosis 1	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[319]
MTDH	Metadherin	O	miR-182-5p	miR-183/96/182	[366]
MYC	MYC proto-oncogene, bHLH transcription factor	O	miR-93-5p	miR-106b/25/93	[222]
			miR-182-5p	miR-183/96/182	[223]
NCOA3	Nuclear receptor coactivator 3	TS	miR-17-5p	miR-17/92a-1	[33]
NEDD9	Neural precursor cell expressed, developmentally down-regulated 9	O	miR-25-5p	miR-106b/25/93	[463]
			miR-18a-5p	miR-17/92a-1	[439]
			miR-203a-3p	miR-203a/203b	[464]
NF2	Neurofibromin 2	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[465]
PDCD10	Programmed cell death 10	TS	miR-425-5p	miR-191/425	[466]
			miR-20a-5p	miR-17/92a-1	[65]
PDCD4	Programmed cell death 4	TS	miR-181b-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[356]

			miR-141-3p	miR-200c/141	[76]
PDE4D	Phosphodiesterase 4D	TS	miR-203a-3p	miR-203a/203b	[384]
PDK4	Pyruvate dehydrogenase kinase 4	TS	miR-23a-3p	miR-23a/27a/24-2	[467]
PEAK1	Pseudopodium enriched atypical kinase 1	O	miR-181d-5p	miR-181c/181d	[161]
PHLPP1	PH domain leucine-rich-repeat protein phosphatase 1	TS	miR-224-5p	miR-452/224	[409]
PHLPP2	PH domain leucine-rich-repeat protein phosphatase 2	TS	miR-224-5p	miR-452/224	[409]
			miR-18a-5p	miR-17/92a-1	[468]
PIAS3	Protein inhibitor of activated STAT 3	TS	miR-181b-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[469]
PLAG1	PLAG1 Zinc Finger	O	miR-181a-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[470]
PLK3	Polo like kinase 3	TS	miR-106b-5p	miR-106b/25/93	[471]
POU5F1	POU Class 5 Homeobox 1	O	miR-20b-5p	miR-106a/363	[75]
PRICKLE2	Prickle planar cell polarity protein 2 EPM5	O	miR-200c-5p	miR-200c/141	[472]
PRKCZ	Protein kinase C zeta	O	miR-25-5p	miR-106b/25/93	[473]
PRRX1	Paired related homeobox 1	TS	miR-106b-5p	miR-106b/25/93	[234]
			miR-106a-3p	miR-106a/363	[474]
			miR-106b-5p miR-93-5p	miR-106b/25/93	[50,234]
PTEN	Phosphatase and tensin homolog	TS	miR-19a-3p miR-17-5p miR-92a-3p	miR-17/92a-1 miR-106a/363	[151,416, 475]
			miR-181a-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[355]
			miR-29a-3p	miR-29b-1/29a	[476]
RASSF1	Ras association domain family member 1	O	miR-181b-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[357]
RB1CC1	RB1 inducible coiled-coil 1	TS	miR-20a-5p	miR-17/92a-1	[433]
RBL2	RB transcriptional corepressor like 2	TS	miR-17-5p	miR-17/92a-1	[150]
RBM4	RNA binding motif protein 4	TS	miR-92a-2-3 p	miR-106a/363 miR-17/92a-1	[320]
RCN2	Reticulocalbin 2	TS	miR-183-5p	miR-183/96/182	[362]
RECK	Reversion inducing cysteine rich protein with kazal motifs	TS	miR-92a-3p	miR-106a/363 miR-17/92a-1	[138]
			miR-96-3p	miR-183/96/182	[477]
RND3	Rho Family GTPase 3	TS	miR-17-5p	miR-17/92a-1	[338]
RNF6	RING finger protein 6	O	miR-203a-3p	miR-203a/203b	[422]
ROBO1	Roundabout guidance receptor 1	O	miR-203a-3p	miR-203a/203b	[478]
RPS15A	Ribosomal protein S15A	O	miR-29a-3p	miR-29b-1/29a	[404]
RXRA	Retinoid X receptor alpha	TS	miR-27a-3p	miR-23a/27a/24-2	[184]

SATB2	SATB homeobox 2	TS	miR-182-5p	miR-183/96/182	[364]
SEMA4C	Semaphorin 4C	O	miR-25-3p	miR-106b/25/93	[61]
SEMA6D	Semaphorin 6D	TS	miR-23a-5p	miR-23a/27a/24-2	[479]
SFRP1	Secreted frizzled related protein 1	TS	miR-27a-3p	miR-23a/27a/24-2	[183]
SFRP2	Secreted frizzled related protein 2	TS	miR-224-5p	miR-452/224	[221]
SGPP1	Sphingosine-1-phosphate phosphatase 1	O	miR-27a-3p	miR-23a/27a/24-2	[480]
SIK1	Salt inducible kinase 1	TS	miR-17-5p	miR-17/92a-1	[152]
SIK2	Salt inducible kinase 2	O	miR-203a-3p	miR-203a/203b	[387]
SIRT1	Sirtuin 1	O	miR-141-3p	miR-200c/141	[78]
			miR-29b-3p	miR-29b-1/29a	[239]
SLAIN2	SLAIN motif family member 2	O	miR-106b-5p	miR-106b/25/93	[74]
SLC4A4	Solute carrier family 4 member 4	O	miR-224-5p	miR-452/224	[440]
SMAD2	SMAD family member 2	O	miR-27a-3p	miR-23a/27a/24-2	[480]
SMAD3	SMAD family member 3	TS	miR-29b-1-5p	miR-29b-1/29a	[481]
SMAD4	SMAD family member 4	TS	miR-18a-5p	miR-17/92a-1	[155,227,
			miR-19b-3p	miR-106a/363	228,415]
SMAD7	SMAD family member 7	TS	miR-224-5p	miR-452/224	[198,482]
			miR-92a-3p	miR-106a/363	[483]
SOX2	SRY-box transcription factor 2	O	miR-25-3p	miR-106b/25/93	[222,336]
			miR-93-5p		
SOX4	SRY-box transcription factor 4	O	miR-200c-3p	miR-200c/141	[418]
SOX9	SRY-box transcription factor 9	O	miR-363-3p	miR-106a/363	[327]
SPHK2	Sphingosine kinase 2	O	miR-18b-5p	miR-106a/363	[57]
SRCIN1	SRC kinase signalling inhibitor 1	O	miR-363-3p	miR-106a/363	[144]
			miR-181a-5p	miR-181a-1/181b-1	[484]
ST6GALNAC2	ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 2	TS	miR-181a-2/181b-2		
			miR-182-5p	miR-183/96/182	[365]
STAT1	Signal transducer and activator of transcription 1	TS	miR-181a-5p	miR-181a-1/181b-1	[485]
TBPL1	TATA box-binding protein-like protein 1	O	miR-181a-2/181b-2		
			miR-18a-5p	miR-17/92a-1	[340]
TCF4	Transcription factor 4	O	miR-181a-5p	miR-181a-1/181b-1	[56]
			miR-181a-2/181b-2		
TF	Tissue factor	O	miR-203a-3p	miR-203a/203b	[225]
			miR-19a-3p	miR-17/92a-1	[486]
TGFB2	Transforming growth factor beta receptor 2	TS	miR-106a-5p	miR-106a/363	[209,411]
			miR-17-5p	miR-17/92a-1	[228,230]
		O	miR-20-5p		

				miR-19a-3p		
TGM2	Transglutaminase 2	TS	miR-19a-3p	miR-17/92a-1	[487]	
THBS1	Thrombospondin 1	TS	miR-182-5p	miR-183/96/182	[237]	
			miR-19a-3p	miR-17/92a-1	[236]	
THBS2	Thrombospondin 2	O	miR-203a-3p	miR-203a/203b	[238]	
TIA1	TIA1 cytotoxic granule associated RNA binding protein	TS	miR-19a-3p	miR-17/92a-1	[488]	
TIAM1	TIAM Rac1 associated GEF 1	O	miR-29b-3p	miR-29b-1/29a	[401]	
TIMP3	TIMP metalloproteinase inhibitor 3	TS	miR-191-5p	miR-191/425	[417]	
TLE5	TLE family member 5, transcriptional modulator	O	miR-203a-3p	miR-203a/203b	[67]	
TNFAIP3	TNF alpha induced protein 3	TS	miR-19a-3p	miR-17/92a-1	[343]	
		O	miR-29a-3p	miR-29b-1/29a	[69]	
TP53	Tumor protein P53	TS	miR-27a-3p	miR-23a/27a/24-2	[396]	
TP53INP1	Tumor protein p53 inducible nuclear protein 1	TS	miR-96-5p	miR-183/96/182	[220]	
TPM1	Tropomyosin 1	TS	miR-96-5p	miR-183/96/182	[363]	
TRAF5	TNF receptor associated factor 5	O	miR-141-3p	miR-200c/141	[179]	
TRIM8	Tripartite motif containing 8	TS	miR-106b-5p	miR-106b/25/93	[489]	
		TS	miR-17-5p	miR-17/92a-1	[489]	
TUSC3	Tumor suppressor candidate 3	O	miR-181b-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[41]	
TYMS	Thymidylate synthetase	O	miR-203a-3p	miR-203a/203b	[490]	
USP3	Ubiquitin specific peptidase 3	TS	miR-224-5p	miR-452/224	[482]	
UVRAG	UV radiation resistance associated	TS	miR-183-5p	miR-183/96/182	[361]	
VANGL	VANGL planar cell polarity protein 1	O	miR-27a-3p	miR-23a/27a/24-2	[491]	
VEGFA	Vascular endothelial growth factor A	O	miR-20a-5p	miR-17/92a-1	[230]	
VHL	von Hippel Lindau tumour suppressor	TS	miR-24-3p	miR-23a/27a/24-2	[394]	
VIM	Vimentin	O	miR-17-5p	miR-17/92a-1	[413]	
VLDLR	Very low-density lipoprotein receptor	TS	miR-200c-3p	miR-200c/141	[372]	
WIF1	WNT inhibitory factor 1	TS	miR-181a-5p	miR-181a-1/181b-1 miR-181a-2/181b-2	[160]	
ZEB1	Zinc finger E-box binding homeobox 1	O	miR-200c-3p miR-141-3p	miR-200c/141	[36,47]	

Function of genes in human CRC cell lines was described according referred study, tumour suppressor function was abbreviated as TS and genes with oncogenic function were abbreviated as O.

<i>Supplementary material S5: List of abbreviated lncRNA and circRNA genes</i>	26
ACVRL1	27
AGER	28
BANCR	29
CA3-AS1	30
CCAT1	31
CDK6	32
CRNDE	33
DUSP2	34
FARSA-AS1	35
FBXL19-AS1	36
FBXW7	37
FENDRR	38
FOXD2-AS1	39
GAS5	40
H19	41
HAND2-AS1	42
HOTAIR	43
HOTAIRM1	44
LIFR-AS1	45
LINC00858	46
LINC01567	47
LINC02595	48
LINC-PINT	49
lncRNA ATB	50
MALAT1	51
MEG3	52
NORAD	53
POLR2J4	54
SMARCA5	55
SNHG15	56
UCA1	57
XIRP2-AS1	58
XIST	59
ZEB1-AS1	60
	61
	62
	63
	64

<i>Supplementary material S6: List of abbreviated target genes of selected miRNA clusters</i>	65
ABCA1	66
ABCF1	67
ADAM9	68
AFDN	69
AGER	70
AKAP12	71
AKT2	72
AMER1	73
ANGPTL8	74
APAF1	75
AQP8	76
ARID4	77
ATG12	78
ATG16L1	79
ATG5	80
ATG7	81
ATM	82
ATXN3	83
BCL2L1	84
BCL2L11	85
BCL9L	86
BID	87
BMI1	88
BNIP2	89
BTG1	90
BTG3	91
CEBPB	92
CALR	93
CCND1	94
CCND2	95
CD274	96
CDC42	97
CDH1	98
CDK19	99
CDK2	100
CDKN1A	101

CDKN2B	Cyclin dependent kinase inhibitor 2B	102
CDS2	CDP-diacylglycerol synthase 2	103
CLU	Clusterin	104
CPEB4	Cytoplasmic polyadenylation element-binding 4	105
CREB1	cAMP responsive element binding protein 1	106
CRY2	Cryptochrome circadian regulator 2	107
CSE1L	Chromosomal segregation 1 like	108
CTNNB1	Catenin Beta 1	109
CTNND1	Catenin delta 1	110
CTSA	Cathepsin A	111
CXCL8	C-X-C motif chemokine ligand 8	112
CYP7B1	Cytochrome P450, family 7, subfamily B, member 1	113
DAB2IP	DAB2 interacting protein	114
DHFR	Dihydrofolate reductase	115
DKK3	Dickkopf WNT signalling pathway inhibitor 3	116
DLC1	DLC1 Rho GTPase activating protein	117
DND1	DND microRNA-mediated repression inhibitor 1	118
DNMT3B	DNA methyltransferase 3 beta	119
DUSP2	Dual-specificity phosphatase 2	120
E2F5	E2F transcription factor 5	121
EGFR	Epidermal growth factor receptor	122
EIF5A2	Eukaryotic initiation factor 5A2	123
ETS1	ETS proto-oncogene 1, transcription Factor	124
EZH2	Enhancer of zeste 2 polycomb repressive complex 2 subunit	125
F2RL3	F2R like thrombin or trypsin receptor 3	126
FAM172A	Family with sequence similarity 172 member A	127
FBXL3	F-box and leucine rich repeat protein 3	128
FBXW7	F-Box and WD repeat domain containing 7	129
FLT1	Fms related receptor tyrosine kinase 1	130
FOXA1	Forkhead box A1	131
FOXF2	Forkhead box F2	132
FOXJ2	Forkhead Box J2	133
FOXO1	Forkhead box protein O1	134
FOXO3a	Forkhead box protein O3a	135
FOXQ1	Forkhead box Q1	136
GABBR1	Gamma-amino-butyric acid type B receptor 1	137
GATA6	GATA Binding Protein 6	138
GEMIN2	Gem nuclear organelle associated protein 2	139

GPC1	Glypican-1	140
GRN	Granulin precursor	141
GSK3B	Glycogen synthase kinase 3 beta	142
HIF1A	Hypoxia inducible factor 1 subunit alpha	143
HNRNPA1	Heterogeneous nuclear ribonucleoprotein A1	144
ING4	Inhibitor of growth family member 4	145
ITGA5	Integrin subunit alpha 5	146
ITGB1	Integrin subunit beta 1	147
ITGB8	Integrin subunit beta 8	148
KIF14	Kinesin family member 14	149
KLF4	Krüppel like factor 4	150
KLK6	Kallikrein related peptidase 6	151
KRAS	KRAS proto-oncogene, GTPase	152
LGALS1	Galectin like	153
MAP2K4	Mitogen-activated protein kinase kinase 4	154
MAP3K5	Mitogen-activated protein kinase kinase kinase 5	155
MAP4K4	Mitogen-activated protein kinase kinase kinase kinase 4	156
MARK1	Microtubule affinity regulating kinase 1	157
MBD2	Methyl-CpG binding domain protein 2	158
MCU	Mitochondrial calcium uniporter	159
MICA	MHC class I polypeptide-related sequence A	160
MMP14	Matrix metalloproteinase 14	161
MMP2	Matrix metalloproteinase 2	162
MOAP1	Modulator of apoptosis 1	163
MTDH	Metadherin	164
MYC	MYC proto-oncogene, bHLH transcription factor	165
NCOA3	Nuclear receptor coactivator 3	166
NEDD9	Neural precursor cell expressed, developmentally down-regulated 9	167
NF2	Neurofibromin 2	168
PDCD10	Programmed cell death 10	169
PDCD4	Programmed cell death 4	170
PDE4D	Phosphodiesterase 4D	171
PDK4	Pyruvate dehydrogenase kinase 4	172
PEAK1	Pseudopodium enriched atypical kinase 1	173
PHLPP1	PH domain leucine-rich-repeat protein phosphatase 1	174
PHLPP2	PH domain leucine-rich-repeat protein phosphatase 2	175
PIAS3	Protein inhibitor of activated STAT 3	176
PLAG1	PLAG1 Zinc Finger	177

PLK3	Polo like kinase 3	178
POU5F1	POU Class 5 Homeobox 1	179
PRICKLE2	Prickle planar cell polarity protein 2 EPM5	180
PRKCZ	Protein kinase C zeta	181
PRRX1	Paired related homeobox 1	182
PTEN	Phosphatase and tensin homolog	183
RASSF1	Ras association domain family member 1	184
RB1CC1	RB1 inducible coiled-coil 1	185
RBL2	RB transcriptional corepressor like 2	186
RBM4	RNA binding motif protein 4	187
RCN2	Reticulocalbin 2	188
RECK	Reversion inducing cysteine rich protein with kazal motifs	189
RND3	Rho Family GTPase 3	190
RNF6	RING finger protein 6	191
ROBO1	Roundabout guidance receptor 1	192
RPS15A	Ribosomal protein S15A	193
RXRA	Retinoid X receptor alpha	194
SATB2	SATB homeobox 2	195
SEMA4C	Semaphorin 4C	196
SEMA6D	Semaphorin 6D	197
SFRP1	Secreted frizzled related protein 1	198
SFRP2	Secreted frizzled related protein 2	199
SGPP1	Sphingosine-1-phosphate phosphatase 1	200
SIK1	Salt inducible kinase 1	201
SIK2	Salt inducible kinase 2	202
SIRT1	Sirtuin 1	203
SLAIN2	SLAIN motif family member 2	204
SLC4A4	Solute carrier family 4 member 4	205
SMAD2	SMAD family member 2	206
SMAD3	SMAD family member 3	207
SMAD4	SMAD family member 4	208
SMAD7	SMAD family member 7	209
SOX2	SRY-box transcription factor 2	210
SOX4	SRY-box transcription factor 4	211
SOX9	SRY-box transcription factor 9	212
SPHK2	Sphingosine kinase 2	213
SRCIN1	SRC kinase signalling inhibitor 1	214
ST6GALNAC2	ST6 N-acetylgalactosaminide alpha-2,6-sialyltransferase 2	215

STAT1	Signal transducer and activator of transcription 1	216
TBPL1	TATA box-binding protein-like protein 1	217
TCF4	Transcription factor 4	218
TF	Tissue factor	219
TGFBR2	Transforming growth factor beta receptor 2	220
TGM2	Transglutaminase 2	221
THBS1	Thrombospondin 1	222
THBS2	Thrombospondin 2	223
TIA1	TIA1 cytotoxic granule associated RNA binding protein	224
TIAM1	TIAM Rac1 associated GEF 1	225
TIMP3	TIMP metalloproteinase inhibitor 3	226
TLE5	TLE family member 5, transcriptional modulator	227
TNFAIP3	TNF alpha induced protein 3	228
TP53	Tumor protein P53	229
TP53INP1	Tumor protein p53 inducible nuclear protein 1	230
TPM1	Tropomyosin 1	231
TRAF5	TNF receptor associated factor 5	232
TRIM8	Tripartite motif containing 8	233
TUSC3	Tumor suppressor candidate 3	234
TYMS	Thymidylate synthetase	235
USP3	Ubiquitin specific peptidase 3	236
UVRAG	UV radiation resistance associated	237
VANGL	VANGL planar cell polarity protein 1	238
VEGFA	Vascular endothelial growth factor A	239
VHL	von Hippel Lindau tumour suppressor	240
VIM	Vimentin	241
VLDLR	Very low-density lipoprotein receptor	242
WIF1	WNT inhibitory factor 1	243
ZEB1	Zinc finger E-box binding homeobox 1	244
ZNF217	Zinc finger protein 217	245
		246

Supplementary material S8: References cited in Supplemental materials, which were not cited in the main text

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