

Table S1: Characteristics of chosen miRNA.

miRN A	Biological Role	Targeted Genes	Correlation of Expression in CRC
Let7	tumor suppression	HMGA2, KRAS, c-MYC,	higher expression was associated with higher CRC-specific mortality
mir16	tumor suppression	cox-2, zyxin	low expression associated with poor survival of CRC patients
mir19	cell survival, proliferation, differentiation and angiogenesis	TG2	high expression associated with poorer survival
mir21	cellular proliferation and differentiation	PDCD4, NFIB, SPRY2	associated with poor survival and response to chemotherapy
mir23			Increased expression associated with liver metastasis
mir29	cell proliferation, cell cycle, cell senescence, differentiation, and apoptosis	CDK6, MCL1, BCR/ABL1	correlated with a poor prognosis in patients with CRC
mir34	tumor suppression	p53	increased expression associated with poor cancer-specific mortality
mir92	cell proliferation, suppress apoptosis of cancer cells, induce tumor angiogenesis	integrin α 5, E-cadherin, Bim	high expression in CRC patients was associated with poor survival
mir222		PTEN, p57Kip2, PDLIM2	correlated with liver metastasis, distant metastasis and shorter overall survival rate of patients with CRC
mir451	tumor suppression	MIF, IL6R, Ywhaz	downregulation correlated with cancer persistence or recurrence after surgery

Table S2. Characteristics of chosen primers (*all* Qiagen GmbH, Hilden, Germany).

miScript Primer Assay	miR Base	miRNA Sequence
Hs_miR-23a_2	MIMAT0000078	5'AUCACAUUGCCAGGGAUUUUCC
Hs_miR-451_1	MIMAT0001631	5'AAACCGUUACCAUUAUCUGAGUU
Hs_miR-34a*_1	MIMAT0004557	5'CAAUCAGCAAGUAUACUGCCCU
Ce_miR-39_1	MIMAT0000010	5'UCACCGGGUGUAAAUCAGCUUG
Hs_miR-92_1	MIMAT0000092	5'UAUUGCACUUGUCCCCGGCCUGU
Hs_miR-16_1	MIMAT0000069	5'UAGCAGCACGUAAAUAUUGGCG
Hs_miR-21_2	MIMAT0000076	5'UAGCUUAUCAGACUGAUGUUGA
Hs_let-7c_1	MIMAT0000064	5'UGAGGUAGUAGGUUGUAUGGUU
Hs_miR-222_2	MIMAT0000279	5'AGCUACAUCUGGCUACUGGGU
Hs_miR-19a_1	MIMAT0000073	5'UGUGCAAUUCUAUGC AAAACUGA
Hs_miR-29a_1	MIMAT0000086	5'UAGCACCAUCUGAAAUCGGUUA
Hs_SNORD43_11	MS00007476	5'CACAGATGATGAACTTATTGAC

Table S3. Median levels of Cel-miR-39 with standard deviations.

Cel-miR-39	Healthy	Adenoma	CRC
exosomes	15.23 \pm 2.14	13.46 \pm 3.17	13.89 \pm 1.87
serum	28.87 \pm 2.87	25.45 \pm 2.34	27.51 \pm 3.33

Table S4. Details of median-normalized miRNA values in the exosomal compartment, shown in Figure 2.

miRNA	Diagnosis	Patients	Outliers	min.	25% Quant.	Median	75% Quant.	Max	mean	Standard Deviation	Standard Error
Let7	healthy	26	0	-7.33	-4.19	-2.75	-1.51	-0.10	-2.87	1.67	0.33
	adenoma	19	1	-3.82	-2.33	-1.87	-0.88	0.59	-1.66	1.26	0.30
	CRC	22	1	-4.50	-2.50	-2.19	-1.34	-0.19	-2.01	1.03	0.22
mir16	healthy	26	0	-6.33	-3.81	-2.26	-0.93	0.78	-2.53	1.96	0.38
	adenoma	20	0	-6.41	-3.52	-2.69	-0.20	1.53	-1.90	2.23	0.50
	CRC	23	0	-4.79	-2.02	-1.56	-0.68	2.79	-1.36	1.48	0.31
mir19	healthy	26	0	-7.54	-5.63	-4.49	-3.57	-0.74	-4.44	1.85	0.36
	adenoma	20	0	-6.32	-4.70	-3.81	-2.37	0.01	-3.51	1.84	0.41
	CRC	23	0	-6.83	-4.71	-4.26	-2.80	0.62	-3.77	1.56	0.33
mir21	healthy	26	0	-8.27	-6.15	-5.02	-3.66	-0.85	-4.81	1.75	0.34
	adenoma	20	0	-8.52	-3.48	-2.75	-2.31	-0.69	-3.17	1.98	0.44
	CRC	23	0	-7.88	-6.25	-4.35	-2.34	0.73	-4.36	2.30	0.48
mir23	healthy	26	0	-7.44	-6.13	-4.44	-3.32	0.02	-4.39	2.12	0.42
	adenoma	20	0	-9.52	-3.36	-2.72	-1.36	0.34	-2.79	2.43	0.54
	CRC	23	0	-6.67	-4.29	-3.46	-2.42	1.49	-3.22	1.71	0.36
mir29	healthy	26	0	-6.24	-4.72	-3.54	-2.22	0.03	-3.36	1.78	0.35
	adenoma	19	1	-4.96	-2.48	-1.72	-1.08	0.91	-1.83	1.63	0.38
	CRC	23	0	-5.03	-3.51	-2.88	-1.61	1.84	-2.52	1.50	0.31
mir34	healthy	26	0	-7.19	-5.86	-5.33	-3.78	-1.22	-4.73	1.67	0.33
	adenoma	20	0	-8.54	-4.69	-3.85	-2.77	0.94	-3.94	2.30	0.51
	CRC	22	1	-7.11	-5.64	-4.84	-3.23	-1.10	-4.60	1.60	0.35
mir92	healthy	26	0	-7.42	-5.09	-3.80	-2.47	-0.09	-3.67	1.81	0.35
	adenoma	20	0	-8.02	-3.57	-2.71	-1.14	1.54	-2.60	2.29	0.51
	CRC	23	0	-5.48	-3.91	-3.07	-1.57	2.01	-2.72	1.69	0.35
mir222	healthy	26	0	-7.34	-5.95	-5.01	-4.10	-1.09	-4.77	1.66	0.33
	adenoma	20	0	-8.06	-4.04	-3.04	-2.29	-0.38	-3.29	1.93	0.43
	CRC	23	0	-6.87	-5.13	-4.58	-2.85	0.66	-3.99	1.67	0.35
mir451	healthy	26	0	-5.79	-3.15	-2.49	-1.06	0.92	-2.23	1.73	0.34
	adenoma	20	0	-7.06	-3.46	-2.79	0.45	1.78	-1.82	2.34	0.52
	CRC	23	0	-4.01	-2.27	-1.90	-0.40	2.98	-1.37	1.55	0.32

Table S5. Areas under the curve (AUC) and sensitivities (SN) at 95% specificity (SP) for the different miRNAs in the exosomal compartment. Comparisons of healthy and non-healthy (adenoma or CRC) patients were made. p -value of Let7 = 0.009, of mir16 = 0.061 and of mir23 = 0.012.

miRNA	Healthy vs. Non-Healthy (Adenoma or CRC)	
	AUC	SN@95%SP
Let7	0.67	38.5%
mir16	0.62	23.1%
mir19	0.61	23.1%
mir21	0.65	3.8%
mir23	0.69	34.6%
mir29	0.68	26.9%
mir34	0.59	3.8%
mir92	0.65	11.5%
mir222	0.68	15.4%
mir451	0.59	23.1%

Table S6. Median-normalized miRNA values in serum. Comparisons of different diagnoses (healthy controls, adenoma patients, carcinoma patients) were made. Differences are shown as *p*-values. *p*-values of < 0.05 (highlighted with *) were considered to be statistically significant.

miRNA	Healthy vs. Adenoma	Healthy vs. CRC	Adenoma vs. CRC
Let7	<0.001 *	0.296	0.005 *
mir16	<0.001 *	0.533	<0.001 *
mir19	<0.001 *	0.193	0.056
mir21	<0.001 *	0.619	<0.001 *
mir23	<0.001 *	0.541	<0.001 *
mir29	<0.001 *	0.742	<0.001 *
mir34	<0.001 *	0.289	0.013 *
mir92	<0.001 *	0.275	0.002 *
mir222	0.017 *	0.310	0.241
mir451	<0.001 *	0.173	0.010 *

Table S7. Details of median-normalized miRNA values in serum.

miRNA	Diagnosis	Patients	Outliers	min.	25% Quant.	Median	75% Quant.	max	mean	Standard Deviation	Standard Error
Let7	healthy	26	0	-7.51	-1.57	-0.27	2.04	4.89	-0.13	2.98	0.58
	adenoma	20	0	0.03	1.67	3.17	5.08	6.22	3.30	1.95	0.44
	CRC	23	0	-4.33	-2.02	0.94	4.07	5.97	0.84	3.40	0.71
mir16	healthy	26	0	-2.81	3.82	4.66	5.68	10.26	4.89	2.78	0.55
	adenoma	20	0	5.25	7.37	8.69	9.86	11.30	8.59	1.81	0.40
	CRC	23	0	1.06	2.51	4.61	8.61	10.65	5.46	3.47	0.72
mir19	healthy	25	1	-11.10	0.92	2.16	3.34	5.67	1.14	4.20	0.86
	adenoma	19	0	-3.11	3.33	5.88	7.43	11.41	5.41	3.56	0.82
	CRC	23	0	-5.11	0.45	1.72	6.17	11.18	2.87	4.80	1.00
mir21	healthy	26	0	-3.37	1.85	3.37	4.73	7.95	3.38	2.55	0.50
	adenoma	20	0	2.68	5.55	8.70	9.54	11.87	7.74	2.55	0.57
	CRC	23	0	-2.29	0.47	3.53	7.00	11.38	3.90	4.31	0.90
mir23	healthy	26	0	-3.44	3.38	4.41	5.97	12.60	4.53	3.14	0.62
	adenoma	20	0	4.00	6.35	8.68	10.73	12.80	8.72	2.83	0.63
	CRC	23	0	-6.74	-0.50	2.92	8.47	12.92	3.73	5.48	1.14
mir29	healthy	25	1	-0.94	0.29	1.30	1.95	4.79	1.45	1.71	0.35
	adenoma	20	0	1.00	2.68	4.26	5.89	8.25	4.47	2.36	0.53
	CRC	23	0	-2.48	-0.97	0.37	3.47	7.62	1.22	2.91	0.61
mir34	healthy	26	0	-10.32	-6.56	-4.73	-2.92	-1.20	-4.73	2.28	0.45
	adenoma	20	0	-3.78	-2.59	-1.45	-0.25	3.96	-0.95	2.35	0.53
	CRC	23	0	-7.75	-6.68	-6.07	-1.68	3.81	-3.66	4.27	0.89
mir92	healthy	26	0	-7.54	-1.54	-0.01	1.71	4.77	0.04	2.57	0.50
	adenoma	20	0	0.24	2.04	3.38	4.88	6.26	3.54	1.79	0.40
	CRC	23	0	-2.89	-1.57	-0.63	3.46	6.25	0.95	3.15	0.66
mir222	healthy	26	0	-7.57	-1.98	-0.40	0.65	4.76	-0.44	2.44	0.48
	adenoma	20	0	-1.89	-0.23	0.90	2.83	6.25	1.46	2.63	0.59
	CRC	23	0	-3.32	-1.77	-0.69	2.29	6.59	0.40	3.19	0.67
mir451	healthy	25	0	-3.54	4.49	5.86	7.76	12.38	6.04	3.55	0.71
	adenoma	16	0	5.98	9.51	12.04	13.35	17.36	11.48	3.39	0.85
	CRC	23	0	1.06	4.39	6.19	10.84	16.65	7.80	5.04	1.05

Table S8. Details for tumor markers CEA and CA 19-9.

Marker	Diagnosis	Patients	Min.	25% Quant.	Median	75% Quant.	Max.	Mean	Standard Deviation	Standard Error
CEA	healthy	24	0.00	0.00	0.35	1.10	4.08	0.76	1.07	0.22
	adenoma	17	0.00	0.00	1.10	2.35	4.53	1.40	1.40	0.34
	CRC	22	0.00	0.69	1.10	1.61	3.40	1.24	0.88	0.19
CA19-9	healthy	24	0.00	0.69	1.70	2.97	5.36	1.87	1.51	0.31
	adenoma	16	0.00	1.52	2.77	3.30	5.17	2.50	1.42	0.35
	CRC	21	0.00	2.40	2.64	3.09	5.46	2.73	1.16	0.25