

Diagnostic value of a plasma microRNA signature in gastric cancer: a microRNA expression analysis

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Table S1. Differently expressed miRNAs in the screening phase

MiRNA	Fold change			Mean fold
	Pool1	Pool2	Pool3	
<i>miR-103</i>	5.95	6.07	8.58	6.87
<i>miR-106a</i>	3.17	4.38	5.33	4.29
<i>miR-106b</i>	3.86	7.15	7.13	6.05
<i>miR-107</i>	4.86	6.64	6.93	6.14
<i>miR-151-5p</i>	4.31	7.30	12.03	7.88
<i>miR-15b</i>	2.77	3.62	5.55	3.98
<i>miR-17</i>	4.85	4.43	9.33	6.21
<i>miR-182</i>	4.02	3.24	15.15	7.47
<i>miR-185</i>	2.68	4.39	5.19	4.09
<i>miR-19a</i>	3.88	2.52	8.14	4.84
<i>miR-20a</i>	3.00	4.02	6.38	4.47
<i>miR-21</i>	4.81	5.84	12.16	7.61
<i>miR-210</i>	2.04	4.68	3.97	3.56
<i>miR-223</i>	3.13	4.51	10.63	6.09
<i>miR-23a</i>	2.26	3.36	5.92	3.85
<i>miR-25</i>	1.88	2.75	2.48	2.37
<i>miR-320a</i>	3.62	3.90	4.53	4.02
<i>miR-335</i>	1.92	3.55	6.18	3.88
<i>miR-421</i>	3.15	4.01	12.73	6.63
<i>miR-532-5p</i>	3.67	1.87	2.86	2.80
<i>miR-584</i>	3.07	3.86	7.25	4.73
<i>miR-652</i>	2.46	2.88	3.66	3.00
<i>miR-92b</i>	2.05	1.67	3.91	2.54
<i>miR-16</i>	2.45	2.64	3.60	2.90
<i>miR-128</i>	3.09	4.90	8.42	5.47
<i>miR-181a</i>	5.89	7.39	9.54	7.61
<i>miR-199a-5p</i>	3.54	5.68	9.48	6.24
<i>miR-26a</i>	5.98	12.20	11.90	10.03
<i>miR-320b</i>	2.42	3.67	4.07	3.39
<i>miR-125a-5p</i>	-2.62	-4.27	-1.94	-2.95
<i>miR-133b</i>	-1.99	-2.29	-2.09	-2.13
<i>miR-133a</i>	-2.63	-3.30	-2.87	-2.93
<i>miR-365</i>	-1.72	-5.52	-3.99	-3.74

Table S2. Expression levels of miRNAs identified from screening phase but not passed through the training stage (presented as mean \pm SD; fmol/L).

MiRNA	Controls	Cases	FC	P value
<i>miR-106a</i>	604 \pm 190	1985 \pm 1767	3.29	0.10
<i>miR-107</i>	412 \pm 403	492 \pm 300	1.19	0.52
<i>miR-128</i>	985 \pm 1062	835 \pm 807	0.85	0.94
<i>miR-133a</i>	156 \pm 235	36.4 \pm 28.3	0.23	0.49
<i>miR-133b</i>	115 \pm 171	26.1 \pm 19.4	0.23	0.85
<i>miR-151-5p</i>	275 \pm 106	351 \pm 151	1.28	0.19
<i>miR-15b</i>	107 \pm 62.1	203 \pm 136	1.89	0.26
<i>miR-16</i>	14060 \pm 10829	21122 \pm 12051	1.50	0.20
<i>miR-182</i>	19.7 \pm 11.9	24.3 \pm 15.8	1.23	0.51
<i>miR-199a-5p</i>	44.7 \pm 24.2	105 \pm 120	2.35	0.52
<i>miR-21</i>	658 \pm 300	1358 \pm 1130	2.06	0.20
<i>miR-223</i>	35393 \pm 15857	56570 \pm 41424	1.60	0.34
<i>miR-23a</i>	947 \pm 413	1698 \pm 1455	1.79	0.77
<i>miR-26a</i>	1026 \pm 415	5084 \pm 5807	4.96	0.09
<i>miR-320a</i>	12069 \pm 3199	20990 \pm 18046	1.74	0.67
<i>miR-320b</i>	1302 \pm 319	2265 \pm 1763	1.74	0.90
<i>miR-335</i>	125 \pm 70.8	106 \pm 62.3	0.85	0.63
<i>miR-365</i>	352 \pm 562	33.9 \pm 33.7	0.10	0.89
<i>miR-421</i>	324 \pm 233	348 \pm 175	1.07	0.12
<i>miR-532-5p</i>	34.3 \pm 28.8	54.5 \pm 40.9	1.59	0.38
<i>miR-584</i>	158 \pm 118	345 \pm 377	2.18	0.76
<i>miR-652</i>	34 \pm 12.9	86.1 \pm 78.3	2.53	0.23

FC: fold change

Table S3. Expression levels of the other 6 miRNAs in the training and testing stages (presented as mean \pm SD; fmol/L).

MiRNA	Training stage				Testing stage				Combined	
	Controls	Cases	FC	P value	Controls	Cases	FC	P value	FC	P value
<i>miR-103-1</i>	94.3 \pm 49.2	261 \pm 169	2.77	<0.001	88.6 \pm 51.3	97.2 \pm 79	1.10	0.23	1.55	0.58
<i>miR-106b</i>	543 \pm 290	1576 \pm 852	2.90	<0.001	1619 \pm 1556	1181 \pm 926	0.73	0.47	0.86	0.81
<i>miR-17</i>	972 \pm 797	1976 \pm 1248	2.03	0.003	972 \pm 670	1225 \pm 1018	1.26	0.79	1.48	0.32
<i>miR-181a</i>	22.5 \pm 13	72.7 \pm 56	3.23	<0.001	30.6 \pm 19.7	43.1 \pm 34.3	1.41	0.50	1.14	0.48
<i>miR-19a</i>	1097 \pm 1070	1957 \pm 1378	1.78	0.003	927 \pm 769	1047 \pm 805	1.13	0.13	1.35	0.15
<i>miR-125a-5p</i>	29.2 \pm 14.7	77.7 \pm 66.6	2.66	0.032	30.7 \pm 16.1	33.9 \pm 25.8	1.10	0.33	1.56	0.72

FC: fold change

Table S4. Expression levels of the five miRNAs in the external cohort (presented as mean \pm SD; fmol/L).

MiRNA	Controls	Cases	FC	P value
<i>miR-185</i>	58.4 \pm 20.3	135 \pm 64.7	2.32	<0.001
<i>miR-20a</i>	2493 \pm 1003	5356 \pm 3739	2.15	0.046
<i>miR-210</i>	13.2 \pm 7.13	42.3 \pm 36.9	3.21	0.022
<i>miR-25</i>	925 \pm 363	2570 \pm 1881	2.78	0.004
<i>miR-92b</i>	9.2 \pm 6.4	44.4 \pm 28.4	4.82	<0.001

FC: fold change

Table S5. Analyses of the five miRNAs in the peripheral plasma compared to those in the arterial plasma (presented as mean \pm SD; fmol/L).

MiRNA	Peripheral	Arterial	FC	P value
<i>miR-185</i>	128 \pm 79.8	56.3 \pm 29.9	0.44	<0.001
<i>miR-20a</i>	5646 \pm 4132	7720 \pm 4627	1.37	0.008
<i>miR-210</i>	36.8 \pm 27.6	86.4 \pm 94.5	2.35	0.013
<i>miR-25</i>	1781 \pm 1289	1754 \pm 919	0.98	0.14
<i>miR-92b</i>	31 \pm 20	103 \pm 93.7	3.34	<0.001

FC: fold change

Table S6. Expression levels of the five miRNAs in the peripheral exosomes of 10 GC patients and controls (presented as mean \pm SD; Δ Ct).

MiRNA	Controls	Cases	P value
<i>miR-185</i>	8.3 \pm 0.5	8.36 \pm 0.74	0.93
<i>miR-20a</i>	4.59 \pm 1.35	4.5 \pm 2.35	0.95
<i>miR-210</i>	7.2 \pm 0.75	7.87 \pm 0.998	0.37
<i>miR-25</i>	2.91 \pm 0.7	3.74 \pm 2	0.63
<i>miR-92b</i>	7.84 \pm 1.03	8.38 \pm 0.38	0.29

Δ Ct=Ct_{miRNA}-Ct_{cel-miR-39}

Table S7. KEGG pathway analysis of the five identified miRNAs

Analysis for <i>miR-185</i>	P Value	Analysis for <i>miR-20a</i>	P Value	Analysis for <i>miR-210</i>	P Value	Analysis for <i>miR-25</i>	P Value	Analysis for <i>miR-92b</i>	P Value
Long-term depression	0.00378729 2	Endocytosis	7.43059E-07	Glycosaminoglycan biosynthesis	0.002932615	FoxO signaling pathway	0.00132694 7	FoxO signaling pathway	0.000905768
Axon guidance	0.00458146 8	Bladder cancer	1.91037E-05	Hepatitis B	0.007958193	Proteoglycans in cancer	0.00636416 7	Proteoglycans in cancer	0.00423138
Arachidonic acid metabolism	0.00522284 7	MAPK signaling pathway	0.000051156	Prostate cancer	0.01244564	Circadian entrainment	0.00731589 7	Circadian entrainment	0.005575269
Glutamatergic synapse	0.00866266 6	Pathways in cancer	0.000146801	Cholinergic synapse	0.02346261	Focal adhesion	0.01283991	Regulation of actin cytoskeleton	0.01323466
Glutathione metabolism	0.00879073 6	TGF-beta signaling pathway	0.000571692	Neuroactive ligand-receptor interaction	0.02904973	Regulation of actin cytoskeleton	0.01862526	MicroRNAs in cancer	0.01627407
Ovarian steroidogenesis	0.00879073 6	Chronic myeloid leukemia	0.00075198	Cocaine addiction	0.03034573	PI3K-Akt signaling pathway	0.01909808	Focal adhesion	0.01936393
Adherens junction	0.00985601 5	Pancreatic cancer	0.000984466	Non-small cell lung cancer	0.03737776	Calcium signaling pathway	0.01991651	Nicotine addiction	0.02152255
Thyroid hormone signaling pathway	0.01003826	Axon guidance	0.001373651	Adrenergic signaling in cardiomyocytes	0.04737275	Nicotine addiction	0.02504522	RNA degradation	0.02738345
Ras signaling pathway	0.01178537	Circadian rhythm	0.002602499	Glioma	0.04896525	ECM-receptor interaction	0.02754333	Salivary secretion	0.02850573
T cell receptor signaling pathway	0.01556694	Prostate cancer	0.004736787			Small cell lung cancer	0.02754333	Dilated cardiomyopathy	0.02850573
VEGF signaling	0.01822438	mTOR signaling	0.004936159			Pantothenate and CoA	0.03231274	Pantothenate and	0.02918549

pathway		pathway		biosynthesis		CoA biosynthesis	
Fatty acid elongation	0.01917427	Melanoma	0.005791707	RNA degradation	0.03298968	Fc gamma R-mediated phagocytosis	0.03020303
Sulfur relay system	0.02482611	Hepatitis B	0.006385244	Adherens junction	0.03298968	Calcium signaling pathway	0.03128138
GnRH signaling pathway	0.02801417	Prolactin signaling pathway	0.006447754	Salivary secretion	0.03489878	Adrenergic signaling in cardiomyocytes	0.03842445
Notch signaling pathway	0.03194996	Glioma	0.008767568	Dilated cardiomyopathy	0.03489878	PI3K-Akt signaling pathway	0.03982208
Thyroid hormone synthesis	0.03444338	Small cell lung cancer	0.009396033	Fc gamma R-mediated phagocytosis	0.03692706	Pancreatic secretion	0.04405333
Endometrial cancer	0.0411774	Neurotrophin signaling pathway	0.01082131	MicroRNAs in cancer	0.04275079	Phosphatidylinositol signaling system	0.04464773
Vascular smooth muscle contraction	0.04684041	TNF signaling pathway	0.01167103	Amino sugar and nucleotide sugar metabolism	0.04613568	Glycosaminoglycan biosynthesis	0.04478341
		Transcriptional misregulation in cancer	0.01218648	Adrenergic signaling in cardiomyocytes	0.04876366		
		FoxO signaling pathway	0.01230724	Glycosaminoglycan biosynthesis	0.04940756		
		Regulation of actin cytoskeleton	0.01238419				
		Cell cycle	0.01439141				

Renal cell carcinoma	0.0262943
PI3K-Akt signaling pathway	0.02682305
Non-small cell lung cancer	0.02744885
Estrogen signaling pathway	0.02849083
p53 signaling pathway	0.03124715
HTLV-I infection	0.03405508
Wnt signaling pathway	0.0363052
Rap1 signaling pathway	0.03660535
Protein processing in endoplasmic reticulum	0.04371815
Osteoclast differentiation	0.0452136
Dopaminergic synapse	0.0452136

Figure S1 Receiver-operating characteristic (ROC) curve analyses of each miRNA to discriminate GC patients from normal controls in the combined two cohorts

