

Supplementary Table S1. Characteristics of classic diagnostic methods of pancreatic ductal adenocarcinoma. [1]

Diagnostic tool	Advantages	Disadvantages
Transabdominal ultrasound	<ul style="list-style-type: none"> • non-invasive • relatively cost-effective 	<ul style="list-style-type: none"> • difficulties in imaging of pancreatic body and tail cancers • highly dependent on the operator's experience
Computed tomography	<ul style="list-style-type: none"> • non-invasive • good spatial resolution • good temporal resolution • wide anatomic coverage • best performance for the evaluation of vascular involvement 	<ul style="list-style-type: none"> • may not depict small metastases to the liver or peritoneum
EUS-guided fine-needle aspiration	<ul style="list-style-type: none"> • high-resolution images of the pancreas • ability to obtain specimens for histopathological diagnosis 	<ul style="list-style-type: none"> • an invasive procedure, however considered safe and accurate
Magnetic resonance imaging	<ul style="list-style-type: none"> • non-invasive • greater soft-tissue contrast of MRI compared with that of CT 	<ul style="list-style-type: none"> • worse spatial resolution compared to CT (requires relatively more time to perform the imaging)

Supplementary Table S2. Diagnostic performance of circulating miRNA (CS – clinical stage, PC-pancreatic cancer, CP-chronic pancreatitis, IPMN – intraductal papillary mucinous neoplasm AUC – area under the curve), 95% CI are provided in square brackets.

*-analysis with Abcam Fireplex™ platform

† - provided with miRBase: the microRNA database

miRNA	Location and predicted target genes †	Author	Year	Normalization control	Source of sample	Expression level compared to non-cancer controls	CS of PC patients	Control	AUC	Sensitivity	Specificity
miR-21	chr17:	Abue et	2015	exogenous cel-	plasma	upregulated	I-IV	healthy patients	0.736	-	-

	59841266-59841337 [+] [82] [83]	al.[84]		miR-39, endogenous miR-16				and IPMN			
miR-483-3p	chr11: 2134134-2134209 [-] [137]	Abue et al.[84]	2015	exogenous cel- miR-39, endogenous miR-16	plasma	upregulated	I-IV	healthy patients and IPMN	0.740	-	-
miR-1202	chr 6: 155946797-155946879 [15]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8833 [0.7246-1.00]	-	-
miR-1275	chr 6: 33999972-34000051 [-] [25]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8333 [0.60049-1.00]	-	-
miR-1915-3p	chr10: 21496562-21496641 [-] [59]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8833 [0.70258-1.00]	-	-
miR-2392	chr14: 100814491-100814574 [+] [105]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8667 [0.75085-0.98249]	-	-
miR-3135-b	chr6: 32749912-	Aita et al. [16]	2021	exogenous UniSp6,	serum	upregulated	I-III	healthy patients	0.8333 [0.70987-0.95680]	-	-

	32749979 [-] [115]			exogenous spike-in mix (UniSp2, UniSp4, UniSp5)							
miR-3679-5p	chr2: 134127125- 134127192 [+] [121]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.85 [0.6431- 1.00]	-	-
miR-371b-5p	chr19: 53787677- 53787742 [-] [122]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.9333 [0.84430- 1.00]	-	-
miR-4327	chr21: 30375294- 30375378 [-] [130]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.9333 [0.84430- 1.00]	-	-
miR-4466	chr6: 156779678- 156779731 [-][131]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8500 [0.58529- 1.00]	-	-
miR-4516	chr16: 2133119- 2133204 [+] [132]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix	serum	upregulated	I-III	healthy patients	0.9167 [0.78255- 1.00]	-	-

				(UniSp2, UniSp4, UniSp5)							
miR-4655-3p	chr7: 1844180- 1844253 [-] [134]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8667 [0.75085- 0.98249]	-	-
miR-4669	chr9: 134379411- 134379472 [+] [135]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8333 [0.56959- 1.00]	-	-
miR-4687-3p	chr11: 3856062- 3856141 [+] [136]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8833 [0.70258- 1.00]	-	-
miR-5100	chr10: 42997563- 42997681 [+] [141]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8667 [0.67646- 1.00]	-	-
miR-574-3p	chr4: 38868032- 38868127 [+] [142]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8333 [0.59329- 1.00]	-	-

				UniSp5)							
miR-6089	chrX: 2609191- 2609254 [+] [145]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8667 [0.63230- 1.00]	-	-
miR-6125	chr12: 62260359- 62260454 [+] [146]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.8833 [0.67896- 1.00]	-	-
miR-6126	chr16: 3485381- 3485469 [-] [147]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.90 [0.79524- 1.00]	-	-
miR-6749-5p	chr11: 64902387- 64902455 [-] [154]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8667 [0.0858- 0.69858]	-	-
miR-6800-5p	chr19: 49832018- 49832099 [+] [155]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.90 [0.74399- 1.00]	-	-
miR-6821-5p	chr22:	Aita et al.	2021	exogenous	serum	upregulated	I-III	healthy patients	0.9667 [0.88761-	-	-

	49962866-49962939 [+] [156]	[16]		UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)					1.00]		
miR-6850-5p	chr8: 144791931-144791991 [-] [157]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.9167 [0.77041-1.00]	-	-
miR-6869-5p	chr20: 1392900-1392961 [-] [158]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.9167 [0.74206-1.00]	-	-
miR-7107-5p	chr12: 121444273-121444352 [-] [161]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8333 [0.59329-1.00]	-	-
miR-7110-5p	chr3: 123161794-123161879 [+] [162]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	healthy patients	0.8167 [0.55014-1.00]	-	-
miR-8485	chr2: 50696172-50696262 [-]	Aita et al. [16]	2021	exogenous UniSp6, exogenous	serum	downregulated	I-III	healthy patients	0.8833 [0.67896-1.00]	-	-

	[167]			spike-in mix (UniSp2, UniSp4, UniSp5)							
miR-939-5p	chr8: 144394149- 144394230 [-] [171]	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	healthy patients	0.90 [0.79524- 1.00]	-	-
miR-181d	chr19: 13874875- 13875011 [+] [50][51]	Akamatsu et al. [52]	2016	exogenous cel- miR-39	serum	upregulated	I-IV	autoimmune pancreatitis	0.882 [0.813 - 0.952]	81%	80%
miR-193b	chr16: 14303967- 14304049 [+] [61] [62]	Akamatsu et al. [52]	2016	exogenous cel- miR-39	serum	upregulated	I-IV	autoimmune pancreatitis	0.804 [0.718 - 0.892]	79%	73%
miR-34a	chr1: 9151668- 9151777 [-] [119][120]	Akamatsu et al. [52]	2016	exogenous cel- miR-39	serum	upregulated	I-IV	autoimmune pancreatitis	0.844 [0.754 - 0.935]	81%	80%
miR-7	chr9: 83969748- 83969857 [-] [159] [160]	Akamatsu et al. [52]	2016	exogenous cel- miR-39	serum	upregulated	I-IV	autoimmune pancreatitis	0.723 [0.603 - 0.844]	72%	73%
miR-21	chr17: 59841266- 59841337 [+] [82] [83]	Aleamar et al. [85]	2016	exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.889 [0.76–1.00]	82.6%	77.8%
miR-34a	chr1: 9151668- 9151777 [-] [119][120]	Aleamar et al. [85]	2016	exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.865 [0.71– 1.00]	91.3%	77.8%
miR-196b	chr7:	Bartsch et	2018	endogenous	serum	upregulated	I-III	healthy patients	0.8938 [0.7395-	80%	50%

	27169480-27169563 [-] [66][67]	al. [68]		miR-24					1.048]		
miR-182	chr7: 129770383-129770492 [-] [53] [54]	Chen et al. [55]	2014	endogenous RNU6B	plasma	upregulated	I-IV	healthy patients, CP	0.775 [0.721–0.856]	64.1 %	82.6 %
miR -106b	chr 7: 100093993-100094074 [6]	Cote et al. [7]	2014	endogenous miRNA-425-5p	plasma	upregulated	I-IV	healthy patients, CP	0.999	100%	98%
miR-10b	chr 2: 176150303-176150412 [13][14]	Cote et al. [7]	2014	endogenous miRNA-425-5p	plasma	upregulated	I-IV	healthy patients, CP	0.980	95%	100%
miR-155	chr21: 25573980-25574044 [+] [34][35]	Cote et al. [7]	2014	endogenous miRNA-425-5p	plasma	upregulated	I-IV	healthy patients, CP	0.975	93%	100%
miR-212	chr17: 2050271-2050380 [-] [89] [90]	Cote et al. [7]	2014	endogenous miRNA-425-5p	plasma	upregulated	I-IV	healthy patients, CP	0.900	90%	83%
miR-30c	chr1: 40757284-40757372 [+] [113][114]	Cote et al. [7]	2014	endogenous miRNA-425-5p	plasma	upregulated	I-IV	healthy patients, CP	0.938	73%	96%
miR-25	chr7: 100093560-100093643 [-] [107] [108]	Deng et al.[109]	2016	directly normalized to the serum volume	serum	upregulated	I-IV	healthy patients, CP	0.915 [0.893-0.937]	-	-
miR-130a-3p*	chr11: 57641198-57641286	Dittmar et al. [29]	2021	endogenous miR-17-5p, miR-20a-5p,	plasma	upregulated	II	healthy patients	0.74 [0.63-0.84]	-	-

	[+][28]			miR-93-5p							
miR-222-3p*	chrX: 45747015- 45747124 [-] [97]	Dittmar et al. [29]	2021	endogenous miR-17-5p, miR-20a-5p, miR-93-5p	plasma	upregulated	II	healthy patients	0.70 [0.58-0.81]	-	-
miR-34a-5p*	chr1: 9151668- 9151777 [-] [119][120]	Dittmar et al. [29]	2021	endogenous miR-17-5p, miR-20a-5p, miR-93-5p	plasma	upregulated	II	healthy patients	0.77 [0.66- 0.87]	-	-
miR-642		Fathi et al. [151]	2022	endogenous RNU6B	plasma	upregulated	-	patients with gastrointestinal symptoms, without malignancy	0.63	58%	78%
miR-8073	chr13: 110340958- 110341029 [+] [166]	Fathi et al. [151]	2022	endogenous RNU6B	plasma	upregulated	-	patients with gastrointestinal symptoms, without malignancy	0.82	77%	78%
let-7d-3p	chr 9: 94178834- 94178920 [4]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.75 [0.61-0.89]	-	-
miR-101-3p	chr 1: 65058434- 65058508 [10]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	downregulated	I-II	healthy patients	0.75 [0.60-0.89]	-	-
miR-106b-5p	chr 7: 100093993- 100094074 [6]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	downregulated	I-II	healthy patients	0.81 [0.68-0.94]	-	-
miR-122-5p	chr 18: 58451074-	Franklin et al [5]	2018	endogenous mean	plasma	upregulated	I-II	healthy patients	0.75 [0.60-0.89]	-	-

	58451158 [17]			expression value normalization							
miR-130b-3p	chr11: 57641198- 57641286 [+][28]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.80 [0.67-0.92]	-	-
miR-144-3p	chr17: 28861533- 28861618 [-] [33]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	downregulated	I-II	healthy patients	0.81 [0.68-0.94]	-	-
miR-197-3p	chr1: 109598893- 109598967 [+] [69]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.76 [0.62-0.90]	-	-
miR-22-5p	chr17: 1713903- 1713987 [-] [104]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.78 [0.64-0.92]	-	-
miR-24-3p	chr9: 95086021- 95086088 [+] [106]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.78 [0.65-0.92]	-	-
miR-26a-5p	chr3: 37969404- 37969480 [+] [111]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	downregulated	I-II	healthy patients	0.77 [0.62-0.91]	-	-
miR-34a-5p	chr1: 9151668- 9151777 [-]	Franklin et al [5]	2018	endogenous mean expression	plasma	upregulated	I-II	healthy patients	0.82 [0.69-0.94]	-	-

	[119][120]			value normalization							
miR-423-3p	chr17: 30117079- 30117172 [+] [127]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.76 [0.62-0.90]	-	-
miR-451a	chr17: 28861369- 28861440 [-] [133]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	downregulated	I-II	healthy patients	0.77 [0.63-0.91]	-	-
miR-574-3p	chr4: 38868032- 38868127 [+] [142]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.83[0.70-0.95]	-	-
miR-885-5p	chr3: 10394489- 10394562 [-] [168]	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	upregulated	I-II	healthy patients	0.79 [0.66-0.93]	-	-
miR-22-3p	chr17: 1713903- 1713987 [-] [101]	Ganepola et al. [102]	2014	endogenous miR-3196	plasma	upregulated	IIA-IIB	healthy patients	0.86 [0.70-1.00]	-	-
miR-642b-3p	chr19: 45674932- 45675008 [-] [152]	Ganepola et al. [102]	2014	endogenous miR-3196	plasma	upregulated	IIA-IIB	healthy patients	0.79 [0.59-0.98]	-	-
miR-885-5p	chr3: 10394489- 10394562 [-] [168]	Ganepola et al. [102]	2014	endogenous miR-3196	plasma	upregulated	IIA-IIB	healthy patients	0.84 [0.68-1.00]	-	-
miR-373	chr19: 53788705-	Hua et al.[125]	2017	endogenous RNU6B	serum	downregulated	I-IV	healthy patients	0.852	80.6%	84.3%

	53788773 [+] [123][124]										
miR-429	chr1: 1169005- 1169087 [+] [128]	Huang et al.[129]	2022	endogenous RNU6B	serum	downregulated	I-IV	healthy patients	0.858 [0.727- 0.989]	-	-
miR-22-3p	chr17: 1713903- 1713987 [-] [101]	Hussein et al.[103]	2017	endogenous miR-3196	serum	upregulated	IB,IIB,I V	healthy patients	0.943	97.14%	93.33%
miR-642b-3p	chr19: 45674932- 45675008 [-] [152]	Hussein et al.[103]	2017	endogenous miR-3196	serum	upregulated	IB,IIB,I V	healthy patients	1.00	100%	100%
miR-885-5p	chr3: 10394489- 10394562 [-] [168]	Hussein et al.[103]	2017	endogenous miR-3196	serum	upregulated	IB,IIB,I V	healthy patients	1.00	100%	100%
miR-107	chr 10: 89592747- 89592827 [11]	Imamura et al.[12]	2017	exogenous cel- miR-39	plasma	downregulated	I-IV	healthy patients	0.851	82%	68.8%
miR-607	chr10: 96828669- 96828764 [-] [143]	Jiang et al. [144]	2021	endogenous RNU6	serum	downregulated	I-IV	healthy patients	0.785 [0.738- 0.831]	64.7%	77.2%
miR-126-5p	chr 9: 136670602- 136670686 [+][23]	Karasek et al. [24]	2018	endogenous miR-106a	plasma	upregulated	I-II	healthy patients	0.85	-	-
miR-1290	chr1: 18897071- 18897148 [-] [26]	Karasek et al. [24]	2018	endogenous miR-106a	plasma	upregulated	I-II	healthy patients	0.78	-	-
miR-155	chr21:	Karasek et	2018	endogenous	plasma	upregulated	I-II	healthy patients	0.86	-	-

	25573980- 25574044 [+] [34][35]	al. [24]		miR-106a							
miR-17-5p	chr13: 91350605- 91350688 [+] [41]	Karasek et al. [24]	2018	endogenous miR-106a	plasma	upregulated	I-II	healthy patients	0.87	-	-
miR-21-5p	chr17: 59841266- 59841337 [+] [82] [83]	Karasek et al. [24]	2018	endogenous miR-106a	plasma	upregulated	I-II	healthy patients	0.99	-	-
miR-375	chr2: 219001645- 219001708 [-][126]	Karasek et al. [24]	2018	endogenous miR-106a	plasma	upregulated	I-II	healthy patients	0.73	-	-
miR-221	chrX: 45746157- 45746266 [-] [94][95]	Kawaguchi et al.[96]	2013		plasma	upregulated	I-IV	healthy patients	0.743	-	-
miR-122-5p	chr 18: 58451074- 58451158 [17]	Khan et al.[18]	2021	exogenous UniSp6	serum	upregulated	I-IV	healthy patients	0.988 [0.927– 0.999]	98%	96%
miR-192-5p	chr11: 64891137- 64891246 [-] [60]	Khan et al.[18]	2021	exogenous UniSp6	serum	upregulated	I-IV	healthy patients	0.720 [0.604– 0.817]	74%	60%
miR-215-5p	chr1: 220117853- 220117962 [-] [91]	Khan et al.[18]	2021	exogenous UniSp6	serum	upregulated	I-IV	healthy patients	0.832 [0.721– 0.904]	72%	72%
miR-30b-5p	chr8: 134800520- 134800607 [-] [112]	Khan et al.[18]	2021	exogenous UniSp6	serum	downregulated	I-IV	healthy patients	0.798 [0.691– 0.883]	76%	68%
miR-320b	chr1:	Khan et	2021	exogenous	serum	upregulated	I-IV	healthy patients	0.922 [0.833–	84%	78%

	116671746-116671817 [+] [117]	al.[18]		UniSp6					0.970]		
miR-223	chrX: 66018870-66018979 [+] [98] [99]	Komatsu et al.[100]	2015	exogenous cel-miR-39	plasma	upregulated	I-II	healthy patients	0.8340	62%	94.1%
miR-200a	chr1: 1167863-1167952 [+] [72][73]	Li et al.[74]	2010	endogenous miR-16	serum	upregulated	-	healthy patients	0.861 [0.774–0.949]	84.4%	87.5%
miR-200b	chr1: 1167104-1167198 [+] [75] [76]	Li et al.[74]	2010	endogenous miR-16	serum	upregulated	-	healthy patients	0.85 [0.763–0.938]	71.1%	96.9%
miR-492	chr12: 94834398-94834513 [+] [139]	Lin et al.[140]	2014	exogenous cel-miR-39	serum	downregulated	I-IV	healthy patients	0.787 [0.689-0.885]	75.5%	70.0%
miR-663a	chr20: 26208186-26208278 [-] [153]	Lin et al.[140]	2014	exogenous cel-miR-39	serum	downregulated	I-IV	healthy patients	0.870 [0.793-0.948]	85.7%	80.0%
miR-196a	chr17: 48632490-48632559 [-] [64]	Liu et al. [46]	2020	endogenous RNU6B	plasma	upregulated	I-IV	healthy patients	0.865 [0.779-0.951]	72.5%	92.5%
miR-155	chr21: 25573980-25574044 [+] [34][35]	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients, CP	0.704 [0.646-0.762]	-	-
miR-16	chr13: 50048973-50049061 [-] [39] [40]	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients, CP	0.749 [0.694-0.803]	-	-
miR-181b	chr1:	Liu et al.	2012	exogenous cel-	plasma	upregulated	I-IV	healthy patients,	0.785 [0.735-	-	-

	198858873-198858982 [-] [44][45]	[36]		miR-39				CP	0.835]		
miR-196a	chr17: 48632490-48632559 [-] [64]	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients, CP	0.816 [0.768-0.864]	-	-
miR-21	chr17: 59841266-59841337 [+] [82] [83]	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients, CP	0.776 [0.725-0.827]	-	-
miR-210	chr11: 568089-568198 [-] [87][88]	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients, CP	0.755 [0.701-0.808]	-	-
miR-181b	chr1: 198858873-198858982 [-] [44][45]	Liu et al. [46]	2020	endogenous RNU6B	plasma	upregulated	I-IV	healthy patients	0.789 [0.681-0.898]	77.5%	85.0%
miR-210	chr11: 568089-568198 [-] [87][88]	Liu et al. [46]	2020	endogenous RNU6B	plasma	upregulated	I-IV	healthy patients	0.834 [0.745-0.923]	82.5%	80.0%
miR-181a	chr1: 198859044-198859153 [-] [42] [43]	Liu J. et al. [36]	2012	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients, CP	0.774 [0.723-0.825]	-	-
miR-744	chr17: 12081899-12081996 [+] [163] [164]	Miyamae et al.[165]	2015	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients	0.8307	59.3%	89.6%
miR-18a	chr13: 91350751-91350821 [+] [56] [57]	Morimura et al. [58]	2011		plasma	upregulated	I-IV	healthy patients	0.9369	-	-

miR-21-5p	chr17: 59841266- 59841337 [+] [82]	Qu et al.[92]	2017	exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.78 [0.66–0.90]	77%	80%
miR-629	chr15: 70079372- 70079468 [-] [148] [149]	Shi et al.[150]	2018		serum	upregulated	I-IV	healthy patients	0.765 [0.679-0.851]	-	-
miR-196		Škrha et al.[63]	2016	endogenous miR-191 and miR-454	serum	upregulated	-	healthy patients	0.74	-	-
miR-200		Škrha et al.[63]	2016	endogenous miR-191 and miR-454	serum	upregulated	-	healthy patients	0.79	-	-
miR-196b	chr7: 27169480- 27169563 [-] [66][67]	Slater et al. [65]	2014	endogenous miR-24	serum	upregulated	I,II,IV	healthy patients	0.86	100%	78%
miR-196a	chr17: 48632490- 48632559 [-] [64]	Slater et al. [65]	2014	endogenous miR-24	serum	upregulated	I,II,IV	healthy patients	0.97	90%	89%
miR-100	chr 11: 122152229- 122152308 [8]	Stroese et al. [9]	2018	exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.81 [0.70-0.92]	-	-
miR-21	chr17: 59841266- 59841337 [+] [82] [83]	Stroese et al. [9]	2018	exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.71 [0.56-0.86]	-	-
miR-99a	chr21: 16539089- 16539169 [+] [172][173]	Stroese et al.[9]	2018	exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.72 [0.59-0.86]	-	-
miR-99b	chr19:	Stroese et	2018	exogenous cel-	serum	upregulated	I-IV	healthy patients	0.76 [0.65-0.88]	-	-

	51692612-51692681 [+] [174][175]	al.[9]		miR-39							
miR-205	chr1: 209432133-209432242 [+] [77] [78]	Traeger et al. [79]	2018	exogenous cel-miR-39	serum	upregulated	II-IV	healthy patients, CP, IPMN	0.669 [0.548–0.789]	64.3%	68.4%
miR-181c	chr19: 13874699-13874808 [+] [47] [48]	Vieira et al. [49]	2021	endogenous RNU-24 and RNU-48	plasma	upregulated	I-IV	healthy patients	0.72	-	-
miR-210	chr11: 568089-568198 [-] [87][88]	Vieira et al. [49]	2021	endogenous RNU-24 and RNU-48	plasma	upregulated	I-IV	healthy patients	0.88	-	-
miR-21-5p	chr17: 59841266-59841337 [+] [82]	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients	0.862 [0.834-0.890]	62.4%	73.5%
miR-320a	chr8: 22244966-22245037 [-] [116]	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients	0.849 [0.819-0.879]	83.0%	78.4%
miR-33a-3p	chr22: 41900944-41901012 [+] [118]	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients	0.857 [0.828-0.886]	87.2%	76.0%
miR-93-5p	chr7: 100093768-100093847 [-] [169]	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients	0.791 [0.755-0.826]	77.9%	67.3%
miR-133a	chr18: 21825698-21825785 [30][31]	Wang et al. [32]	2019	endogenous RNU6B	serum	downregulated	I-III	healthy patients	0.893	87.2%	90.6%

miR-155	chr21: 25573980- 25574044 [+] [34][35]	Wang et al.[37]	2009	endogenous miRNA-16	plasma	upregulated	I-IV	healthy patients	0.67 [0.51–0.82]	-	-
miR-196a	chr17: 48632490- 48632559 [-] [64]	Wang et al.[37]	2009	endogenous miRNA-16	plasma	upregulated	I-IV	healthy patients	0.69 [0.53–0.84]	-	-
miR-21	chr17: 59841266- 59841337 [+] [82] [83]	Wang et al.[37]	2009	endogenous miRNA-16	plasma	upregulated	I-IV	healthy patients	0.62 [0.45–0.77]	-	-
miR-210	chr11: 568089- 568198 [-] [87][88]	Wang et al.[37]	2009	endogenous miRNA-16	plasma	upregulated	I-IV	healthy patients	0.65 [0.49–0.80]	-	-
miR-1246	chr 2: 176600980- 176601052 [19]	Wei et al.[20]	2020	* three independent experiments	serum	upregulated	I-IV	healthy patients, pancreatic disease	0.81 [0.75 - 0.87]	-	-
miR-1290	chr1: 18897071- 18897148 [-] [26]	Wei et al.[20]	2020	* three independent experiments	serum	upregulated	I-IV	healthy patients, pancreatic disease	0.91 [0.87 - 0.95]	-	-
miR-1290	chr1: 18897071- 18897148 [-] [26]	Xu [27]	2021	endogenous miR-16-5p, exogenous cel- miR-39	serum	upregulated	I-IV	healthy patients	0.8857	60.9%	90.0%
miR-126-3p	chr 9: 136670602- 136670686 [+] [21]	Xu et al.[22]	2016	endogenous RNU6B, miR- 16	plasma	upregulated	I-IV	healthy patients	0.618 [0.550– 0.682]	61.5%	60%
miR-486-5p	chr8: 41660441- 41660508 [-]	Xu et al.[22]	2016	endogenous RNU6B, miR- 16	plasma	upregulated	I-IV	healthy patients	0.861 [0.808– 0.904]	75%	87.7%

	[138]										
miR-938	chr10: 29602264- 29602346 [-] [170]	Xu et al.[22]	2016	endogenous RNU6B, miR- 16	plasma	upregulated	I-IV	healthy patients	0.693 [0.628– 0.753]	61.5%	73%
miR-155	chr21: 25573980- 25574044 [+] [34][35]	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	-	healthy patients	0.822 [0.707– 0.937]	-	-
miR-196a	chr17: 48632490- 48632559 [-] [64]	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	-	healthy patients	0.791 [0.665– 0.916]	-	-
miR-20a	chr13: 91351065- 91351135 [+] [80][81]	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	-	healthy patients	0.884 [0.790– 0.978]	-	-
miR-21	chr17: 59841266- 59841337 [+] [82] [83]	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	-	healthy patients	0.845 for [0.740–0.949]	-	-
miR-210	chr11: 568089- 568198 [-] [87][88]	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	-	healthy patients	0.687 [0.543– 0.831]	-	-
miR-25	chr7: 100093560- 100093643 [-] [107] [108]	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	-	healthy patients	0.763 [0.635– 0.891]	-	-
miR-25	chr7: 100093560- 100093643 [-] [107] [108]	Yu et al.[110]	2020	endogenous let-7d, let-7g, let-7i	serum	upregulated	I-IV	healthy patients	0.939 [0.903- 0.975]	82.5%	93.64%
miR-21	chr17:	Yuan et	2016	exogenous cel-	plasma	upregulated	I-IV	healthy patients	0.809(0.743-	-	-

	59841266-59841337 [+] [82] [83]	al.[86]		miR-39					0.875)		
miR-25	chr7: 100093560-100093643 [-] [107] [108]	Yuan et al.[86]	2016	exogenous cel-miR-39	plasma	upregulated	I-IV	healthy patients	0.655(0.570-0.740)	-	-
let-7b-5p	chr 22: 46113686-46113768 [2]	Zou et al. [3]	2019	exogenous cel-miR-39	serum	upregulated	I-IV	healthy patients	0.703 [0.636-0.771]	79.8%	59.8%
miR-192-5p	chr11: 64891137-64891246 [-] [60]	Zou et al. [3]	2019	exogenous cel-miR-39	serum	upregulated	I-IV	healthy patients	0.684 [0.615-0.754],	77.5%	57.0%
miR-19a-3p	chr13: 91350891-91350972 [+] [70]	Zou et al. [3]	2019	exogenous cel-miR-39	serum	upregulated	I-IV	healthy patients	0.771 [0.712-0.831]	71.3%	78.5%
miR-19b-3p	chr13: 91351192-91351278 [+] [71]	Zou et al. [3]	2019	exogenous cel-miR-39	serum	upregulated	I-IV	healthy patients	0.788 [0.729-0.846]	65.1%	81.3%
miR-223-3p	chrX: 66018870-66018979 [+] [99]	Zou et al. [3]	2019	exogenous cel-miR-39	serum	upregulated	I-IV	healthy patients	0.901 [0.861-0.941]	78.3%	91.6%
miR-25-3p	chr7: 100093560-100093643 [-][108]	Zou et al. [3]	2019	exogenous cel-miR-39	serum	upregulated	I-IV	healthy patients	0.726 [0.659-0.792]	66.7%	80.4%

Supplementary Table S3. Diagnostic performance of circulating miRNA panels. CS- clinical stage, PC –pancreatic cancer, AUC – area under the curve, CA19-9 - Carbohydrate antigen 19-9

Markers included in the panel and their relative levels ↓/↑	Author	Year	Normalization control	Source of sample	CS of PC patients	AUC	Sensitivity	Specificity
miR-483-3p ↑ miR-21 ↑	Abue et al.[84]	2015	exogenous cel-miR-39, endogenous miR-16	plasma	I-IV	0.839	-	-
miR-21 ↑ miR-34a ↑	Aleamar et al. [85]	2016	exogenous cel-miR-39	serum	I-IV	0.894 [0.771–1.0]	-	-
miR-196b ↑ TIMP1 ↑ LCN2 ↑	Bartsch et al. [68]	2018	endogenous miR-24	serum	I-III	0.93 [0.8162 to 1.044]	80%	80%
miRNA-10b ↑ miRNA -106b ↑	Cote et al. [7]	2014	endogenous miRNA-425-5p	plasma	I-IV	-	100%	100%
miR-8073 ↑ miR-642 ↑	Fathi et al. [151]	2022	endogenous RNU6B	plasma	-	0.79	77%	78%
miR-574-3p ↑ miR-885-5p ↑ miR-144-3p ↓ miR-130b-3p ↑ miR-34a-5p ↑ miR-24-3p ↑ miR-106b-5p ↓ miR-22-5p ↑ miR-451a ↓ let-7d-3p ↑ miR-101-3p ↓ miR-26a-5p ↓ miR-197-3p ↑ miR-423-3p ↑ miR-122-5p ↑	Franklin et al [5]	2018	endogenous mean expression value normalization	plasma	I-II	0.96 [0.92-1.00]	-	-
miR-642b-3p ↑ miR -885-5p ↑	Ganepola et al. [102]	2014	endogenous miR-3196	plasma	IIA-IIB	0.97 [0.90-1.00]	-	-

miR- 22-3p↑								
miR-607↓ CA19.9↑ CEA↑	Jiang et al. [144]	2021	endogenous RNU6B	serum	I-IV	0.863	76.6%	83.1%
miR-16 ↑ miR-24↓ miR-27.a↓ miR-30a-5p↓ miR-323-3p↓ miR-20a↑ miR-25↓ miR-29c↓ miR-483-5p ↑	Johansen et al.[176]	2016	endogenous controls	serum	I-IV	0.7207	-	-
miR-16↑ miR-18.a↑ miR-24↓ miR-27a↓ miR-30a-5p↓ miR-323-3p↓ miR-20a↑ miR-25↓ miR-29c↓ miR-191↓ miR-345↑ miR-483-5p ↑	Johansen et al.[176]	2016	endogenous controls	serum	I-IV	0.7237		
miR-221↑ miR-375↓	Kawaguchi et al.[96]	2013		plasma	I-IV	0.762	-	-
miR-215-5p↑ miR-122-5p↑ miR-192-5p↑ miR-30b-5p↓ miR-320b↑	Khan et al.[18]	2021	exogenous UniSp6	serum	I-IV	0.811 [0.744– 0.829]	-	-
miR-492↓ miR-663a↓	Lin et al.[140]	2014	exogenous cel-miR- 39	serum	I-IV	0.869 [0.791- 0.947]	85.7%	80.0%
miR-181b↑ miR-210↑	Liu et al. [46]	2020	endogenous RNU6B	plasma	I-IV	0.830 [0.743- 0.917]	80.0%	70.0%

miR-196a↑ miR-210↑	Liu et al. [46]	2020	endogenous RNU6B	plasma	I-IV	0.888 [0.805- 0.970]	87.5%	80.0%
miR-181b↑ miR-196a↑	Liu et al. [46]	2020	endogenous RNU6B	plasma	I-IV	0.944 [0.887- 1.001]	92.5%	90.0%
miR-181b↑ miR-196a↑ miR-210↑	Liu et al. [46]	2020	endogenous RNU6B	plasma	I-IV	0.968 [0.924- 1.011]	95.0%	97.5%
miR-16↑ miR-196a↑	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	I-IV	0.895 [0.850- 0.939]	-	-
miR-16↑ miR-196a↑ CA19-9↑	Liu et al. [36]	2012	exogenous cel-miR-39	plasma	I-IV	0.979 [0.962- 0.996]	92.0%	95.6%,
miR-20a↑ miR-21↑ miR-24↑ miR-25↑ miR-99a↑ miR-185↑ miR-191↑	Liu et al.[177]	2012	directly normalized to the serum volume	serum	I-IV	0.985	94%	93%
miR-145↓ miR-150↓ miR-223↑ miR-636↓	Schultz et al. [178]	2014	endogenous RNU44 and RNU48	whole blood	I-IV	0.88 [0.85- 0.92]	85%	73%
miR-26b↑ miR-34a↑ miR-122↑ miR-126↓ miR-145↑ miR-150↓ miR-223↑ miR-505↑ miR-636↓ miR-885-5p↑	Schultz et al. [178]	2014	endogenous RNU44 and RNU48	whole blood	I-IV	0.93 [0.89- 0.96]	85%	86%
miR-196↑	Škrha et	2016	endogenous miR-	serum	-	-	94%	82%

miR-200 ↑ CA 19-9↑	al.[63]		191 and miR-454v					
miR-196a↑ miR-196b↑	Slater et al. [65]	2014	endogenous miR-24	serum	I,II,IV	1.00	100%	100%
miR-210↑ miR-21↑ CA19-9↑	Vieira et al. [49]	2021	endogenous RNU-24 and RNU-48	plasma	I-IV	1.00	100%	100%
miR-33a-3p↑ miR-320a↑	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	I-IV	0.906 [0.93-0.88]	89%	85%
miR-33a-3p↑ miR-320a↑ CA19-9↑	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	I-IV	0.956 [0.97-0.94]	86%	91%
miR-21↑ miR-210↑ miR-155↑ miR-196a↑	Wang et al.[37]	2009	endogenous miRNA-16	plasma	I-IV	0.82 [0.70–0.94]	64%	89%
miR-1290↑ miR-1246↑ CA19-9↑	Wei et al.[20]	2020	* three independent experiments	serum	I-IV	0.97 [0.96-1.00]	92.5%	93.7%
miR-25↑ MIC-1↑ CA19-9↑	Yuan et al.[86]	2016	exogenous cel-miR-39	plasma	I-IV	0.967 [0.938-0.995]	84.1%	100%
miR-21↑ MIC-1↑ CA19-9↑	Yuan et al.[86]	2016	exogenous cel-miR-39	plasma	I-IV	0.972 [0.946-0.999]	87.8%	98.9%
miR-122-5p↑ miR-125b-5p↑ miR-192-5p↑ miR-193b-3p↑ miR-221-3p↑ miR-27b-3p↑	Zhou et al. [179]	2018	endogenous miR-103a	plasma	I-IV	0.937 [0.894–0.979]	88.7%	89.1%
let-7b-5p↑ miR-192-5p↑ miR-19a-3p↑ miR-19b-3p↑ miR-223-3p↑	Zou et al. [3]	2019	exogenous cel-miR-39	serum	I-IV	0.978 [0.966-0.998]	93.3%	96.0%

miR-25-3p↑								
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Supplementary Table S4. Diagnostic performance of circulating miRNA compared to CA19-9. CS – clinical stage, PC – pancreatic cancer, AUC –area under the curve, CA19-9 - Carbohydrate antigen 19-9

* analysis with Abcam Fireplex™ platform

miRNA	Author	Year	Normaliza tion control	Source of sample	Expression level compared to non- cancer controls.	CS of PC patients	Compared with CA19-9 alone	AUC in panel with CA19.9	Sensitivity in panel with CA19-9	Specificity in panel with CA19-9
miR-21	Abue et al.[84]	2015	exogenous cel- miR-39,	plasma	upregulated	I-IV	worse results	-	-	-

			endogenous miR-16							
miR-483-3p	Abue et al.[84]	2015	exogenous cel-miR-39, endogenous miR-16	plasma	upregulated	I-IV	worse results	-	-	-
miR-1202	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-1275	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-1915-3p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-2392	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-3135-b	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-3679-5p	Ait. et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-

miR-371b-5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-4327	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-4466	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-4516	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-4655-3p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-4669	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-4687-3p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-5100	Aita et al.	2021	exogenous	serum	upregulated	I-III	better results	-	-	-

	[16]		UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)							
miR-574-3p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-6089	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-6125	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-6126	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-6749- 5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-6800- 5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike- in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-6821- 5p	Aita et al. [16]	2021	exogenous UniSp6,	serum	upregulated	I-III	better results	-	-	-

			exogenous spike-in mix (UniSp2, UniSp4, UniSp5)							
miR-6850-5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-6869-5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-7107-5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-7110-5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-8485	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	downregulated	I-III	better results	-	-	-
miR-939-5p	Aita et al. [16]	2021	exogenous UniSp6, exogenous spike-in mix (UniSp2, UniSp4, UniSp5)	serum	upregulated	I-III	better results	-	-	-
miR-182	Chen et al [55]	2014	endogenous RNU6B	plasma	upregulated	I-IV	better results	0.837 [0.769–0.894]	84.68 %	86.77 %

miR-25	Deng et al.[109]	2016	directly normalized to the serum volume	serum	upregulated	I-IV	better results	-	-	-
miR-130a-3p*	Dittmar et al. [29]	2021	endogenous miR-17-5p, miR-20a-5p, miR-93-5p	plasma	upregulated	II	worse results	0.94 [0.89-0.98]	-	-
miR-222-3p*	Dittmar et al. [29]	2021	endogenous miR-17-5p, miR-20a-5p, miR-93-5p	plasma	upregulated	II	worse results	0.92 [0.87-0.97]	-	-
miR-34a-5p*	Dittmar et al. [29]	2021	endogenous miR-17-5p, miR-20a-5p, miR-93-5p	plasma	upregulated	II	worse results	0.92 [0.86 - 0.97]	-	-
miR-22-3p	Hussein et al.[103]	2017	endogenous miR-3196	serum	upregulated	IB,IIB,IV	better results	-	-	-
miR-642b-3p	Hussein et al.[103]	2017	endogenous miR-3196	serum	upregulated	IB,IIB,IV	better results	-	-	-
miR-885-5p	Hussein et al.[103]	2017	endogenous miR-3196	serum	upregulated	IB,IIB,IV	better results	-	-	-
miR-607	Jiang et al. [144]	2021	endogenous RNU6B	serum	downregulated	I-IV	better results	-	-	-
miR-181b	Liu et al. [46]	2020	endogenous RNU6B	plasma	upregulated	I-IV	worse results	-	-	-
miR-196a	Liu et al. [46]	2020	endogenous RNU6B	plasma	upregulated	I-IV	worse results	-	-	-
miR-210	Liu et al. [46]	2020	endogenous RNU6B	plasma	upregulated	I-IV	worse results	-	-	-
miR-629	Shi et al.[150]	2018	-	serum	upregulated	I-IV	better results	0.812 [0.733 - 0.8927]	-	-
miR-205	Traeger et al. [79]	2018	exogenous cel-miR-39	serum	upregulated	II-IV	worse results	0.890 [0.782–0.995]	86.7%	93.3%
miR-210	Vieira et al. [49]	2021	endogenous RNU-24 and RNU-48	plasma	upregulated	I-IV	worse results	0.99	-	-
miR-21-5p	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	better results	-	-	-

miR-320a	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	better results	-	-	-
miR-33a-3p	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	better results	-	-	-
miR-93-5p	Vila-Navarro et al.[93]	2019	exogenous cel-miR-39	plasma	upregulated	I-IV	worse results	-	-	-
miR-1246	Wei et al.[20]	2020	* three independent experiments	serum	upregulated	I-IV	worse results	0.93 [0.89-0.96]	85.8 %	86.2 %
miR-1290	Wei et al.[20]	2020	* three independent experiments	serum	upregulated	I-IV	better results	0.96 [0.94-0.99]	84.2 %	96.2 %
miR-25	Yu et al.[110]	2020	endogenous let-7d, let-7g, let-7i	serum	upregulated	I-IV	better results	0.985 [0.972-0.998]	-	-
miR-21	Yuan et al.[86]	2016	exogenous cel-miR-39	plasma	upregulated	I-IV	worse results	-	-	-
miR-25	Yuan et al.[86]	2016	exogenous cel-miR-39	plasma	upregulated	I-IV	worse results	-	-	-
miR-122-5p	Zhou et al. [179]	2018	endogenous miR-103a	plasma	upregulated	I-IV	-	0.81 [0.762–0.859]	-	-
miR-125b-5p	Zhou et al. [179]	2018	endogenous miR-103a	plasma	upregulated	I-IV	-	0.646 [0.585–0.707]	-	-
miR-192-5p	Zhou et al. [179]	2018	endogenous miR-103a	plasma	upregulated	I-IV	-	0.693 [0.634–0.753]	-	-
miR-193b-3p	Zhou et al. [179]	2018	endogenous miR-103a	plasma	upregulated	I-IV	-	0.775 [0.722–0.828]	-	-
miR-221-3p	Zhou et al. [179]	2018	endogenous miR-103a	plasma	upregulated	I-IV	-	0.625 [0.562–0.688]	-	-
miR-27b-3p	Zhou et al.	2018	endogenous	plasma	upregulated	I-IV	-	0.656	-	-

	[179]		miR-103a					[0.594–0.718]		
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Supplementary Table S5. Prognostic performance of circulating miRNA. OS-overall survival

*-in unresectable patients

†-in patients undergoing pancreatoduodenectomy

miRNA	Author	Year	Normalization control	Source of sample	Expression level compared to non-cancer controls.	Prognosis with increased level of miRNA expression	OS with high levels of expression in months	OS with low levels of expression in months	Univariate analysis p value	Multivariate analysis p value
miR-21*	Abue et al.[84]	2015	exogenous cel-miR-39, endogenous miR-16	plasma	upregulated	poor	3.0	13.8	p=0.005	-
let-7a	Ali et al.[180]	2015	-	plasma	downregulated	good	-	-	p=0.063	-
miR-508	Ali et al.[180]	2015	-	plasma	upregulated	poor	-	-	p=0.212	-
let-7d	Ali et al.[181]	2010	endogenous miR-16	plasma	downregulated	good	-	-	-	p=0.0044
miR-21	Ali et al.[181]	2010	endogenous miR-16	plasma	upregulated	poor	-	-	-	p=0.0032
miR-182	Chen et al [55]	2014	endogenous RNU6B	plasma	upregulated	poor	25.023, [22.122–27.878]	37.025, [32.753–41.247]	p=0.001	p<0.001
miR-200c-3p†	Gablo et al. [182]	2020	endogenous miR-93-5p	plasma	-	poor	-	-	p =0.012	-
miR-365a-3p†	Gablo et al. [182]	2020	endogenous miR-93-5p	plasma	-	good	-	-	p =0.013	-
miR-99a-5p†	Gablo et	2020	endogenous miR-	plasma	-	good	-	-	p =0.006	-

	al. [182]		93-5p							
miR-373	Hua et al.[125]	2017	endogenous RNU6B	serum	downregulated	good	-	-	-	p=0.014
miR-107	Imamura et al.[12]	2017	exogenous cel-miR-39	plasma	downregulated	good	-	-	p=0.0038	p=0.0424
miR-607†	Jiang et al. [144]	2021	endogenous RNU6B	serum	downregulated	good	-	-	p=0.011	p=0.036
miR-21-5p†	Karasek et al. [24]	2018	endogenous miR-106a	plasma	upregulated	poor	-	-	p=0.0499	p=0.0379
miR-196a	Kong et al. [183]	2011	exogenous cel-miR-39	serum	upregulated	poor	6.1 [4.49–7.72]	12.0 [5.92–18.08]	p = 0.007	
miR-21	Liu et al.[177]	2012	directly normalized to the serum volume	serum	upregulated	poor	-	-	p=0.02	p=0.00
miR-744	Miyamae et al.[165]	2015	exogenous cel-miR-39	plasma	upregulated	poor	-	-	p=0.0063	p=0.0007†
miR-629	Shi et al.[150]	2018	-	serum	upregulated	poor	-	-	p=0.001	p=0.006
miR-100	Stroese et al. [9]	2018	exogenous cel-miR-39	serum	upregulated	poor	-	-	p = 0.002	p = 0.046
miR-21	Stroese et al.[9]	2018	exogenous cel-miR-39	serum	upregulated	poor	-	-	p = 0.001	p = 0.004
miR-205	Traeger et al. [79]	2018	exogenous cel-miR-39	serum	upregulated	poor	6.93	11.93	p = 0.176	-
miR-17-3p	Van der Sijde et al.[184]	2021	endogenous miR-26a-5p, miR-30b-5p	serum	-	-	-	-	p = 0.032	p = 0.192
miR-194-5p	Van der Sijde et al.[184]	2021	endogenous miR-26a-5p, miR-30b-5p	serum	-	-	-	-	p = 0.145	-
miR-373-3p	Van der Sijde et al.[184]	2021	endogenous miR-26a-5p, miR-30b-5p	serum	-	-	-	-	p = 0.141	-
miR-21	Wang et al. [185]	2013	exogenous cel-miR-39	serum	upregulated	poor	6.2	11.6	p = 0.002	p = 0.008
miR-196a	Yu et al	2017	exogenous cel-	plasma	upregulated	poor	6.3 [2.3–10.3]	12.5 [10.0–	p=0.001	p=0.013

	[38]		miR-39					15.0]		
miR-210	Yu et al [38]	2017	exogenous cel- miR-39	plasma	upregulated	good	11.7 [6.8– 16.5]	6.6 [5.3–7.9]	p = 0.003	p=0.021
miR-21	Yuan et al.[86]	2016	exogenous cel- miR-39	plasma	upregulated	good	8.30 [5.69- 10.91]	7.30 [5.94- 8.66]	p=0.768	-
miR-25	Yuan et al.[86]	2016	exogenous cel- miR-39	plasma	upregulated	good	8.30 [4.73- 11.87]	7.30[6.04- 8.56]	p= 0.759	-
miR-125b-5p	Zhou et al. [179]	2018	endogenous miR- 103a	plasma	upregulated	good	-	-	p=0.004	p=0.011
miR-19a-3p	Zou et al. [3]	2019	exogenous cel- miR-39	serum	upregulated	poor	-	-	p=0.036	p=0.042

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