Supplemental Data include two figures, thirty-six tables and references of included studies.

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ESM Table 36. Robust microRNA-gene interaction pairs supported by 1966 articles (n=3290)

ESM Fig. 1. Funnel plots of publication bias on different microRNAs

ESM Fig. 2. The Venn diagram of microRNA categories and flow chart of systematic review

Appendix

References of included studies

ESM Table 1. Characteristics of human miRNA expression profiling studies [T2D vs nondiabetic controls (CTR)]

Study	T2D								Differentially expressed miRNAs		
	Country	Period	Tissue	Clinical status	No. of samples (T2D/CTR)	Age (years)	BMI (kg/m^2)	HbA1c (%)	Platform	Cut-off criteria	Total (Up/Down)
Al-Hayali MA 2019 [1]	Turkey	NR	Serum	Diagnosed	T2D: 45 T2D+CAD: 45 T2D+HF: 45 CTR: 45	61.50±5.08 61.61±6.02 62.07±5.26 60.23±6.27	29.86±3.18 29.62±2.63 29.21±1.66 23.33±1.39	10.23±9.67 7.46±1.42 5.63±0.73 4.74±0.47	StepOnePlus RT-PCR system (Applied Biosystems) with MPLIFYME SYBR UniversalMix (BLIRT)	*p<0.05*	2 (1/1)
Alicka M 2019 [2]	Poland	NR	ASC (adipose); extracellular vesicles of ASC	Diagnosed	12 (6/6) 12 (6/6)	36-49 38-56	41.50±5.50 15.45±2.21	NR	CFX Connect^{TM} RT- PCR Detection System (Bio-Rad)	*p<0.05*	6 (5/1) 6 (6/0)
Alipoor B 2018 [3]	Iran	NR	PBMCs Plasma	Diagnosed	60 (30/30)	57 50.5	27.13±4.15 27.22±3.26	7.4 5.1	RT-PCR with SYBR Premix Ex TaqTM II (Takara)	*p*<0.05	1 (0/1) 1 (0/1)
Al-Kafaji G 2015 [4]	Kingdom of Bahrain	NR	Peripheral whole blood	Diagnosed	48 (24/24)	52±6.0 49±9.1	25.3±1.8 24.2±1.0	7.5±0.8 4.8±0.6	TaqMan miRNA Assays and RT-PCR system (Applied Biosystems)	*p*<0.05	1 (0/1)
Al-Kafaji G 2016 [5]	Kingdom of Bahrain	NR	Peripheral whole blood	Diagnosed	T2D: 52, T2D+DN: 50, CTR: 50	62.0±10.5 64.6±6.3 56±5.2	25.2±4.5 26.3±5.2 24.2±4.1	8.9±2.7 9.3±1.8 4.9±0.7	TaqMan miRNA Assays and 7900HT PCR system (Thermo Fisher Scientific)	*p*<0.05	1 (0/1)
Al-Kafaji G 2017 [6]	Kingdom of Bahrain	NR	Peripheral whole blood	Diagnosed	T2D: 45 T2D+CAD: 45 CTR: 45	61±12 64±11.7 53±8.6	25.4±4.8 26.1±4.3 24±4.5	7.4±8.3 9.6±3.2 3.64±1.1	TaqMan miRNA Assays (Applied BioSystems)	*p*<0.05 Ct <35	1 (0/1)
Avgeris M 2020 [7]	Greece	NR	Peripheral whole blood	Diagnosed	Screening: 12 (6/6) Validation: 77 (40/37)	NR 35-75 19-69	NR 21.5-46.5 21.3-36.3	NR 5.2-12.1 5.0-6.1	miScript PCR Array and SYBR Green kit (Qiagen) in 7500 RT-PCR system (Applied Biosystems)	*p*<0.05	7 (0/7) 3 (0/3)

Bai L 2019 [8]	NR	NR	Blood	Diagnosed	40 (20/20)	60±5.3 61.2±5.5	34±6.5 32.5±5.5	7.8±7.1 5.0±4.1	RT-PCR	$p<0.05$	1 (1/0)
Bai X 2016 [9]	China	2012 to 2014	Plasma	Diagnosed	T2D+DN/CTR: 47 (27/20)	NR	NR	NR	miR-130b miScript Primer Assays (Qiagen)	$p<0.05$	1 (0/1)
Balasubramanyam M 2011 [10]	Chennai India	NR	PBMCs	Diagnosed	40 (20/20)	43.7±5.1 42.0±4.7	26.4±3.7 25.8±4.0	7.9±1.8 5.5±0.2	miRCURY LNA miRNA PCR system (Exiqon)	$p<0.05$	1 (0/1)
Baldeon RL 2015 [11]	Ecuador	2009 to 2012	PBMCs	Diagnosed	82 (48/34)	NR	NR	NR	TaqMan miRNA Assays and 7900 HT RT-PCR system (Applied Biosystems)	$p\leq0.05$	2 (2/0)
Baltaci OF 2018 [12]	Turkey	NR	Blood	Diagnosed	8 (5/3)	NR	NR	NR	TaqMan probes (Thermo Fisher Scientific) with qRT-PCR	$p<0.05$	1 (1/0)
Bao L 2015 [13]	China	2011 and 2013	Plasma	Diagnosed	T2D: 34 Pre-diabetes: 27 CTR: 30	NR	NR	NR	SYBR Green Master Mix; TaqMan Universal Master Mix II.	$p<0.05$	1 (0/1)
Blum A 2019 [14]	Israel	NR	Serum	Diagnosed	37 (15/22)	65±9 39±10	NR	NR	TaqMan Advanced miRNA assays (Applied Biosystems)	$p<0.05$	1 (0/1)
Bork-Jensen J 2015 [15]	Denmark	NR	Skeletal muscle	Diagnosed	22 (11/11)	68±8 68±8	32.5±6.7 30.4±6.5	7.7±1.5 5.9±0.5	miRCURY LNA array (Exiqon,)	pFDR<0.1	20 (0/20)
Brovkina O 2019 [16]	Russia	NR	Adipose	Diagnosed	70 (35/35)	48.5 44.5	41.80 43.02	8.00 5.40	TaqMan Advanced miRNA Assays (Thermo Fisher Scientific)	$p<0.05$	7 (5/2)
Candia PD 2017 [17]	Italy	NR	Plasma	Newly diagnosed	18 (9/9)	60.2±8 57.9±8.9	29.6±7.8 23.7±3.3	6.40±0.58 5.52±0.2	miRCURY RNA PCR panels (Exiqon, Denmark,)	$p<0.05$	3 (1/2)
Cheng S 2018 [18]	China	Aug 2016 to May 2017	$CD34^+$ cells from blood	Diagnosed	33 (18/15)	NR	NR	NR	SYBR PrimeScript miRNA RT-PCR (Takara)	$p<0.05$	1 (0/1)

Cheng Y 2020 [19]	Shanghai China	2015 to 2017	Kidney	Diagnosed	17 (10/7)	54.0±3.6 48.0±6.7	NR	NR	TaqMan miRNA Assay Kit (Life Technologies)	$p<0.05$	1 (0/1)
Conserva F 2019 [20]	Italy	NR	Kidney	Diagnosed	Discovery: (CTR: 4, T2D+DN: 6, T2D+MN: 6 Validation:17 (12/5)	38±14 59±16 63±16 NR	26±4 33±4 26±4 NR	NR	Agilent Human miRNA Microarray; miScript SYBR Green PCR Kit	FC≥1.5 & $pFDR\leq0.05$	65 (29/36) 1 (0/1)
Corral-Fernandez NE 2013 [21]	Mexico	NR	PBMCs	Diagnosed	40 (20/20)	40-60 18-28	31.9±7.4 23.1±2.5	7.9±1.7 4.8±0.7	TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	2 (0/2)
Cui X 2017 [22]	Nanjing China	NR	Serum	Newly diagnosed	183 (101/82)	57.5±12.2 49.3±7.73	26.8±4.19 24.3±3.22	NR	TaqMan and ViiA7 qRT-PCR system (Applied Biosystems)	FC≥2 & $p\leq0.05$	3 (3/0)
Dahlmans D 2017 [23]	Netherlands	NR	Skeletal muscle	Diagnosed	n=12 for each group (T2D, obese, lean and athlete)	58.64±1.22 57±2.29 21.91±0.72 25.08±1.25	32.37±1.11 30.83±1.14 21.84±0.57 20.98±0.44	NR	384-well Pick-&-Mix miRNA PCR Panel plates (Exiqon)	$p<0.05$	4 (4/0)
Dai X 2016 [24]	Shanghai China	Apr 2009 to Oct 2012	Serum	Newly diagnosed	T2D+PC/CTR: 80/80	60.1±10.7 59.5±13.5	NR	NR	TaqMan low-density array; ABI7500 RT-PCR system (Applied Biosystems)	$p<0.05$	6 (6/0)
Dangwal S 2015 [25]	Germany	NR	Plasma	Diagnosed	43 (23/20)	61.0±2.1 NR	29.1±0.9 NR	8.6±0.4 NR	Affymetrix miRNA array; TaqMan assays.	$p\leq0.05$	2 (0/2)
Deng X 2017 [26]	China	Sep 2015 to Jan 2016	Blood	Diagnosed	T2D+CHD: 28 CHD: 35 CTR: 31	65.1±7.2 61.3±6.6 60.3±7.3	NR	NR	qRT-PCR with ABI7500 system (Applied Biosystems)	$p<0.05$	1 (0/1) 1 (0/1)
El Samaloty NM 2019 [27]	Egypt	NR	Serum	Diagnosed	T2D: 21, T2D+HCV: 19, HCV: 21, CTR: 19	44.2±1.6 42±1.5 41.1±1.4 39.4±1.2	24.4±0.3 24.2±0.4 24±0.3 23.5±0.3	7.6±0.1 6.5±0.14 5.2±0.15 5.1±0.19	miScript SYBR Green kit (Qiagen) with StepOne Plus RT-PCR system (Applied Biosystem)	$p<0.05$	2 (1/1)

Elemeery MN 2019 [28]	Egypt	NR	Serum	Diagnosed	T2D: 200 T2D+TCC: 200 CTR: 225	53.68±9.48 56.23±8.14 49.92±7.14	NR	NR	TaqMan miRNA assay (Applied Biosystems)	$p<0.05$	12 (5/7)
Fejes Z 2017 [29]	Debrecen, Hungary	NR	Platelets; Plasma	Diagnosed	T2D: 28 Obese CTR: 19 CTR: 23	50-59 48-57 34-60	32.9 35.8 24	7.5 5.5 NR	TaqMan miRNA assay kits (Applied Biosystems)	$p\leq0.05$	3 (0/3) 4 (0/4)
Fomison-Nurse I 2018 [30]	New Zealand	NR	Heart Plasma Plasma	Diagnosed	T2D+IHD/IHD: 10/11 for heart and plasma; T2D: 11, 14, or 14 for plasma at different duration CTR: 32	67.07 64.56 61.45 67.36 70.86 69.25	31.06 30.27 27.92 27.47 25.84 26.42	7.42 5.74 7.07 7.54 7.91 5.79	TaqMan hybridization probe	$p<0.05$	1 (1/0) 1 (1/0) 1 (1/0)
Fulzele S 2015 [31]	USA	NR	Vitreous	Diagnosed	12 (8/4)	NR	NR	NR	miScript reagents (Qiagen) & SYBR Green I	$p<0.05$	1 (0/1)
Gallagher IJ 2010 [32]	Scotland, UK	NR	Skeletal muscle tissue	Diagnosed	92 (45/47)	54.8±10.2 51.3±10.7	31.4±6.2 31.1±7.2	7.4±1.8 5.5±0.2	miRCURY LNA miRNA array (Exiqon) and TaqMan Assays (Applied Biosystems)	SAM; FDR<0.1 (FC>1.3)	62 (29/33)
Giannella A 2017 [33]	Padua Italy	NR	Plasma	Diagnosed	121 (68/53)	60±1 57±1	30±1.6 25±0.4	NR	TaqMan microRNA kit (Applied Biosystems) & PCR with CFX96 (Biorad)	$p<0.05$	1 (0/1)
Guo J 2017 [34]	Zhengzhou China	Oct 2014 to Jul 2015	Plasma	Diagnosed	68 (33/35)	55.9±2.96 45.33±4.12	25.57±1.64 22.26±0.44	9.10±0.44 5.25±0.16	miRCURY LNA miRNA array (Exiqon)	FC>2	1 (1/0)
Guglielmi V 2017 [35]	NR	NR	Subcutaneous adipose tissue	4 diagnosed; 5 newly diagnosed	16 (9/7)	43.5±8 39.2±10.9	47.6±8.1 45.9±9.9	7.57±1.64 5.41±0.90	TaqMan miRNA array with ABI 7000 PRISM (Applied Biosystems)	$p<0.05$	1 (1/0)
Han YL 2016 [36]	Shandong,	Jan 2012 to	Blood	Diagnosed	T2D+BC/BC: 72/144	52.72±6.23	24.68±4.74	10.57±2.11	ABI 7500 quantitative PCR	$p<0.05$	2 (1/1)

	China	Jan 2015				50.08±4.76	23.21±3.25	5.64±1.57	System (Life Technologies)		
He X 2016 [37]	China	NR	Plasma	12 diagnosed; 20 Newly diagnosed	n=12 for each group (CTR, ASO, T2D+ASO); T2D: 20	NR	NR	NR	miRCURY LNA array (v.18.0); miScript SYBR Green PCR kit in ABI StepOne Plus PCR system	$p<0.05$	4 (3/1)
He X 2018 [38]	China	NR	Vascular tissues	Diagnosed	T2D+ASO/CTR: 26 (16/10)	NR	NR	NR	miScript SYBR Green PCR kit in ABI StepOne Plus PCR system	$p<0.05$	1 (1/0)
Henriksen TI 2017 [39]	Denmark	NR	Muscle stem cells	Diagnosed	16 (8/8)	51-65 50-67	26.2±2.8 25.4±1.8	NR	miRCURY LNA miRNA array (Exiqon)	$p<0.05$	5 (0/5)
Hou XY 2016 [40]	China	2010 to 2015	Plasma	Diagnosed	T2D+DN/CTR: 60 (30/30)	NR	NR	NR	TaqMan miRNA array; ABI7500 RT-PCR system (Applied Biosystems)	$p<0.05$	1 (1/0)
Hou X 2016 [41]	China	NR	Islets	Diagnosed	68 (34/34)	54±8 52±7	34±5 31±4	6.08±0.46 5.26±0.37	miScript SYBR Green PCR Kit (Qiagen)	$p<0.05$	1 (1/0)
Jansen F 2016 [42]	Bonn, Germany	Aug 2012 to Jul 2013	Plasma	Diagnosed	135 (55/80)	67.6±10.6 65.5±11.1	30.5±5.4 26.9±4.5	7.2±1.2 5.9±0.4	TaqMan miRNA Assays and 7500 HT RT-PCR system (Applied Biosystems)	$p<0.05$	2 (0/2)
Jiang Q 2017 [43]	Changchun, China	May 2013 to Mar 2015	Plasma	Diagnosed	T2D: 65 T2D+BDR: 73 T2D+PDR: 51 CTR: 115	47.76±8.05 48.83±7.13 50.75±10.2 48.53±7.26	22.67±1.98 23.06±1.85 23.13±2.02 22.82±2.33	6.25±0.58 7.02±0.66 8.16±0.79 4.30±0.42	qRT-PCR (Qiagen Company)	$p<0.05$	1 (1/0)
Jiang X 2015 [44]	Nanjing, China	Jul 2012 to Dec 2013.	Serum	Diagnosed	T2D+ED/CTR: 40/40	47.37±5.81 46.9±5.69	26.2±3.47 23.79±3.47	8.22±1.08 4.97±0.83	PCR 7500 (Applied Biosystems)	$p<0.05$	3 (3/0)
Jiao Y 2015 [45]	Urumqi China	NR	Peripheral blood Adipose tissues	Diagnosed	36 (12/24)	56±10 49±13	30.9±5.8 26.3±3.6	NR	miRCURY array and chip (Exiqon); MiScript SYBR	$p<0.05$	3 (0/3)

					24 (12/12)	57±11 53±14	27.9±4.2 25.7±4.2		Green PCR (Qiagen)		1 (0/1)
Jones A 2017 [46]	New Zealand	NR	Plasma	Diagnosed	27 (15/12)	45±8 44±9	44.2±4.2 22.9±2.6	7.5±1.7 NR	miRCURY LNA miRNA PCR ExiLENT SYBR green master mix	*Adjusted* p<0.05	42 (13/29)
Kamalden TA 2017 [47]	NR	NR	Plasma	Diagnosed	T2D: 41, T2D+BDR: 22, CTR: 19	62.1±13.2 61.4±8.7 64.5±8.3	NR	7.2±1.2 9.0±2.6 NR	miScript SYBR Green PCR kit (Qiagen)	p<0.05	1 (1/0)
Karolina DS 2011 [48]	Singapore	Jul 2008 to Apr 2009	Whole blood	Diagnosed	15 (8/7)	46.7±3.4 46.3±7.5	24.5±1.1 22.4±2.3	NR	miRCURY LNA miRNA array (Exiqon) and TaqMan Assays (Applied Biosystems)	p<0.05	82 (48/34)
Karolina DS 2012 [49]	Singapore	Jul 2008 to Jul 2012	Whole blood	Diagnosed	96 (50/46)	42.02 43.22	26.03 23.29	NR	miRCURY LNA miRNA array (Exiqon) and TaqMan Assays (Applied Biosystems)	p<0.05	11 (5/6)
Katayama M 2019 [50]	Sweden	NR	Exosomal from serum	Diagnosed	8 (4/4) 41 (21/20)	NR 61±1 60±1	NR 29.5±0.6 28.8±0.4	NR 6.34±0.3 4.6±0.1	StepOne Plus PCR (Applied Biosystems); miRCURY LNA miRNA PCR System (Exiqon)	p<0.05	6 (3/3) 2 (2/0)
Khan R 2020 [51]	India	NR	Serum	Diagnosed	Screening:10 (5/5) Validation: same sample 10 (5/5)	42±7.16 34±6.26	23.3 ± 0.89 21.4 ± 0.89	NR	Illumina Next Seq500; miscript SYBR green PCR kit (GmBH)	p<0.05; FC ≥ ± 2.	28 (9/19) 7 (3/4)
Kloting N 2009 [52]	Germany	6 months	Subcutaneous (SC)/omental adipose	Newly diagnosed	15 (6/9)	67±2.8 66±3.3	31.2±2.1 28.6±2.0	6.7±0.8 5.4±0.4	TaqMan miRNA Assays (Applied Biosystems)	p<0.05	11 (3/8)
Kokkinopoulou I 2019 [53]	NR	NR	Peripheral blood	Diagnosed	77 (40/37)	35-75 19-69	21.5-46.5 21.3-36.3	5.2-12.1 5.0-6.1	7500 RT-PCR System (Applied Biosystems)	p<0.05	6 (0/6)
Kong L 2010 [54]	Shandong,	Feb 2009 to	Serum	Newly	44 (18/26)	47.33±2.62	26.26±0.79	NR	TaqMan miRNA Assays (ABI	C_t=40;	1 (1/0)

	China	Jun 2009		diagnosed		43.81±2.22	25.57±3.58		company)	$p<0.01$	
Kong L 2011 [55]	Shandong, China	NR	Serum	Newly diagnosed	37 (18/19)	47.33±2.62 41.00±2.62	26.26±0.79 26.63±0.80	NR	TaqMan miRNA Assays (Applied BioSystems)	$p<0.05$	7 (7/0)
Krause C 2020 [56]	Germany	NR	Liver	Diagnosed	78 (29/49)	49.84±11.9 39.6±10.87	51.35±9.27 53.93±11.39	8.15±1.68 5.48±1.02	TaqMan miRNAAssays (Applied BioSystems)	$p<0.05$	1 (1/0)
Kuschnerus K 2019 [57]	Switzerland	NR	M2-like macrophages； Aortic wall	Diagnosed	T2D+CAD/CAD: 7/7 T2D+CAD/CAD: 7/5	NR	NR	NR	miRCURY LNA miRNA RT-PCR Kit and In Situ Hybridization kit (Exiqon)	$p<0.05$	1 (1/0) 1 (1/0)
Lareyre F 2019 [58]	France	NR	PBMCs PBMCs Serum Aneurysmal tissue (ANT)	Diagnosed	Screening: 6 (3/3) Validation: 20 (10/10) for PBMCs and serum; 6 (3/3) for ANT	NR 63.8-75.3 66-74.5 NR	NR 24.4-28.8 22.2-27.6 NR	NR	miRCURY LNA Universal RT miRNA PCR (Exiqon-Qiagen)	$p<0.05$	4 (3/1) 3 (3/0) 1 (1/0) 2 (2/0)
Latouche C 2016 [59]	Australia	NR	Skeletal muscle	Diagnosed	11 (6/5)	53±2 48±3	33±2 25±1	NR	Agilent 8x60K Human miRNA microarray	$p<0.05$	23 (13/10)
Latreille M 2014 [60]	Sweden	NR	Islets	Diagnosed	19 (9/10)	54.2±8.3 56.9±7.9	28.4±4.3 26.7±3.3	6.6±0.5 5.5±0.2	TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	1 (0/1)
Li H 2019 [61]	China	Jan 2012 to Oct 2014	Heart Plasma	Diagnosed	16 (8/8) 30 (15/15)	52±4.3 46±3.2 60±4.0 59±1.8	NR	NR	miRCURY LNA miRNA Arrays (Exiqon)	$p<0.05$	1 (1/0) 1 (1/0)
Li MY 2016 [62]	Shandong China	NR	Serum	Newly diagnosed	T2D: 30 T2D+BC: 30 BC-CTR: 30 CTR: 20	60.79±11.11 61.13±10.58 61.89±9.33 59.78±11.23	28.88±1.18 27.24±1.37 29.24±1.32 20.12±1.69	7.60±0.33 7.57±0.36 5.30±0.33 4.56±0.45	RT-PCR with SYBR ExTaq Mix	$p<0.05$	2 (2/0)
Li YB 2017 [63]	Hubei	May 2014 to	Plasma	Diagnosed	20 (10/10)	NR	NR	NR	RT-PCR Master Mix	$p<0.05$	1 (1/0)

	China	Mar 2015 Jul 2011 to Oct 2015	Lower limb skin	Diagnosed	60 (30/30)				SYBR-Green PCR (Toyobo Co., Ltd., Osaka, Japan)		1 (1/0)
Lian W 2018 [64]	Shanghai, China	NR	EPCs from blood	Diagnosed	50 (25/25)	58.2±8.3 60.1±8.7	23.23±4.90 13.35±2.90	NR	TaqMan qPCR	$p<0.05$	1 (1/0)
Liang L 2016 [65]	USA	NR	Fibroblasts from foot skin specimens	Diagnosed	T2D+DFU: 7 CTR: 8	NR	NR	NR	nCounter microRNA expression (NanoString); Quantification System (Quanta BioSciences)	FC≥2.0; $p<0.05$	3 (3/0)
Liang YZ 2018 [66]	Beijing China	First stage: 2015; validation stage: 2017	Plasma	Newly diagnosed	First 20 (10/10); Validation T2D: 112 pre-diabetic: 72 CTR: 94	49.10±3.84 49.00±3.97 54.75±7.53 52.53±7.51 52.84±8.85	26.84±2.85 22.74±1.91 27.11±3.17 26.26±2.97 23.86±3.27	8.66±0.87 4.97±0.24 7.58±1.54 5.74±0.60 5.16±0.39	Agilent miRNA microarrays; miScript RT Kit (Qiagen) with GeneAmp PCR System 9700 (Applied Biosystems)	FC≥2.0, $p<0.05$	51 (33/18) 4 (3/1) 2 (2/0)
Liang Z 2018 [67]	Shenzhen, China	NR	Serum	Diagnosed	17 (11/6)	NR	NR	NR	SYBR-Green PCR Master Mix (Applied Biosystems)	FC≥2.0, FDR<0.05	4 (4/0)
Liu H 2016 [68]	Shandong China	Jan2011 to Dec 2014	Epithelial BC tissues	Diagnosed	T2D+BC/BC: 257 (117/140)	53.57±6.08 54.36±5.52	22.83±2.78 24.05±3.32	NR	ABI PRISM 7000 detection system (Applied Biosystems)	$p<0.05$	1 (0/1)
Liu Y 2017 [69]	China	Aug 2014 to Feb 2017	Serum	Diagnosed	42 (21/21)	46.9±2.0 37.4±3.3	NR	NR	Real-time PCR with AB7300 (Stratagene, Valencia, CA)	$p<0.05$	1 (0/1)
Locke JM 2014 [70]	USA and UK	NR	Pancreatic islets	Diagnosed	20 (11/9) 20 (10/10)	53±8/47±9 55±9/51±6	36±14/30±6 32±4/29±5	NR	TaqMan miRNA Assays (Life Technologies)	$p<0.05$	2 (2/0)
Long Y 2017 [71]	Hunan, China	Mar 2013 to Sep 2014	PBMCs	Diagnosed	34 (16/18)	57±9 53±11	NR	NR	TaqMan miRNA Assays (Applied BioSystems)	$p<0.05$	1 (0/1)
Lu H 2010 [72]	UK	NR	Left ventricular biopsies	Diagnosed	12 (6/6)	59±7 58±14	27.7±4.3 27.0±2.5	6.6±1.0 5.5±0.2	TaqMan miRNA Assay (Applied Biosystems)	FC<-2 or >2,	18 (10/8)

										$p \le 0.05$	
Luo M 2015 [73]	Sichuan China	NR	Peripheral blood platelets	Diagnosed	T2D: 43 T2D+CHD: 36, CTR: 46	59±9.3 64.8±9.8 51.4±9.4	23.3±5.4 23.4±4.6 21.9±2.9	7.0±1.3 7.8±1.1 5.±0.5	SYBR Green Master Mix (TaKaRa); ABI PRISM 7500 system	$p<0.05$	1 (0/1)
Luo M 2019 [74]	Sichuan China	Sep 2017 to Oct 2018	Plasma	Diagnosed	T2D:47; T2D+CHD: 27; CHD: 34; CTR: 32	60.5±11.14 64.5±6.5 60.9±5.3 58.6±8.1	24.76±3.29 25.02±3.12 24.57±3.01 24.49±2.30	9.15±1.02 9.13±1.01 6.28±0.69 5.36±0.35	Stem-loop qRT-PCR	$p<0.05$	1 (0/1)
Luo M 2019 [75]	Sichuan China	Aug 2018 to Jan 2019	Plasma	Diagnosed	T2D: 48 Pre-diabetic: 47 CTR: 50	52.6±9.13 49.23±6.45 45.62±8.58	25.52±2.89 25.47±3.02 24.56±3.40	9.16±1.05 6.78±0.73 5.15±0.32	Stem-loop qRT-PCR	$p<0.05$	2 (1/1)
Mao G 2014 [76]	Jinan China	Jan 2013 to Dec 2013	Serum	Diagnosed	66 (33/33)	35-72 30-76	NR	NR	qPCR	$p<0.05$	1 (0/1)
Massaro JD 2019 [77]	Brazil	NR	PBMCs	Diagnosed	72 (32/40) with complication T2D +DN: 5; T2D+DC: 21; T2D+DU:5	59.31±8.56 44.55±13.6	21.4–47.45 23.8 ± 5.1	8.13±1.70 NR	MiSeq Reagent Kit v2 on MiSeq system (Illumina)	$p \leqslant 0.05$, $\|FC\|>1.0$, $FDR<0.1$	10 (3/7)
Massart J 2017 [78]	NR	NR	Skeletal muscle	Diagnosed	22 (12/10)	62±1 59±1.5	31.6±1 29.0±0.5	6.0±0.2 4.6±0.1	TaqMan miRNA Assays	$p<0.05$	2 (2/0)
Matsha TE 2018 [79]	South Africa	NR	Whole blood	Newly diagnosed	T2D: 12 pre-diabetic: 12 CTR: 12	54.8±7.5 53.5±8.5 52.1±7.8	33.5±8.9 33.3±9.1 27.3±5.8	NR	Illumina HiSeq with Agilent 2100 Bioanalyzer	$\|FC\|\ge 1.3$, $p<0.1$	31 (30/1) 15 (6/9)
Mazloom H 2015 [80]	Iran	NR	PBMCs	Diagnosed	40 (20/20)	46.5±5.8 47.5±4.4	28.7±4.9 26.2±4.0	7.02±0.5 5.7±0.7	SYBR Premix EX Taq II (Takara); Rotogene Q (Qiagene)	$p<0.05$	1 (0/1)
Meng S 2012 [81]	Shanghai,	NR	EPCs from	Diagnosed	30 (15/15)	67±8	29±9	NR	miRNA array probes (LC	$p<0.01$	5 (0/5)

	China		PBMCs			65±9	27±7		Sciences) and TaqMan miRNA Assays (Applied BioSystems)		
Meng S 2013 [82]	Shanghai China	NR	EPCs from blood	Diagnosed	40 (20/20)	64±8 62±9	28±7 26±9	NR	Roche LightCycler 480 system	*p*<0.05	1 (0/1)
Mensà E 2019 [83]	Italy	NR	Plasma	Diagnosed	158 (66/92)	NR	NR	NR	RT q-PCR	*p<0.05*	1 (0/1)
Monfared YK 2020 [84]	Iran	NR	Plasma	Newly diagnosed	80 (40/40)	53.69±5.69 33.59±7.58	30.11±1.01 25.23±2.43	9.13±0.41 4.67±1.22	Platinum SYBR Green qPCR SuperMix-UDG	*p<0.05*	1 (1/0)
Mononen N 2019 [85]	Finland	NR	Whole blood	Diagnosed	T2D: 24 Pre-diabetic: 252 CTR: 589	45.1±3.5 43.2±4.7 41.9±4.9	30.7±6.7 28.2±5.5 25.3±3.9	6.6±1.0 5.6±0.3 5.4±0.2	TaqMan OpenArray miRNA Panel (Applied BioSystems)	*p<0.05*	4 (3/1)
Ortega FJ 2010 [86]	Girona, Spain	NR	Adipose	Diagnosed	T2D+obese: 9 CTR+obese: 13 CTR: 6	45±10 41±9 42±9	44.5±4.9 44.5±3.0 26.6±2.7	5.7±1.4 4.9±0.4 4.4±0.2	miRNA microarrays (Agilent Technologies) TaqMan miRNA Assays (Applied BioSystems)	*p*<0.05	8 (4/4)
Ortega FJ 2014 [87]	Girona, Spain	NR	Plasma	Diagnosed	T2D/CTR:30/35 T2D+obese/obese:18 /10	54±10 48.1±10.1 57.7±8 50.6±14.4	26.4±2.4 25.2±1.8 33.4±3.3 32.2±2.4	7.67±1.46 4.73±0.35 7.06±2.14 4.81±0.33	TaqMan Low-Density Arrays (Applied Biosystems)	*p*<0.05	6 (3/3)
Ou L 2019 [88]	China	Jan to Dec 2016	Gingival tissues	Diagnosed	T2D+P: 63 Non-T2D+P: 45 CTR: 50	50-60 for all samples	29.43±2.78 27.20±5.16 24.90±5.16	8.39±0.83 5.59±0.41 5.61±0.49	Bulge-Loop miRNA qPCR Kit (Ribobio)	*p<0.05*	1 (1/0)
Parrizas M 2015 [89]	NR	NR	Serum	Newly diagnosed	27 (10/17)	NR	NR	NR	384-well panels (Exiqon) LC480 II thermocycler (Roche);	*p*<0.05	3 (2/1)
Parrizas M 2020 [90]	Spain	NR	Serum	Newly diagnosed	T2D: 7 pre-diabetic: 17	NR	NR	NR	384-well panels (Exiqon) in 7900HT RT-PCR system	*p<0.05*	4 (2/2)

					CTR: 8				(Thermo Fisher Scientific)		
Pek SLT 2016 [91]	Singapore	Jul 2008 to Mar 2012	Whole blood;	Newly diagnosed;	T2D-lean: 8 T2D-obese: 8 CTR-Lean: 8	50.5±9.8 38.0±8.1 42.3±9.3	22.4±2.6 37.0±13.0 21.3±1.4	NR	LNA qPCR	$p<0.05$	5 (0/5)
		NR	Visceral adipose tissues	Diagnosed	CTR-obese: 8 83 (26/57)	36.6±6.72 42.7±12.3 38.1±10.2	33.3±5.8 39.1±7.4 41.1±8.3				1 (0/1)
Peng R 2015 [92]	Chongqing, China	Jan 2012 to Sep 2014	Plasma	Diagnosed	T2D+DN: 20, CTR: 20	52.2±5.1 50.3±5.7	NR	7.6±1.0 NR	TaqMan miRNA Assays (Applied BioSystems)	$p<0.05$	2 (0/2)
Pescador N 2013 [93]	Madrid, Spain	NR	Serum	Diagnosed	T2D: 13 T2D+obese: 16 obese: 20 CTR: 20	69.40±7.12 67.55±11 41.7±11.18 42.9±12.13	24.86±1.49 33.38±2.86 42.73±4.67 22.7±2.43	NR	MiRCURY LNA microRNA PCR system	FC>5	4 (2/2)
Poddar S 2016 [94]	NR	NR	Skeletal muscle	Diagnosed	6 (3/3)	65-75 for all samples	NR	NR	TaqMan miRNA Assays and 7900 HT RT-PCR system (Applied Biosystems)	$p<0.05$	1 (0/1)
Polina ER 2019 [95]	Brazil	NR	Plasma	Diagnosed	20 each for T2D, T2D+PDR, T2D+NPDR, CTR	63±8 for all T2D groups	NR	8.4±1.5 for all T2D groups	TaqMan miRNA RT-PCR (Thermo Fisher Scientific)	$p<0.05$	1 (0/1)
Prabu P 2015 [96]	India	NR	Serum	Diagnosed	T2D: 49 Pre-diabetes: 47 CTR: 49	44.4±8.1 44.1±7.0 44.3±6.9	25.7±3.5 24.9±2.9 24.5±2.6	7.8±1.6 6.3±0.8 5.6±0.4	miRCURY LNA & SYBR Green Master Mix (Exiqon); ABI 7000 thermocycler	$p<0.05$	2 (2/0)
Prabu P 2020 [97]	India	NR	Serum	Diagnosed	40 each for T2D, T2D+DEP, CTR	54±6.0 54±7.0 48±10	25.4±4.9 25.5±3.7 26.0±4.2	8.8±2.0 8.6±2.2 5.7±0.45	miRCURY LNA & SYBR Green Master Mix (Exiqon)	$p<0.05$	1 (1/0)
Radović N 2018	Serbia	NR	Gingival	Diagnosed	T2D: 24	33.2	26.93	NR	TaqMan miRNA Assays and	$p<0.05$	2 (2/0)

[98]			crevicular fluid		T2D+CP: 24 CTR: 24	54.9 33.4	25.45 26.37		7500 HT RT-PCR system (Applied Biosystems)		
Ramirez HA 2015 [99]	Miami, USA	NR	Foot skin	Diagnosed	20 (10/10)	62.2±7.6 53.6±15.1	NR	NR	miRCURY LNA (Exiqon); Quanta qScript miRNA Quantification System	$p \le 0.05$	1 (1/0)
Rawal S 2017 [100]	New Zealand	NR	Right atrial appendage & left ventricular	Diagnosed	T2D+IHD: 8 IHD: 8 CTR: 5	NR	NR	NR	Quantitative RT-PCR analysis	$p<0.05$	2 (0/2)
Rawal S 2019 [101]	New Zealand	NR	Right atrial appendage & left ventricular	Diagnosed	T2D+IHD: 10 IHD: 10 CTR: 5	70.2±11.79 69.9±10.65 NR	28.74±5.59 27.51±3.58 NR	6.94±1.38 5.30±0.44 NR	Taqman hybridization probes ((Thermofisher, NZ)	$p<0.05$	1 (1/0)
Regmi A 2019 [102]	Hubei China	May 2014 to Mar 2015	Serum	Diagnosed	T2D: 50 T2D+DN: 42 CTR: 25	50.3±10.3 51.5±9.3 47.6±7.9	25.5±4.4 24.4±3.4 22.8±3.4	8.97±1.72 10.08±2.25 5.45±0.13	PrimeScript RT reagent kit with SYBR Premix Ex Taq (Takara Japan)	$p<0.05$	4 (2/2)
Rezk NA 2016 [103]	Egypt	NR	Serum	Diagnosed and newly diagnosed	T2D: 100 Pre-diabetes: 86 CTR: 100	48.2±8.2 46.3±7.9 45.7±8.4	22.9±5.1 21.6±3.8 23±3.1	8.7±1.9 6.6±0.72 5.4±0.6	MiScript SYBR Green PCR (Qiagen); ABI7500 RT-PCR system (Applied Biosystems)	$p<0.05$	1 (0/1)
Riches K 2014 [104]	Leeds, UK	Aug 2008 to Jan 2014	Smooth muscle cells of vessels	Diagnosed	20 (10/10)	NR	NR	NR	TaqMan miRNA Assays and 7500 HT RT-PCR system (Applied Biosystems)	$p<0.05$	2 (2/0)
Rojas LB 2016 [105]	Quito, Ecuador	2009 to 2012	Serum	Diagnosed	96 (56/40) for miR-146a 90 (53/37) for miR-574-3p	37-85 for all T2D 32-87 for all CTR	22-49 for all T2D 23-42 for all CTR	7.0 for all T2D 5.6 for all CTR	TaqMan miRNA Assays and 7900 HT RT-PCR system (Applied Biosystems)	$p \le 0.05$	2 (0/2)
Rong Y 2013 [106]	Hubei, China	Mar 2011 to Jun 2011	Plasma	Newly diagnosed	180 (90/90)	48.5 48	24.58±3.66 23.38±2.95	NR	TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	1 (1/0)

Rubie C 2019 [107]	Germany	NR	PBMCs	Diagnosed	56 (20/36)	56-88 for all samples	NR	NR	TaqMan miRNA RT Kit (Thermo Fisher)	$p<0.05$	1 (0/1)
Santovito D 2014 [108]	NR	NR	Plasma exosome	Diagnosed	30 (18/12)	57.2±9.6 48.5±12.4	31.6±5.1 32.9±5.4	9.6±1.5 5.7±0.5	mirCURY LNA (Exiqon); 7900HT (Applied Biosystems)	$p<0.05$	3 (1/2)
Sebastiani G 2015 [109]	NR	NR	Pancreatic islets	Diagnosed	11 (5/6)	71.2±9.8 NR	26.36 NR	NR	TaqMan miRNA Assays and 7900 HT RT-PCR system (Applied Biosystems)	$p<0.05$	1 (1/0)
Silva M 2019 [110]	Brazil	Mar 2015 to Nov 2017	Plasma	Diagnosed	111 (91/20) for miR-29b 199 (179/20) for miR-200b	61.1±8.2 for all T2D 45.5±7.5 for CTR	31.1±6.3 for all T2D NR for CTR	8.4±1.6 for all T2D NR for CTR	StepOnePlus RT-PCR System (Life Technologies)	$p<0.05$	2 (1/1)
Smit-McBride Z 2020 [111]	USA	Jun 2011 to Apr 2014	First: aqueous humor, plasma, vitreous humor validation: plasma	Diagnosed	First: T2D+PDR: 6 T2D+NPDR: 4 CTR: 10 Validation: same sample	NR	NR	NR	Affymetrix miRNA Array 3.0 (Affymetrix, Santa Clara) TaqMan assays (ThermoFisher Scientific)	$\|logFC\|\geq1.5$ $p<0.05$ $p<0.05$	3 (3/0) 35 (6/29) 16 (14/2) 28 (0/2)
Spinetti G 2013 [112]	NR	NR	Serum and PACs from PBMCs	Diagnosed	T2D+CLI/CTR:99(101)/18; T2D/CTR:6/5 T2D+CLI/CLI:6/6 T2D/CTR:52/17	71.2±9.3 for all T2D; 77.7±9.7 for CLI; 36.7±7.3for all CTR	NR	7.8±1.5 for all T2D	TaqMan-validated RT-PCR (Applied Biosystems)	$p<0.05$	19 (17/2)
Spinetti G 2020 [113]	NR	NR	BM-CD34⁺ cells BM-CD34⁺ cells; plasma, extracellular	Diagnosed	Screening: T2D: 7, T2D+CLI: 6, CTR: 6; Validation1:T2D: 4,T2D+CLI: 4, 5 for	NR	NR	NR	Screening: miRCURY LNA Universal RT-PCR (Exiqon) Validation: QuantStudio 6 Flex RT-PCR with miR	$p<0.05$	16 (8/8) 3 (0/3)

			vesicles of plasma		CRT; validation2: 4/4; validation3: 9/10; validation4: 4/5				TaqMan probes (Thermo Fisher)		1 (0/1) 1 (0/1) 1 (0/1)
Stępień EL 2018 [114]	Poland	NR	Ectosomes from plasma	Diagnosed	22 (11/11)	NR	NR	NR	miRCURY LNA PCR Panel with SYBR Green Master Mix Universal RT (Exiqon)	FC>2 & $p<0.05$	8 (7/1)
Sucharita S 2018 [115]	India	NR	Plasma	Diagnosed	60 (30/30)	50.5±6.3 42.1±7.8	27.3±4.6 27.3±4.7	8.4±2.0 5.5±0.4	TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	1 (1/0)
Sun K 2014 [116]	Xinjiang, China	2010 to 2011	Plasma	Diagnosed	200 (100/100)	51.33±11.75 48.55±12.41	26.30±4.08 24.44±4.63	NR	TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	1 (1/0)
Sun Q 2020 [117]	Sichuan China	Jun to Oct 2019	Serum	Newly diagnosed	60 (30/30)	42 – 75 for all samples	NR	NR	RT-qPCR	$p<0.05$	2 (2/0)
Tang WB 2018 [118]	China	Dec 2013 to Mar 2015	Serum	Diagnosed	T2D: 22 T2D+Micro:20 CTR: 30	59.5±8.7 60.7±9.6 59.8±12.4	25.1±3.9 26.2±3.5 24.3±5.6	9.4±2.3 8.9±2.3 NR	RT-qPCR	$p<0.05$	1 (1/0) 1 (1/0)
Togliatto G 2018 [119]	Torino Italy	NR	Carotid vascular tissue	Diagnosed	17 (11/6)	74.4±6.07 73.6±4.3	NR	NR	TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	1 (1/0)
Wang C 2016 [120]	Nanjing, China	Sep 2013 to Mar 2015.	Serum	Diagnosed and newly diagnosed	T2D: 92 T2D+complication: 92; CTR: 92 n=31 for each group of 4 miRNAs	47.7±13.9 52.4±13.1 50.2±14.2 NR	25.6±4.5 25.5±2.9 23.6±2.0 NR	9.8±2.9 10.3±2.7 5.3±0.4 NR	RT-qPCR	$p<0.05$	5 (5/0) 4 (4/0)
Wang H 2012 [121]	Guangxi, China	Mar 2010 to Mar 2011	PBMCs	Diagnosed	116 (30/86)	NR	NR	NR	All-in-One miRNA Q-PCR (GeneCopoeia)	$p<0.05$	1 (1/0)
Wang H 2018 [122]	China	Jan 2016 to	Serum	Diagnosed	56 (36/20)	52.5±7.0	NR	NR	miScript SYBR-Green PCR	$p<0.05$	1 (0/1)

		Jan 2017				55.6±4.5			kit (Qiagen)		
Wang JM 2014 [123]	China	NR	BM-Angiogenccells	Newly diagnosed	11 (6/5)	56±6.3 54±1.8	NR	NR	ABI PRISM 7500 Sequence Detection System (Ambion)	p<0.05	1 (0/1)
Wang S 2019 [124]	Jilin China	NR	Serum	Diagnosed	62 (33/29)	57.55±1.34 53.52±1.67	25.38±0.46 24.17±0.41	8.70±0.21 5.38±0.08	FastStart Universal SYBR Green Master (Roche)	p<0.05	2 (2/0)
Wang SS 2017 [125]	Beijing China	Mar 2015 to Oct 2015	PBMCs	Newly diagnosed	T2D: 117 Pre-diabetic: 74 CTR: 105	51.68±8.77 51.09±7.48 49.26±9.09	27.44±3.08 26.70±3.25 24.18±2.86	7.51±1.42 5.75±0.59 5.19±0.42	GeneAmp PCR System 9700; TaqMan miRNA assay (Applied Biosystems)	p<0.05	2 (1/1) 1 (1/0)
Wang WY 2019 [126]	Tianjin China	Oct 2014 to Jun 2015	Serum	Diagnosed	T2D: 69 T2D+CAD: 117 CTR: 68	64.29±3.77 64.73±8.22 62.98±7.42	25.61±5.76 26.44±3.31 24.08±2.42	6.80±2.41 8.22±2.64 5.29±0.33	SYBR Premix Ex Taq TM II (TaKaRa) with 7300 q-PCR system (Applied Biosystems)	p<0.05	1 (1/0)
Wang X 2014 [127]	Sweden and Iraq	Feb 2010 to Mar 2010	Plasma	Diagnosed	152 (33/119)	55.76±5.8 for all samples	28.33±1.27 for all samples	NR	miRCURY LNA miRNA PCR system (Exiqon)	FC>1.5	9 (9/0)
Widlansky ME 2018 [128]	USA	NR	Arterioles	Diagnosed	38 (18/20)	57±8 51±11	37.5±7.6 26.5±4.2	7.1±1.6 5.3±0.5	TaqMan chemistry with SYBR Green chemistry	p<0.05	3 (3/0)
Witkowski M 2020 [129]	Germany	NR	Plasma	Diagnosed	66 (46/20)	65.6±9.3 48.7±7.3	30.6 27.0±4.2	8.39±1.61 5.27±0.2	SYBR Green assays with SYBR Select Master Mix (applied Biosystems)	p<0.05	1 (0/1)
Wu L 2015 [130]	Guangzhou China	NR	Serum	Diagnosed	T2D: 25 T2D+obesity: 25 Obesity: 25 CTR: 25	46.7±8.6 46.1±12.6 42.6±11.8 45.5±10.2	23.5±2.1 33.1±1.9 34.2±1.5 22.6±2.6	NR	miRNeasy Mini Kit (Qiagen) 7900HT Fast RT-PCR System (Life Technologies)	p<0.05	4 (1/3)
Xavier DJ 2015 [131]	Brazil	NR	PBMCs	Diagnosed	18 (9/9) T2D+Hy/CTR: 9/9	NR	NR	NR	Human miRNAMicroarray kit (Agilent Technologies)	p<0.01, PFP<0.05	19 (13/6) 6 (4/2)
Xiang Y 2015 [132]	USA	NR	Plasma	Diagnosed	38 (30/8)	NR	NR	NR	qPCR	p<0.05	1 (0/1)

Xu Q 2014 [133]	Shanghai China	NR	EPCs from blood	Diagnosed	6 (3/3)	NR	NR	BR	TaqMan miRNA assay kits (Applied Biosystems)	p<0.05	1 (0/1)
Yan S 2016 [134]	Guizhou China	NR	Plasma	Newly diagnosed	T2D: 50 Pre-diabetic: 50 CTR: 50	46.22±6.90 44.18±6.13 45.52±6.22	25.41±0.32 25.39±0.32 25.56±0.38	8.69±0.36 6.53±0.31 5.41±0.29	MiScript SYBR Green PCR (Qiagen); ABI7500 RT-PCR system (Applied Biosystems)	p<0.05	3 (1/2) 4 (2/2)
Yan YX 2020 [135]	Beijing China	Aug 2016 to Dec 2017	Plasma	Newly diagnosed	362 (179/183)	56.9±10.17 55.2±10.65	26.80±3.20 24.47±3.34	7.47±1.45 5.23±0.42	LightCycler 480 SYBR Green I Master (Roche)	p<0.05	1 (1/0)
Yang F 2020 [136]	Jilin China	Aug 2017 to Jun 2018	Blood	Newly diagnosed	6 (3/3)	46.67 51.33	27.55 24.82	NR	Illumina Hiseq 4000 and 2500/2000 (Illumina Inc.)	|logFC|≥1.5 p<0.05	40 (20/20)
Yang S 2019 [137]	Jiangsu China	NR	Plasma	Diagnosed	150 (75/75)	NR	NR	BR	TaqMan miRNA assay kits with ABI RT-PCR 7900 system (Applied Biosystems)	p<0.05	12 (12/2)
Yang TT 2015 [138]	Shandong China	NR	Peripheral blood	Diagnosed	20 each for T2D, T2D+BDR, T2D+PDR, CTR	38-70 for all T2D, 35-65 for CTR	NR	NR	SYBR® Premix Ex Taq (Takara); CFX96TM RT PCR Detection System amplifier	p<0.05	1 (1/0)
Yang X 2017 [139]	Tianjin China	Jul 2015 to Mar 2016	Serum	Diagnosed	T2D: 92 T2D+micro: 87 T2D+macro: 51 CTR: 53	55.19±12.58 58.28±11.68 58.40±11.78 58.26±9.50	25.86±2.41 25.29±2.34 23.39±2.74 22.00±1.41	8.61±0.23 8.71±0.26 6.31±0.40 5.37±0.09	Mir-X miRNA qRT-PCR SYBR Kit (Takara)	p<0.05	2 (1/1)
Yang Z 2014 [140]	Zhejiang China	NR	Serum	Diagnosed	T2D: 24 Pre-diabetes: 20, CTR: 20	51.13±9.21 52.63±11.25 46.65±16.18	25.27±2.90 25.68±2.25 25.55±5.27	9.49±2.45 6.89±1.19 5.98±0.80	Solexa deep sequencing (Illumina); Platinum SYBR Green qPCR (Invitrogen)	p<0.05	8 (0/8)
Yang ZM 2016 [141]	Guangzhou, China	Oct 2013 to Dec 2013	Serum	Diagnosed	T2D+SDS: 5, T2D+BSS: 5, CTR: 5	57.0±7.0 59.4±9.0 NR	NR	NR	miRCURY LNA Universal RT miRNA PCR system (Exiqon)	FC>2.0 or <0.5; p<0.05	11 (11/0)
Yang ZM 2017	Guangzhou,	Oct 2013 to	Serum	Diagnosed	15 (10/5)	58.2±7.7	NR	NR	miRCURY LNA Universal RT	FC>3 or	7 (4/3)

[142]	China	Dec 2013				56.4±3.7			miRNA PCR system (Exiqon)	<0.33 *p*<0.05	
Ye M 2015 [143]	Shanghai China	NR	EPCs from blood	Diagnosed	40 (20/20)	64±9 60±10	24.7±5.1 24.7±1.8	NR	TaqMan real-time PCR (Germany)	*p*<0.05	1 (0/1)
Yi B 2016 [144]	Changsha, China	2012 and 2015	PBMCs	Diagnosed	30 each for T2D+Micro, CTR, T2D+Normo, T2D+Macro	NR	NR	NR	Applied Biosystems 7300 Real-time PCR system	*p*<0.05	1 (1/0)
Yin C 2020 [145]	Shandong China	2015 to 2017	Serum	Diagnosed	T2D: 40 T2D+NPDR: 60 T2D+PDR: 50 CTR: 60	50.23±3.81 50.73±3.80 51.40±3.93 50.85±5.20	21.78±1.84 22.07±2.732 2.61±3.1221 .81±2.20	6.61±0.59 7.31±0.28 8.00±0.34 4.92±0.46	SYBR green I Master Mix kit (Invitrogen) and 7300 PCR system (Applied Biosystems)	*p*<0.05	1 (1/0)
Zampetaki A 2010 [146]	Bolzano, Italy	1995 to 2005	Plasma	Diagnosed	160 (80/80)	66.3±8.9 66.3±8.9	28.0±4.4 25.0±4.0	6.5±1.4 5.4±0.3	TaqMan miRNA Assays (Applied Biosystems)	*p*<0.05	13 (1/12)
Zhang J 2017 [147]	Nanjing China	NR	Peripheral blood	Diagnosed	T2D: 93, T2D+DFU: 90 CTR: 79	66.22 67.19 63.04	25.0±3.9 23.8±4.3 24.1±3.2	NR	Taqman microRNA RT kit (Invitrogen); 7300 PCR System (Thermo Fisher Scientific)	*p*<0.05	1 (0/1)
Zhang JY 2016 [148]	Tianjin China	NR	Plasma	Diagnosed	T2D+DA/CTR: 240/240	NR	NR	NR	TaqMan miRNA Assays (Invitrogen)	*p*<0.05	6 (4/2)
Zhang T 2013 [149]	Shenzhen, China	NR	Plasma	Diagnosed	60 (30/30)	63±8.56 61±9	NR	NR	Bio-Rad CFX-96 qPCR system (Bio-Rad)	*p*<0.05	1 (0/1)
Zhang T 2015 [150]	Shenzhen China	2011 to 2013	Plasma	Diagnosed	40 (20/20)	61.20±10.62 57.25±9.64	24.53±2.87 23.90±2.34	NR	SYBR® Premix Dimer-Eraser kit (TaKaRa); Roche LightCycler RT-PCR	*p*<0.05	1 (0/1)
Zhang Y 2015	Jinan,	May 2012 to	Peripheral blood	Diagnosed	T2D+LLI-LM: 70	60.5±8.53	24.75±3.13	8.25±2.11	SYBR-green fluorescence	*p*<0.05	1 (0/1)

[151]	China	Dec 2013	platelets		T2D+LLI-S: 69 Nonidabetic: 60	60.8±8.2 51.0±10.2	26.42±3.51 22.32±1.73	8.66±1.78 5.09±0.41	RT-PCR		
Zhao B 2016 [152]	China	NR	Serum	Diagnosed	42 (21/21)	46.9±2.0 37.4±3.3	NR	NR	Quantitative RT-PCR analysis	$p<0.05$	1 (0/1)
Zhao H 2010 [153]	Hong Kong, China	NR	Pancreatic tissue	Diagnosed	55 (40/15)	69±13 54±14	NR	NR	TaqMan miRNA Assays (Applied BioSystems)	$p<0.05$	1 (1/0)
Zhou J 2013 [154]	Chongqing, China	2010 to 2012	Whole blood	Diagnosed	16 (7/9)	NR	NR	NR	LC sciences (Houston) TaqMan miRNA Assays (Applied Biosystems)	$p<0.05$	1 (1/0)
Zhu J 2020 [155]	Xinjiang China	2016 to 2018	Serum	Diagnosed	131 (59/72)	48.45±7.36 44.56±3.58	28.50±4.69 21.94±1.33	NR	miRcute plus miRNA SYBR Green qPCR Kit (cat#FP401, TianGen).	$p<0.05$	2 (2/0)
Zou HL 2017 [156]	Nanjing, China	Apr 2013 to Apr 2015	Plasma	Diagnosed	T2D: 65; T2D+DR: 75 CTR: 127	49.28±8.54 48.33±8.58 47.25±9.75	21.86±1.65 21.75±1.14 22.08±1.59	8.94±2.35 12.41±1.56 4.28±0.65	qRT-PCR (Qiagen Company)	$p<0.05$	1 (1/0)

Age, BMI and HbA1c are presented as mean±SD, range or mean. ASC, adipose-derived mesenchymal stem cells; ASO, arteriosclerosis of low extremity artery; BC, breast cancer; BDR, background diabetic retinopathy; BM, bone marrow-derived; BMI, body mass index; BSS, blood stasis syndrome; CAD, coronary artery disease; CHD, coronary heart disease; CLI, critical limb ischemia; CP or P, chronic periodontitis or periodontitis; DA, diabetic atherosclerosis; DC, diabetic complication; DFU, diabetic foot ulcers; DN, diabetic nephropathy; DR, diabetic retinopathy; DU, diabetic neuropathy; ED, erectile dysfunction; EPCs, endothelial progenitor cells; FC, fold change; FDR, false discovery rate; HCC, hepatocellular carcinoma; HF, heart failure; Hy, hyperglycemia; IHD, ischaemic heart disease; LLI-LM, low to moderate lower limb ischemia; LLI-S, severe lower limb ischemia; Macro, macroalbuminuria; Micro, microalbuminuria; MN, membranous nephropathy; Normo, normal albuminuria; NR, not reported; PACs, proangiogenic cells; PBMCs, peripheral blood mononuclear cells; PC, pancreatic cancer; (N)PDR, (non-)proliferative diabetic retinopathy, PFP, prediction of false positive; SAM, significance analysis of microarray; SDS, spleen-deficiency syndrome; T2D, type 2 diabetes

ESM Table 2. Quality assessment according to the MIAME and MIQE guideline

Source of bias	Raw data of hybridization	Actual data processing	Sample annotation and experimental variables	Experiment design	Annotation of array design	Experimental and data processing protocols
Al-Hayali MA 2019	H	L	U	U	L	L
Alicka M 2019	H	L	U	U	L	L
Alipoor B 2017	H	L	U	U	U	L
Al-Kafaji G 2015	H	L	L	L	U	L
Al-Kafaji G 2016	H	L	U	L	U	L
Al-Kafaji G 2017	H	L	L	L	L	L
Avgeris M 2020	H	L	U	L	L	L
Bai L 2019	H	L	U	H	H	L
Bai X 2016	H	L	H	U	U	L
Balasubramanyam M 2011	H	L	L	U	H	L
Baldeon RL 2015	H	L	H	H	H	L
Baltaci OF 2018	H	L	H	H	U	U
Bao L 2015	H	L	H	U	H	L
Blum A 2019	H	L	H	U	U	U
Bork-Jensen J 2015	L	L	H	U	U	U
Brovkina O 2019	H	L	U	H	U	U
Candia PD 2017	L	L	L	H	U	L
Cheng S 2018	H	L	H	H	L	U
Cheng Y 2020	H	U	H	H	U	H
Conserva F 2019	L	L	U	U	L	L
Corral-Fernandez NE 2013	H	L	H	H	U	L
Cui X 2017	H	L	U	H	U	U
Dahlmans D 2017	H	L	U	U	U	L

Dai X 2016	H	L	U	U	H	L
Dangwal S 2015	L	U	U	H	H	U
Deng X 2017	H	U	H	L	U	L
El Samaloty NM 2019	H	L	L	U	U	L
Elemeery MN 2019	H	L	H	H	L	L
Fejes Z 2017	H	L	L	L	U	L
Fomison-Nurse I 2018	H	L	U	H	U	L
Fulzele S 2015	H	U	H	H	H	H
Gallagher IJ 2010	L	L	U	L	L	L
Giannella A 2017	H	L	U	H	U	U
Guglielmi V 2017	H	U	H	U	H	L
Guo J 2017	H	U	H	U	U	L
Han YL 2016	H	L	U	L	L	L
He X 2016	H	L	U	U	L	L
He X 2018	H	L	H	U	U	L
Henriksen TI 2017	L	L	U	U	U	L
Hou X 2016	H	L	U	U	U	U
Hou XY 2016	H	L	H	U	U	L
Jansen F 2016	H	L	L	U	U	L
Jiang Q 2017	H	L	L	U	U	L
Jiang X 2015	H	L	L	L	U	L
Jiao Y 2015	H	L	H	H	H	L
Jones A 2017	H	L	L	H	L	L
Kamalden TA 2017	H	U	U	U	U	U
Karolina DS 2011	L	L	U	U	H	U
Karolina DS 2012	H	L	U	H	H	U

Katayama M 2019	L	L	H	H	L	U
Khan R 2020	L	L	L	U	U	U
Kloting N 2009	H	U	U	H	H	L
Kokkinopoulou I 2019	H	L	U	L	U	L
Kong L 2010	H	L	H	L	H	U
Kong L 2011	H	L	L	L	U	L
Krause C 2020	H	L	U	U	U	L
Kuschnerus K 2019	H	U	H	H	U	U
Lareyre F 2019	H	L	U	H	L	L
Latouche C 2016	L	L	U	H	U	L
Latreille M 2014	L	U	U	H	U	U
Li H 2019	H	L	H	U	U	U
Li MY 2016	H	L	L	U	H	L
Li YB 2017	H	L	U	U	U	L
Lian W 2018	H	L	L	H	L	L
Liang L 2016	L	L	H	U	U	L
Liang YZ 2018	L	L	L	L	L	L
Liang Z 2018	H	L	L	L	L	L
Liu H 2016	H	L	U	U	U	L
Liu Y 2017	H	L	H	H	U	L
Locke JM 2014	H	L	H	H	H	U
Long Y 2017	H	L	U	U	U	L
Lu H 2010	L	L	U	U	L	U
Luo M 2015	H	L	H	L	U	L
Luo M 2019 [74]	H	L	H	H	H	L
Luo M 2019 [75]	H	L	L	H	U	L

Mao G 2014	H	U	H	H	U	L
Massaro JD 2019	L	L	U	L	L	L
Massart J 2017	H	L	U	H	U	U
Matsha TE 2018	H	L	H	H	U	U
Mazloom H 2015	H	U	U	H	U	L
Meng S 2012	H	L	U	U	U	U
Meng S 2013	H	U	U	U	U	U
Mensà E 2019	H	L	H	H	H	L
Monfared YK 2019	H	L	H	U	U	U
Mononen N 2019	H	L	L	H	L	L
Ortega FJ 2010	L	L	U	U	U	L
Ortega FJ 2014	H	L	U	H	U	U
Ou L 2019	H	L	U	U	U	U
Parrizas M 2015	H	L	U	H	L	L
Parrizas M 2019	H	L	U	H	L	L
Pek SLT 2016	H	L	U	H	H	L
Peng R 2015	H	L	H	L	U	L
Pescador N 2013	L	L	L	H	U	U
Poddar S 2016	H	L	H	U	U	U
Polina ER 2019	L	L	U	L	L	L
Prabu P 2015	H	L	L	H	U	L
Prabu P 2020	H	L	L	H	U	L
Radović N 2018	H	L	U	H	U	L
Ramirez HA 2015	L	L	H	U	U	L
Rawal S 2017	H	L	H	H	U	U
Rawal S 2019	H	L	U	H	U	U

Regmi A 2019	H	L	L	U	L	L
Rezk NA 2016	H	U	L	U	U	L
Riches K 2014	H	L	H	H	H	U
Rojas LB 2016	H	L	U	U	H	L
Rong Y 2013	H	L	U	U	U	L
Rubie C 2019	H	L	H	L	U	U
Santovito D 2014	H	L	H	H	H	L
Sebastiani G 2015	H	L	H	L	U	L
Silva M 2019	L	L	U	L	L	L
Smit-McBride Z 2020	L	U	U	U	U	L
Spinetti G 2013	H	L	U	U	U	U
Spinetti G 2020	H	L	H	H	L	L
Stępień EL 2018	H	L	L	U	U	L
Sucharita S 2018	H	L	L	L	U	U
Sun K 2014	H	L	U	U	U	L
Sun Q 2020	H	L	H	H	H	U
Tang WB 2018	H	U	U	H	H	H
Togliatto G 2018	H	L	U	U	U	L
Wang C 2016	H	L	L	L	U	L
Wang H 2012	H	L	H	L	H	U
Wang H 2018	H	L	U	L	U	L
Wang JM 2014	H	L	U	H	U	U
Wang S 2019	H	L	H	H	U	U
Wang SS 2017	H	L	L	L	U	L
Wang WY 2019	H	L	U	L	L	L
Wang X 2014	H	U	U	L	U	L

Widlansky ME 2018	L	L	L	H	U	L
Witkowski M 2020	H	L	U	H	U	L
Wu L 2015	H	L	H	H	U	U
Xavier DJ 2015	L	L	H	H	H	L
Xiang Y 2015	H	L	H	U	H	U
Xu Q 2014	H	U	H	U	H	U
Yan S 2016	H	L	L	L	U	L
Yan YX 2020	H	U	U	U	U	U
Yang F 2020	U	L	H	U	U	L
Yang S 2019	H	U	H	L	U	L
Yang TT 2015	H	U	U	H	H	U
Yang X 2017	H	L	L	L	U	U
Yang Z 2014	H	L	U	L	U	L
Yang ZM 2016	H	L	H	U	H	L
Yang ZM 2017	H	L	U	U	H	L
Ye M 2015	H	L	U	H	U	U
Yi B 2016	H	L	U	H	U	L
Yin C 2020	H	L	U	H	U	L
Zampetaki A 2010	H	L	L	L	H	U
Zhang J 2017	H	L	H	H	U	L
Zhang JY 2016	H	L	H	H	H	L
Zhang T 2013	H	U	H	H	U	U
Zhang T 2015	H	L	H	H	H	U
Zhang Y 2015	H	L	H	L	U	L
Zhao B 2016	H	L	H	H	H	U
Zhao H 2010	H	U	H	L	U	L

Zhou J 2013	H	U	H	U	H	U
Zhu J 2020	H	L	U	U	U	L
Zou HL 2017	H	L	L	L	U	L

Abbreviations: H, high risk; L, low risk; U, unclear risk.

ESM Table 3. Statistically significant dysregulation of miRNAs in type 2 diabetes (n= 60)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-29a-3p	8	352	6.838	[5.4211, 8.2548]	2.77E-19
	miR-375	4	307	7.8447	[5.7837, 9.9057]	7.69E-12
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	1.10E-11
	miR-4463	5	138	6.6571	[4.8722, 8.4420]	2.38E-11
	miR-346	3	180	8.2217	[5.9401, 10.5034]	1.45E-10
	miR-9-5p	4	152	6.8044	[4.8003, 8.8084]	2.53E-09
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-302a-3p	4	124	6.4617	[4.4525, 8.4709]	2.59E-08
	miR-208a	4	70	5.769	[3.7527, 7.7854]	1.82E-06
	miR-181a-2-3p	2	116	7.77	[4.9635, 10.5764]	5.12E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	6.41E-05
	miR-142-5p	2	110	7.5032	[4.3913, 10.6150]	2.04E-04
	miR-140-3p	3	48	5.576	[3.2412, 7.9109]	2.55E-04
	miR-19b-3p	3	49	5.5337	[3.1943, 7.8730]	3.16E-04
	miR-148a-3p	4	913	7.7662	[4.4735, 11.0589]	3.37E-04
	miR-32-5p	2	45	6.2739	[3.4413, 9.1064]	1.26E-03
	miR-187-3p	2	40	6.0845	[3.2472, 8.9218]	2.34E-03
	miR-589	2	107	7.3325	[3.8801, 10.7850]	2.80E-03
	miR-136-5p	2	37	5.7482	[2.8907, 8.6058]	7.17E-03
	miR-4695-5p	2	32	5.6095	[2.7527, 8.4663]	1.06E-02
	miR-29c-3p	8	178	4.8667	[2.3283, 7.4050]	1.52E-02
	miR-296-5p	2	29	5.4174	[2.5522, 8.2826]	1.88E-02
	miR-302b-3p	2	28	5.3521	[2.4830, 8.2212]	2.28E-02
	miR-483-3p	2	26	5.2619	[2.3911, 8.1327]	2.91E-02
	miR-455-3p	2	28	5.2417	[2.3620, 8.1214]	3.20E-02
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	3.56E-02
	miR-320a	14	867	5.2885	[2.2857, 8.2914]	4.96E-02
Down-regulation	miR-30c-5p	6	305	7.4205	[5.7924, 9.0485]	3.68E-17
	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	5.27E-17
	miR-198	2	850	12.1054	[9.3304, 14.8805]	1.09E-15
	miR-593	4	200	7.8637	[5.8846, 9.8427]	6.08E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	7.89E-13
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	1.11E-10
	miR-10b-5p	3	150	7.4974	[5.2028, 9.7920]	1.34E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	3.69E-08
	miR-423-3p	4	149	6.5331	[4.4836, 8.5826]	3.70E-08

miR-374b-5p	3	134	7.1157	[4.8121, 9.4194]	1.25E-07
miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.59E-07
miR-4477a	2	133	8.3626	[5.5690, 11.1563]	3.95E-07
miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	3.95E-07
miR-378	4	64	5.6664	[3.6496, 7.6832]	3.25E-06
miR-126a	2	93	7.5237	[4.7159, 10.3316]	1.34E-05
miR-182-5p	3	56	5.8221	[3.4929, 8.1512]	8.56E-05
miR-1228-3p	3	37	5.0521	[2.6954, 7.4087]	2.36E-03
miR-766-3p	3	35	4.9924	[2.6343, 7.3505]	2.96E-03
miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	3.84E-03
miR-1281	3	34	4.9235	[2.5616, 7.2853]	3.91E-03
miR-660-5p	3	35	4.9138	[2.5467, 7.2809]	4.21E-03
miR-409-3p	2	37	5.8618	[3.0131, 8.7104]	4.90E-03
miR-1246	3	30	4.7846	[2.4197, 7.1495]	6.52E-03
miR-1275	2	30	5.44	[2.5724, 8.3076]	1.78E-02
miR-1973	2	30	5.44	[2.5724, 8.3076]	1.78E-02
miR-199b-5p	2	104	7.1309	[3.2754, 10.9865]	2.57E-02
miR-331-3p	2	104	7.1309	[3.2754, 10.9865]	2.57E-02
miR-18b-5p	2	26	5.1858	[2.3077, 8.0638]	3.68E-02
miR-30a-3p	2	25	5.1408	[2.2614, 8.0203]	4.16E-02

ESM Table 4. Statistically significant dysregulation of miRNAs in pancreas (n=1)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-187-3p	2	40	6.0845	[3.2472-8.9218]	2.63E-05

ESM Table 5. Statistically significant dysregulation of miRNAs in heart (n=2)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-208a	4	70	5.7690	[3.7527, 7.7854]	4.10E-08
Down-regulation	miR-15b-5p	3	42	5.3777	[3.0372, 7.7181]	1.34E-05

ESM Table 6. Statistically significant dysregulation of miRNAs in kidney (n=1)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-1228-3p	3	37	5.0521	[2.6954, 7.4087]	1.09E-03

ESM Table 7. Statistically significant dysregulation of miRNAs in adipose (n=6)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-125b-5p	2	85	7.051	[4.0961, 10.0059]	1.75E-05
	miR-140-3p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-145-5p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-146a-5p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-16-5p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-24-3p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03

ESM Table 8. Statistically significant dysregulation of miRNAs in muscle (n=5)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-143-3p	2	112	7.6017	[4.6859-10.5174]	1.61E-06
Down-regulation	miR-10b-5p	2	114	7.6901	[4.8813-10.4989]	4.02E-07
	miR-10a-5p	2	108	7.3939	[4.0640-10.7237]	6.75E-05
	miR-27b-3p	2	108	7.3939	[4.0640-10.7237]	6.75E-05
	miR-363-3p	2	33	5.6293	[2.7711-8.4876]	5.65E-04

ESM Table 9. Statistically significant dysregulation of miRNAs in blood (n=50)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-29a-3p	4	272	7.8323	[5.8456, 9.8190]	6.71E-13
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	7.56E-12
	miR-346	3	180	8.2217	[5.9401, 10.5034]	9.94E-11
	miR-9-5p	4	152	6.8044	[4.8003, 8.8084]	1.73E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-4463	4	112	6.686	[4.6910, 8.6810]	3.10E-09
	miR-572	2	200	9.2302	[6.4447, 12.0157]	5.08E-09
	miR-128-3p	2	160	8.7889	[6.0000, 11.5778]	4.00E-08
	miR-302a-3p	3	112	6.8914	[4.5807, 9.2022]	3.09E-07
	miR-374a-5p	2	120	7.7535	[4.8930, 10.6139]	6.59E-06
	miR-375	3	252	7.836	[4.9199, 10.7521]	8.48E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	4.39E-05
	miR-320c	3	49	5.6282	[3.2948, 7.9617]	1.38E-04
	miR-148a-3p	4	913	7.7662	[4.4735, 11.0589]	2.31E-04
	miR-193b-3p	2	49	6.4626	[3.6362, 9.2890]	4.52E-04
	miR-101-3p	2	45	6.2739	[3.4413, 9.1064]	8.66E-04
	miR-32-5p	2	45	6.2739	[3.4413, 9.1064]	8.66E-04
	miR-1260a	2	42	6.165	[3.3298, 9.0002]	1.24E-03
	miR-19b-3p	2	39	5.9061	[3.0575, 8.7546]	2.95E-03
	miR-136-5p	2	37	5.7482	[2.8907, 8.6058]	4.92E-03
	miR-302b-3p	2	28	5.3521	[2.4830, 8.2212]	1.56E-02
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	2.44E-02
	miR-335-5p	2	165	7.8129	[3.4098, 12.2160]	3.05E-02
	miR-132-3p	2	23	5.0466	[2.1656, 7.9277]	3.63E-02
	miR-135a-5p	2	90	6.8317	[2.9193, 10.7441]	3.78E-02
	miR-188-3p	2	26	5.0382	[2.1401, 7.9363]	4.00E-02
Down-regulation	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	3.61E-17
	miR-30c-5p	5	295	7.9181	[6.1442, 9.6919]	1.32E-16
	miR-198	2	850	12.1054	[9.3304, 14.8805]	7.50E-16
	miR-593	4	200	7.8637	[5.8846, 9.8427]	4.17E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	5.41E-13
	miR-197-3p	3	283	8.6733	[6.3905, 10.9560]	5.83E-12
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.09E-07
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	2.71E-07
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	2.71E-07
	miR-378	4	64	5.6664	[3.6496, 7.6832]	2.23E-06

miR-152-3p	2	100	7.8637	[5.0648, 10.6625]	2.23E-06
miR-126a	2	93	7.5237	[4.7159, 10.3316]	9.21E-06
miR-503-5p	2	69	7.1099	[4.2982, 9.9217]	4.39E-05
miR-182-5p	3	56	5.8221	[3.4929, 8.1512]	5.87E-05
miR-423-3p	3	57	5.6437	[3.3040, 7.9835]	1.38E-04
miR-374b-5p	2	42	6.1041	[3.2648, 8.9434]	1.53E-03
miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	2.64E-03
miR-660-5p	3	35	4.9138	[2.5467, 7.2809]	2.89E-03
miR-409-3p	2	37	5.8618	[3.0131, 8.7104]	3.36E-03
miR-214-3p	2	89	6.9567	[3.4471, 10.4663]	6.22E-03

ESM Table 10. Statistically significant dysregulation of miRNAs in PBMCs (n = 12)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-18a-5p	2	413	10.6376	[7.8589, 13.4163]	7.48E-13
	miR-346	3	180	8.2217	[5.9401, 10.5034]	1.96E-11
	miR-29b-3p	2	36	5.8889	[3.0451, 8.7327]	5.93E-04
	miR-222-3p	2	36	5.8889	[3.0451, 8.7327]	5.93E-04
	miR-186-5p	2	36	5.8889	[3.0451, 8.7327]	5.93E-04
	miR-188-3p	2	26	5.0382	[2.1401, 7.9363]	7.87E-03
	miR-20a-5p	2	26	5.0382	[2.1401, 7.9363]	7.87E-03
Down-regulation	miR-146a-5p	3	140	7.6934	[5.4058, 9.9810]	5.22E-10
	miR-144-5p	2	133	8.3626	[5.5690, 11.1563]	5.33E-08
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	5.33E-08
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	5.33E-08
	miR-155-5p	2	80	7.4271	[4.6217, 10.2326]	2.54E-06

ESM Table 11. Statistically significant dysregulation of miRNAs in whole blood (n = 25)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-122-5p	2	889	10.5404	[7.7535, 13.3273]	3.10E-12
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	3.10E-12
	miR-155-5p	3	120	7.4271	[5.1365, 9.7177]	5.20E-09
	miR-103a-3p	2	120	7.8123	[5.0062, 10.6185]	1.22E-06
	miR-15b-5p	2	48	6.4378	[3.6111, 9.2645]	2.01E-04
	miR-26b-5p	2	39	5.9944	[3.1524, 8.8363]	8.90E-04
	miR-151a-5p	2	39	5.9944	[3.1524, 8.8363]	8.90E-04
	miR-150-5p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-192-5p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-27a-3p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-320a	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-148a-3p	3	895	8.3771	[4.0588, 12.6953]	3.58E-03
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	1.00E-02
	miR-151a-3p	2	21	4.7465	[1.8376, 7.6554]	3.45E-02
Down-regulation	miR-24-3p	4	211	7.6194	[5.6304, 9.6085]	1.50E-12
	miR-378	4	64	5.6664	[3.6496, 7.6832]	9.13E-07
	miR-486-5p	2	48	6.4378	[3.6111, 9.2645]	2.01E-04
	miR-342-3p	2	48	6.305	[3.4702, 9.1397]	3.25E-04
	miR-17-5p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-210-3p	2	32	5.6664	[2.8143, 8.5186]	2.47E-03
	let-7f-5p	2	89	6.9567	[3.4471, 10.4663]	2.55E-03
	miR-214-3p	2	89	6.9567	[3.4471, 10.4663]	2.55E-03
	miR-20a-5p	2	21	4.7465	[1.8376, 7.6554]	3.45E-02
	miR-660-5p	2	21	4.7465	[1.8376, 7.6554]	3.45E-02

ESM Table 12. Statistically significant dysregulation of miRNAs in serum (n = 38)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-210-3p	4	540	9.6747	[7.7066, 11.6429]	2.29E-20
	miR-221-3p	6	793	8.7013	[6.8069, 10.5957]	8.80E-18
	miR-29a-3p	3	257	8.5626	[6.2811, 10.8441]	7.60E-12
	miR-15a-5p	4	209	6.8546	[4.8481, 8.8610]	8.60E-10
	miR-125b-5p	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-130b-3p	2	194	9.1696	[6.3837, 11.9555]	4.44E-09
	miR-99b-5p	4	162	6.6902	[4.6173, 8.7631]	1.01E-08
	miR-128-3p	2	160	8.7889	[6.0000, 11.5778]	2.62E-08
	miR-302a-3p	3	112	6.8914	[4.5807, 9.2022]	2.02E-07
	miR-9-5p	3	107	6.8083	[4.4964, 9.1202]	3.14E-07
	miR-27b-3p	3	85	6.1699	[3.8419, 8.4978]	8.20E-06
	miR-24-3p	4	200	6.5303	[4.0615, 8.9991]	8.68E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	2.88E-05
	miR-124-3p	2	47	6.0729	[3.2224, 8.9235]	1.19E-03
	miR-194-5p	2	39	5.9049	[3.0577, 8.7521]	1.92E-03
	miR-150-5p	2	49	5.9913	[2.9747, 9.0079]	3.96E-03
	miR-20b-5p	2	49	5.9913	[2.9747, 9.0079]	3.96E-03
	miR-107	2	23	5.0466	[2.1656, 7.9277]	2.39E-02
	miR-132-3p	2	23	5.0466	[2.1656, 7.9277]	2.39E-02
	miR-1304-5p	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
	miR-302d-3p	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
Down-regulation	miR-198	2	850	12.1054	[9.3304, 14.8805]	4.92E-16
	miR-593	4	200	7.8637	[5.8846, 9.8427]	2.73E-13
	miR-1-3p	3	270	9.0217	[6.7461, 11.2973]	3.13E-13
	miR-192-5p	4	381	7.7446	[5.3532, 10.1360]	8.76E-09
	miR-152-3p	2	100	7.8637	[5.0648, 10.6625]	1.46E-06
	miR-186-5p	2	88	7.6054	[4.8027, 10.4081]	4.20E-06
	miR-503-5p	2	69	7.1099	[4.2982, 9.9217]	2.88E-05
	miR-423-3p	3	57	5.6437	[3.3040, 7.9835]	9.08E-05
	let-7i-5p	2	54	6.2461	[3.3984, 9.0939]	6.88E-04
	miR-1246	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
	miR-6131	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
	miR-98-5p	2	20	4.7958	[1.9007, 7.6908]	4.67E-02

ESM Table 13. Statistically significant dysregulation of miRNAs in plasma (n = 25)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-144-3p	6	951	9.2375	[7.4044, 11.0707]	1.37E-21
	miR-93-5p	4	564	9.3044	[7.2507, 11.3582]	1.75E-17
	miR-34a-5p	5	183	7.0493	[5.2683, 8.8303]	2.25E-13
	miR-4463	4	112	6.686	[4.6910, 8.6810]	1.32E-09
	miR-572	2	200	9.2302	[6.4447, 12.0157]	2.16E-09
	miR-29c-3p	2	95	7.5697	[4.7632, 10.3762]	3.25E-06
	miR-30b-5p	2	172	8.1724	[4.4843, 11.8604]	3.64E-04
	miR-199a-3p	2	42	6.1802	[3.3460, 9.0144]	4.99E-04
	miR-320c	2	34	5.6717	[2.8136, 8.5298]	2.60E-03
Down-regulation	miR-30c-5p	4	280	8.4854	[6.5111, 10.4596]	9.46E-16
	miR-223-3p	4	309	8.4201	[6.4439, 10.3962]	1.76E-15
	miR-130b-3p	3	140	7.5897	[5.2989, 9.8804]	2.18E-09
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	4.65E-08
	miR-185-5p	2	125	8.2932	[5.4995, 11.0870]	1.55E-07
	miR-126-3p	14	1421	7.5404	[4.8784, 10.2024]	7.36E-07
	miR-26a-5p	2	162	8.2401	[5.1650, 11.3151]	3.90E-06
	miR-126a	2	93	7.5237	[4.7159, 10.3316]	3.93E-06
	miR-125b-5p	2	93	7.5237	[4.7159, 10.3316]	3.93E-06
	miR-26b-5p	2	78	7.2781	[4.4681, 10.0880]	9.98E-06
	miR-195-5p	2	85	7.2492	[4.4345, 10.0639]	1.16E-05
	miR-197-3p	2	187	8.4249	[4.9854, 11.8644]	4.11E-05
	miR-192-5p	2	79	6.8486	[3.7805, 9.9167]	3.15E-04
	miR-15b-5p	2	41	5.9617	[3.1116, 8.8118]	1.08E-03
	miR-182-5p	2	41	5.9617	[3.1116, 8.8118]	1.08E-03
	miR-20a-5p	2	30	5.4271	[2.5589, 8.2953]	5.41E-03

ESM Table 14. Statistically significant dysregulation of miRNAs in blood fractions (n=87)

miRNA	Whole blood	PBMCs	Serum	Plasma
let-7f-5p	-1			
let-7i-5p			-1	
miR-1-3p			-1	
miR-103a-3p	1			
miR-107			1	
miR-122-5p	1			
miR-124-3p			1	
miR-1246			-1	
miR-125b-5p			1	-1
miR-126-3p				-1
miR-126a				-1
miR-128-3p			1	
miR-1303			1	
miR-130b-3p			1	-1
miR-132-3p			1	
miR-1304-5p			1	
miR-144-3p				1
miR-144-5p		-1		
miR-146a-5p		-1		
miR-148a-3p	1			
miR-150-5p	1		1	
miR-151a-3p	1			
miR-151a-5p	1			
miR-152-3p			-1	
miR-155-5p	1	-1		
miR-15a-5p			1	
miR-15b-5p	1			-1
miR-17-5p	-1			
miR-182-5p				-1
miR-185-5p				-1
miR-186-5p		1	-1	
miR-188-3p		1		
miR-18a-5p		1		
miR-192-5p	1		-1	-1
miR-194-5p			1	
miR-195-5p				-1
miR-197-3p				-1
miR-198			-1	
miR-199a-3p				1
miR-20a-5p	-1	1		-1
miR-20b-5p			1	
miR-200b-3p				-1

miR-210-3p	-1		1	
miR-214-3p	-1			
miR-221-3p			1	
miR-222-3p		1		
miR-223-3p				-1
miR-24-3p	-1		1	
miR-26a-5p				-1
miR-26b-5p	1			-1
miR-27a-3p	1			
miR-27b-3p			1	
miR-29a-3p			1	
miR-29b-3p		1		
miR-29c-3p				1
miR-30b-5p				1
miR-30c-5p				-1
miR-302a-3p			1	
miR-302d-3p			1	
miR-320a	1			
miR-320c				1
miR-342-3p	-1			
miR-346		1		
miR-34a-5p				1
miR-376a-3p			1	
miR-378	-1			
miR-423-3p			-1	
miR-4463				1
miR-4477a		-1		
miR-4714-3p		-1		
miR-486-5p	-1			
miR-503-5p			-1	
miR-548o-3p	1			
miR-571			1	
miR-572				1
miR-589-3p	1			
miR-593			-1	
miR-6131			-1	
miR-652-3p	-1			
miR-660-5p	-1			
miR-661			1	
miR-770-5p			1	
miR-892b			1	
miR-9-5p			1	
miR-93-5p				1
miR-98-5p			-1	

miR-99b-5p	1

"1" indicates up-regulation and "-1" indicates down-regulation

ESM Table 15. Statistically significant dysregulation of miRNAs detected by PCR-based methods (n = 61)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-144-3p	12	1105	7.4909	[5.9441, 9.0376]	1.99E-19
	miR-29a-3p	8	352	6.838	[5.4211, 8.2548]	2.74E-19
	miR-29c-3p	7	172	6.1063	[4.5842, 7.6284]	3.30E-13
	miR-375	4	307	7.8447	[5.7837, 9.9057]	7.60E-12
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	1.09E-11
	miR-4463	5	138	6.6571	[4.8722, 8.4420]	2.35E-11
	miR-346	3	180	8.2217	[5.9401, 10.5034]	1.43E-10
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-302a-3p	3	114	6.9902	[4.6842, 9.2962]	2.49E-07
	miR-148a-3p	3	907	9.0134	[5.9592, 12.0675]	6.42E-07
	miR-9-5p	3	107	6.8083	[4.4964, 9.1202]	6.90E-07
	miR-208a	4	70	5.769	[3.7527, 7.7854]	1.80E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	6.34E-05
	miR-142-5p	2	110	7.5032	[4.3913, 10.6150]	2.02E-04
	miR-19b-3p	3	49	5.5337	[3.1943, 7.8730]	3.12E-04
	miR-30b-5p	3	182	7.0629	[3.9743, 10.1516]	6.51E-04
	miR-32-5p	2	45	6.2739	[3.4413, 9.1064]	1.25E-03
	miR-187-3p	2	40	6.0845	[3.2472, 8.9218]	2.31E-03
	miR-589	2	107	7.3325	[3.8801, 10.7850]	2.77E-03
	miR-136-5p	2	37	5.7482	[2.8907, 8.6058]	7.09E-03
	miR-4695-5p	2	32	5.6095	[2.7527, 8.4663]	1.05E-02
	miR-296-5p	2	29	5.4174	[2.5522, 8.2826]	1.85E-02
	miR-483-3p	2	26	5.2619	[2.3911, 8.1327]	2.88E-02
	miR-455-3p	2	28	5.2417	[2.3620, 8.1214]	3.17E-02
	miR-140-3p	2	24	5.1299	[2.2535, 8.0063]	4.16E-02
	miR-320a	14	867	5.2885	[2.2857, 8.2914]	4.90E-02
Down-regulation	miR-30c-5p	6	305	7.4205	[5.7924, 9.0485]	3.63E-17
	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	5.21E-17
	miR-198	2	850	12.1054	[9.3304, 14.8805]	1.08E-15
	miR-100-5p	6	239	6.7735	[5.1393, 8.4077]	3.98E-14
	miR-593	4	200	7.8637	[5.8846, 9.8427]	6.01E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	7.81E-13
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	1.10E-10
	miR-10b-5p	3	150	7.4974	[5.2028, 9.7920]	1.33E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	3.65E-08

	miR-374b-5p	3	134	7.1157	[4.8121, 9.4194]	1.24E-07
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.58E-07
	miR-423-3p	3	139	7.0851	[4.6864, 9.4838]	6.22E-07
	miR-98-5p	3	179	7.5765	[4.9474, 10.2056]	1.43E-06
	miR-378	4	64	5.6664	[3.6496, 7.6832]	3.21E-06
	miR-126a	2	93	7.5237	[4.7159, 10.3316]	1.33E-05
	miR-363-3p	4	55	5.2327	[3.1969, 7.2685]	4.14E-05
	miR-182-5p	3	56	5.8221	[3.4929, 8.1512]	8.47E-05
	miR-30e-3p	2	49	6.4626	[3.6362, 9.2890]	6.52E-04
	miR-1228-3p	3	37	5.0521	[2.6954, 7.4087]	2.33E-03
	miR-766-3p	3	35	4.9924	[2.6343, 7.3505]	2.93E-03
	miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	3.80E-03
	miR-1281	3	34	4.9235	[2.5616, 7.2853]	3.86E-03
	miR-409-3p	2	37	5.8618	[3.0131, 8.7104]	4.85E-03
	miR-1275	2	30	5.44	[2.5724, 8.3076]	1.76E-02
	miR-1973	2	30	5.44	[2.5724, 8.3076]	1.76E-02
	miR-660-5p	2	29	5.3927	[2.5242, 8.2612]	2.02E-02
	miR-199b-5p	2	104	7.1309	[3.2754, 10.9865]	2.54E-02
	miR-331-3p	2	104	7.1309	[3.2754, 10.9865]	2.54E-02
	miR-223-3p	8	392	5.9465	[2.7269, 9.1661]	2.59E-02
	miR-18b-5p	2	26	5.1858	[2.3077, 8.0638]	3.63E-02
	miR-30a-3p	2	25	5.1408	[2.2614, 8.0203]	4.11E-02

ESM Table 16. Statistically significant dysregulation of miRNAs detected by RNA-Seq (n=11)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-15b-5p	2	48	6.4378	[3.6111, 9.2645]	8.86E-05
	miR-99b-5p	2	34	5.6364	[2.7761, 8.4967]	1.23E-03
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	4.40E-03
Down-regulation	miR-144-3p	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-144-5p	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-486-5p	3	58	5.9077	[3.5816, 8.2339]	7.07E-06
	miR-126-5p	2	16	4.3543	[1.4258, 7.2828]	3.93E-02
	miR-16-5p	2	16	4.3543	[1.4258, 7.2828]	3.93E-02
	miR-30b-5p	2	16	4.3543	[1.4258, 7.2828]	3.93E-02

ESM Table 17. Statistically significant dysregulation of miRNAs in sensitivity analysis based on sample sizes (n=90)

Sample size	Direction of regulation	miRNA	No. of sub-studies	Pooled sample size	Overall effect		
					LogOR	[95%CI]	Adjusted *p* values
No less than 25	Up- regulation	miR-93-5p	5	716	9.7747	[8.0145, 11.5348]	7.67E-26
		miR-210-3p	4	540	9.6747	[7.7066, 11.6429]	3.20E-20
		miR-29a-3p	4	295	8.2552	[6.2771, 10.2333]	1.60E-15
		miR-222-3p	4	203	7.7746	[5.7929, 9.7562]	8.29E-13
		miR-30d-5p	3	313	8.7249	[6.4439, 11.0060]	3.67E-12
		miR-148a-3p	2	889	10.5404	[7.7535, 13.3273]	6.94E-12
		miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	6.94E-12
		miR-375	3	292	8.5832	[6.3000, 10.8664]	9.69E-12
		miR-346	3	180	8.2217	[5.9401, 10.5034]	9.13E-11
		miR-1303	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-661	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-892b	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-571	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-572	2	200	9.2302	[6.4447, 12.0157]	4.66E-09
		miR-9-5p	3	142	7.4373	[5.1390, 9.7355]	1.27E-08
		miR-4463	3	90	6.8025	[4.5007, 9.1044]	3.89E-07
		miR-146b-5p	2	221	8.8849	[5.8523, 11.9175]	5.23E-07
		miR-302a-3p	2	102	7.871	[5.0718, 10.6702]	1.99E-06
		miR-451a	2	119	7.8737	[5.0699, 10.6776]	2.08E-06
		miR-29c-3p	2	95	7.5697	[4.7632, 10.3762]	7.00E-06
		miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	4.03E-05

	miR-4306	2	64	6.9324	[4.1164, 9.7485]	7.84E-05
	miR-19a-3p	2	187	8.4249	[4.9854, 11.8644]	8.85E-05
Down-regulation	miR-223-3p	5	343	8.16	[6.3904, 9.9296]	8.96E-18
	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	3.32E-17
	miR-197-3p	4	353	8.6362	[6.6601, 10.6123]	6.05E-16
	miR-198	2	850	12.1054	[9.3304, 14.8805]	6.89E-16
	miR-30c-5p	4	280	8.4854	[6.5111, 10.4596]	2.04E-15
	miR-144-5p	3	746	9.2328	[6.9538, 11.5119]	1.13E-13
	miR-593	4	200	7.8637	[5.8846, 9.8427]	3.82E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	4.97E-13
	miR-23a-3p	4	211	7.7607	[5.7785, 9.7428]	9.35E-13
	miR-26b-5p	4	176	7.54	[5.5565, 9.5234]	5.20E-12
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	7.00E-11
	miR-320b	2	200	9.2302	[6.4447, 12.0157]	4.66E-09
	let-7f-5p	3	134	7.4077	[5.1138, 9.7017]	1.38E-08
	miR-130a-3p	3	116	7.3221	[5.0293, 9.6148]	2.17E-08
	miR-96-5p	3	133	7.3394	[5.0404, 9.6385]	2.20E-08
	miR-100-5p	2	175	8.8902	[6.1015, 11.6790]	2.32E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	2.32E-08
	miR-98-5p	2	169	8.8885	[6.1004, 11.6766]	2.32E-08
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.00E-07
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	2.49E-07
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	2.49E-07
	miR-423-3p	2	129	8.1601	[5.3621, 10.9580]	6.10E-07
	miR-10b-5p	2	128	8.097	[5.2971, 10.8969]	8.06E-07
	miR-342-3p	2	125	8.0642	[5.2646, 10.8637]	9.18E-07

		miR-374b-5p	2	119	7.8737	[5.0699, 10.6776]	2.08E-06
		miR-186-5p	2	88	7.6054	[4.8027, 10.4081]	5.88E-06
		miR-26a-5p	2	162	8.2401	[5.1650, 11.3151]	8.40E-06
		miR-126a	2	93	7.5237	[4.7159, 10.3316]	8.46E-06
		miR-126-3p	24	2748	5.8539	[2.9560, 8.7519]	4.21E-03
No less than 50	Up-regulation	miR-93-5p	5	716	9.7747	[8.0145, 11.5348]	5.34E-26
		miR-221-3p	5	781	9.3868	[7.6232, 11.1503]	6.90E-24
		miR-210-3p	4	540	9.6747	[7.7066, 11.6429]	2.23E-20
		miR-148a-3p	2	889	10.5404	[7.7535, 13.3273]	4.84E-12
		miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	4.84E-12
		miR-27a-3p	3	218	8.5517	[6.2725, 10.8309]	7.49E-12
		miR-99b-5p	3	212	8.4823	[6.2024, 10.7622]	1.19E-11
		miR-346	3	180	8.2217	[5.9401, 10.5034]	6.36E-11
		miR-222-3p	3	175	8.1404	[5.8577, 10.4231]	1.08E-10
		miR-15b-5p	2	275	9.7437	[6.9607, 12.5267]	2.65E-10
		miR-30d-5p	2	276	9.4392	[6.6525, 12.2258]	1.23E-09
		miR-1303	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
		miR-661	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
		miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
		miR-892b	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
		miR-571	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
		miR-572	2	200	9.2302	[6.4447, 12.0157]	3.24E-09
		miR-375	2	255	9.2294	[6.4389, 12.0199]	3.52E-09
		miR-29a-3p	2	220	9.1972	[6.4098, 11.9846]	3.90E-09
		miR-302a-3p	2	102	7.871	[5.0718, 10.6702]	1.39E-06
		miR-138-5p	2	100	7.8637	[5.0648, 10.6625]	1.43E-06

Down-regulation	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	2.31E-17
	miR-198	2	850	12.1054	[9.3304, 14.8805]	4.80E-16
	miR-30c-5p	4	280	8.4854	[6.5111, 10.4596]	1.42E-15
	miR-197-3p	3	326	9.2808	[7.0061, 11.5554]	4.99E-14
	miR-144-5p	3	746	9.2328	[6.9538, 11.5119]	7.88E-14
	miR-593	4	200	7.8637	[5.8846, 9.8427]	2.66E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	3.46E-13
	miR-223-3p	3	262	8.6563	[6.3763, 10.9364]	3.90E-12
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	4.88E-11
	miR-320b	2	200	9.2302	[6.4447, 12.0157]	3.24E-09
	miR-100-5p	2	175	8.8902	[6.1015, 11.6790]	1.62E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	1.62E-08
	miR-98-5p	2	169	8.8885	[6.1004, 11.6766]	1.62E-08
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	1.73E-07
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	1.73E-07
	miR-26b-5p	2	102	7.8932	[5.0946, 10.6918]	1.26E-06

ESM Table 18. The characteristics of databases for human microRNA-target gene interactions

Database	miRTarBase	miRecords	TransmiR
No. of miRNA-target interactions	380639	1685	2255
No. of microRNAs	2599	224	402
No. of target genes	15064	1097	369
No. of articles	7204	541	1075
Release date of the latest version	15 Sept 2021	27 Apr 2013	May 2018
Present version	9.0	4.0	2.0

ESM Table 19. Pathway analysis on dysregulated microRNAs from meta-analyses with newly built microRNA regulated pathways

Pathway name	Original ID	totalAcc	pPert	pORA	pComb	pPert.fdr	pORA.fdr	pComb.fdr
MAPK signaling pathway	hsa04010	587.8251	0.0165	3.10E-37	3.12E-07	0.3670	9.84E-36	7.68E-06
Regulation of actin cytoskeleton	hsa04810	601.8163	0.0140	1.90E-28	2.67E-07	0.3568	1.40E-27	7.68E-06
Diabetic cardiomyopathy	hsa05415	338.1408	0.0110	4.68E-25	2.12E-07	0.3495	1.96E-24	7.68E-06
Chemokine signaling pathway	hsa04062	381.1079	0.0180	1.80E-23	3.39E-07	0.3670	6.15E-23	7.68E-06
Prolactin signaling pathway	hsa04917	403.4317	0.0100	3.47E-23	1.94E-07	0.3495	1.17E-22	7.68E-06
p53 signaling pathway	hsa04115	275.2800	0.0270	1.08E-26	4.97E-07	0.4235	6.16E-26	8.45E-06
Platelet activation	hsa04611	338.3987	0.0295	4.04E-18	5.41E-07	0.4296	8.71E-18	8.49E-06
Cell cycle	hsa04110	12566.8436	0.0365	5.87E-30	6.61E-07	0.4651	5.92E-29	8.99E-06
Vascular smooth muscle contraction	hsa04270	245.2489	0.0880	1.42E-14	1.52E-06	0.6351	2.46E-14	1.19E-05
AGE-RAGE signaling pathway in diabetic complications	hsa04933	302.4132	0.1324	4.59E-28	2.23E-06	0.6351	3.18E-27	1.24E-05
Insulin resistance	hsa04931	183.9960	0.2284	5.67E-23	3.72E-06	0.7359	1.83E-22	1.37E-05
PI3K-Akt signaling pathway	hsa04151	356.9245	0.4468	9.91E-40	6.98E-06	0.9024	5.50E-38	1.58E-05
Lipid and atherosclerosis	hsa05417	421.1504	0.4943	3.07E-28	7.67E-06	0.9620	2.20E-27	1.69E-05
MicroRNAs in cancer	hsa05206	252.9818	0.7571	4.29E-42	1.14E-05	0.9866	4.77E-40	1.71E-05
Type II diabetes mellitus	hsa04930	208.8111	0.6967	2.82E-14	1.06E-05	0.9866	4.74E-14	1.71E-05

ESM Table 20. Potential microRNA biomarkers enriched in T2D pathway and their priority verification order

Priority	miRNA	Direction	Presented in following meta-analyses
1	miR-29a-3p	1	overall, blood, serum, sensi-25, sensi-50
2	miR-221-3p	1	serum, sensi-50
3	miR-126-3p	-1	plasma, sensi-25
3	miR-26a-5p	-1	plasma, sensi-25
4	miR-503-5p	-1	blood, serum
5	miR-100-5p	-1	sensi-25, sensi-50
6	miR-101-3p	1	blood
6	miR-103a-3p	1	whole blood
6	miR-122-5p	1	whole blood
6	miR-199a-3p	1	plasma
6	miR-30b-5p	1	plasma
7	miR-130a-3p	-1	sensi-25
7	miR-143-3p	1	muscle
7	miR-145-5p	1	adipose
7	miR-19a-3p	1	sensi-25
7	miR-331-3p	-1	overall

“1” indicates up-regulation and “-1” indicates down-regulation; “sensi-25” and “sensi-50” indicates sensitivity analysis with sample size no less of 25 and 50, respectively.

The priority is according to the following order of importance (a) detectable in blood or blood fractions; (b) statistically significance in different analyses.

ESM Table 21. Contradictory findings on overall effect of human microRNAs between previous and present meta-analysis due to newly included studies

microRNA	Meta 2015			Meta 2022		
	Significant*	Up	Down	Significant*	Up	Down
miR-1-3p	No	0	0	Yes	0	4
miR-103a-3p	Yes	2	0	No	8	4
miR-103b	No	0	0	Yes	0	3
miR-106b-5p	Yes	2	0	No	3	4
miR-107	Yes	2	0	No	2	2
miR-10b-5p	No	0	1	Yes	0	3
miR-1228-3p	No	0	0	Yes	0	3
miR-1246	No	0	0	Yes	0	3
miR-1275	No	0	0	Yes	0	2
miR-1281	No	0	0	Yes	0	3
miR-1303	No	0	0	Yes	2	0
miR-133a-3p	No	0	1	Yes	0	2
miR-136-5p	No	0	0	Yes	2	0
miR-140-3p	No	0	0	Yes	3	0
miR-140-5p	Yes	2	0	No	2	2
miR-142-3p	Yes	4	0	No	4	4
miR-142-5p	No	1	0	Yes	2	0
miR-144-3p	Yes	3	0	No	12	2
miR-148a-3p	No	0	0	Yes	4	0
miR-152-3p	No	0	1	Yes	0	3
miR-155-5p	Yes	0	2	No	7	11
miR-16-5p	Yes	4	0	No	12	5
miR-181a-2-3p	No	1	0	Yes	2	0
miR-18a-5p	Yes	2	0	No	5	2
miR-18b-5p	No	0	0	Yes	0	2
miR-182-5p	No	0	1	Yes	0	3
miR-185-5p	Yes	2	0	No	2	3
miR-1973	No	0	0	Yes	0	2
miR-198	No	0	0	Yes	0	2
miR-19b-3p	No	1	0	Yes	3	0
miR-200b-3p	No	0	0	Yes	0	2
miR-208a	No	0	0	Yes	4	0
miR-20b-5p	Yes	0	2	No	3	5
miR-221-3p	Yes	3	0	No	9	2
miR-296-5p	No	1	0	Yes	2	0
miR-29c-3p	No	1	0	Yes	7	1
miR-302a-3p	No	1	0	Yes	4	0
miR-302b-3p	No	0	0	Yes	2	0
miR-30a-3p	No	0	1	Yes	0	2
miR-30c-5p	No	0	1	Yes	0	6
miR-30e-5p	Yes	0	3	No	1	7
miR-32-5p	No	0	0	Yes	2	0
miR-342-3p	Yes	0	2	No	2	4
miR-346	No	0	0	Yes	3	0
miR-34a-5p	Yes	2	0	No	11	2
miR-378	No	0	0	Yes	0	4
miR-409-3p	No	0	0	Yes	0	2
miR-423-3p	No	0	1	Yes	0	4
miR-4463	No	0	0	Yes	5	0
miR-4477a	No	0	0	Yes	0	2

miR-455-3p	No	0	0	Yes	2	0
miR-4695-5p	No	0	0	Yes	2	0
miR-4714-3p	No	0	0	Yes	0	2
miR-483-3p	No	0	0	Yes	2	0
miR-548o-3p	No	0	0	Yes	2	0
miR-571	No	0	0	Yes	2	0
miR-589-3p	No	0	0	Yes	2	0
miR-593	No	0	0	Yes	0	4
miR-660-5p	No	0	1	Yes	0	3
miR-661	No	0	0	Yes	2	0
miR-665	Yes	2	0	No	2	1
miR-766-3p	No	0	0	Yes	0	3
miR-770-5p	No	0	0	Yes	2	0
miR-892b	No	0	0	Yes	2	0
miR-9-5p	No	1	0	Yes	4	0

*indicates whether the microRNA was statistical significant in corresponding meta-analysis and number under Up and Down indicates the number of sub-studies reported the corresponding microRNA up-regulated and down-regulated, respectively.

ESM Table 22. Statistically significant dysregulation of miRNAs in humans by empirical Bayes estimation (n = 60)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-29a-3p	8	352	6.838	[5.4211, 8.2548]	2.77E-19
	miR-375	4	307	7.8447	[5.7837, 9.9057]	7.69E-12
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	1.10E-11
	miR-4463	5	138	6.6571	[4.8722, 8.4420]	2.38E-11
	miR-346	3	180	8.2217	[5.9401, 10.5034]	1.45E-10
	miR-9-5p	4	152	6.8044	[4.8003, 8.8084]	2.53E-09
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	3.92E-09
	miR-302a-3p	4	124	6.4617	[4.4525, 8.4709]	2.59E-08
	miR-208a	4	70	5.769	[3.7527, 7.7854]	1.82E-06
	miR-181a-2-3p	2	116	7.77	[4.9635, 10.5764]	5.12E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	6.41E-05
	miR-142-5p	2	110	7.5032	[4.3913, 10.6150]	2.04E-04
	miR-140-3p	3	48	5.576	[3.2412, 7.9109]	2.55E-04
	miR-19b-3p	3	49	5.5337	[3.1943, 7.8730]	3.16E-04
	miR-148a-3p	4	913	7.7659	[4.4635, 11.0683]	3.60E-04
	miR-32-5p	2	45	6.2739	[3.4413, 9.1064]	1.26E-03
	miR-187-3p	2	40	6.0845	[3.2472, 8.9218]	2.34E-03
	miR-589	2	107	7.3325	[3.8801, 10.7850]	2.80E-03
	miR-136-5p	2	37	5.7482	[2.8907, 8.6058]	7.17E-03
	miR-4695-5p	2	32	5.6095	[2.7527, 8.4663]	1.06E-02
	miR-29c-3p	8	178	4.8661	[2.3085, 7.4237]	1.71E-02
	miR-296-5p	2	29	5.4174	[2.5522, 8.2826]	1.88E-02
	miR-302b-3p	2	28	5.3521	[2.4830, 8.2212]	2.28E-02
	miR-483-3p	2	26	5.2619	[2.3911, 8.1327]	2.91E-02
	miR-455-3p	2	28	5.2417	[2.3620, 8.1214]	3.20E-02
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	3.56E-02
	miR-320a	14	867	5.2885	[2.2827, 8.2899]	4.92E-02
Down-regulation	miR-30c-5p	6	305	7.4205	[5.7924, 9.0485]	3.68E-17
	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	5.27E-17
	miR-198	2	850	12.1054	[9.3304, 14.8805]	1.09E-15
	miR-593	4	200	7.8637	[5.8846, 9.8427]	6.08E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	7.89E-13
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	1.11E-10
	miR-10b-5p	3	150	7.4974	[5.2028, 9.7920]	1.34E-08
	miR-423-3p	4	149	6.5335	[4.4917, 8.5753]	3.18E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	3.69E-08
	miR-374b-5p	3	134	7.1157	[4.8121, 9.4194]	1.25E-07
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.59E-07
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	3.95E-07
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	3.95E-07
	miR-378	4	64	5.6664	[3.6496, 7.6832]	3.25E-06
	miR-126a	2	93	7.5237	[4.7159, 10.3316]	1.34E-05
	miR-182-5p	3	56	5.8221	[3.4929, 8.1512]	8.56E-05
	miR-1228-3p	3	37	5.0521	[2.6954, 7.4087]	2.36E-03
	miR-766-3p	3	35	4.9924	[2.6343, 7.3505]	2.96E-03
	miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	3.84E-03
	miR-1281	3	34	4.9235	[2.5616, 7.2853]	3.91E-03
	miR-660-5p	3	35	4.9138	[2.5467, 7.2809]	4.21E-03
	miR-409-3p	2	37	5.8618	[3.0131, 8.7104]	4.90E-03

	miR-1246	3	30	4.7846	[2.4197, 7.1495]	6.52E-03
	miR-1275	2	30	5.44	[2.5724, 8.3076]	1.78E-02
	miR-1973	2	30	5.44	[2.5724, 8.3076]	1.78E-02
	miR-199b-5p	2	104	7.1309	[3.2754, 10.9865]	2.57E-02
	miR-331-3p	2	104	7.1309	[3.2754, 10.9865]	2.57E-02
	miR-18b-5p	2	26	5.1858	[2.3077, 8.0638]	3.68E-02
	miR-30a-3p	2	25	5.1408	[2.2614, 8.0203]	4.16E-02

ESM Table 23. Statistically significant dysregulation of miRNAs in human pancreas by empirical Bayes estimation (n=1)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-187-3p	2	40	6.0845	[3.2472-8.9218]	2.63E-05

ESM Table 24. Statistically significant dysregulation of miRNAs in human heart by empirical Bayes estimation (n=2)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-208a	4	70	5.7690	[3.7527, 7.7854]	4.10E-08
Down-regulation	miR-15b-5p	3	42	5.3777	[3.0372, 7.7181]	1.34E-05

ESM Table 25. Statistically significant dysregulation of miRNAs in kidney by empirical Bayes estimation (n=1)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-1228-3p	3	37	5.0521	[2.6954, 7.4087]	1.09E-03

ESM Table 26. Statistically significant dysregulation of miRNAs in adipose by empirical Bayes estimation (n=6)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-125b-5p	2	85	7.051	[4.0961, 10.0059]	1.75E-05
	miR-140-3p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-145-5p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-146a-5p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-16-5p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03
	miR-24-3p	2	24	5.1299	[2.2535, 8.0063]	2.84E-03

ESM Table 27. Statistically significant dysregulation of miRNAs in human muscle by empirical Bayes estimation (n=5)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up- regulation	miR-143-3p	2	112	7.6017	[4.6859-10.5174]	1.61E-06
Down-regulation	miR-10b-5p	2	114	7.6901	[4.8813-10.4989]	4.02E-07
	miR-10a-5p	2	108	7.3939	[4.0640-10.7237]	6.75E-05
	miR-27b-3p	2	108	7.3939	[4.0640-10.7237]	6.75E-05
	miR-363-3p	2	33	5.6293	[2.7711-8.4876]	5.65E-04

ESM Table 28. Statistically significant dysregulation of miRNAs in human blood by empirical Bayes estimation (n=50)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted *p* values
Up-regulation	miR-29a-3p	4	272	7.8323	[5.8456, 9.8190]	6.71E-13
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	7.56E-12
	miR-346	3	180	8.2217	[5.9401, 10.5034]	9.94E-11
	miR-9-5p	4	152	6.8044	[4.8003, 8.8084]	1.73E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	2.68E-09
	miR-4463	4	112	6.686	[4.6910, 8.6810]	3.10E-09
	miR-572	2	200	9.2302	[6.4447, 12.0157]	5.08E-09
	miR-128-3p	2	160	8.7889	[6.0000, 11.5778]	4.00E-08
	miR-302a-3p	3	112	6.8914	[4.5807, 9.2022]	3.09E-07
	miR-374a-5p	2	120	7.7535	[4.8930, 10.6139]	6.59E-06
	miR-375	3	252	7.836	[4.9199, 10.7521]	8.48E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	4.39E-05
	miR-320c	3	49	5.6282	[3.2948, 7.9617]	1.38E-04
	miR-148a-3p	4	913	7.7659	[4.4635, 11.0683]	2.46E-04
	miR-193b-3p	2	49	6.4626	[3.6362, 9.2890]	4.52E-04
	miR-101-3p	2	45	6.2739	[3.4413, 9.1064]	8.66E-04
	miR-32-5p	2	45	6.2739	[3.4413, 9.1064]	8.66E-04
	miR-1260a	2	42	6.165	[3.3298, 9.0002]	1.24E-03
	miR-19b-3p	2	39	5.9061	[3.0575, 8.7546]	2.95E-03
	miR-136-5p	2	37	5.7482	[2.8907, 8.6058]	4.92E-03
	miR-302b-3p	2	28	5.3521	[2.4830, 8.2212]	1.56E-02
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	2.44E-02
	miR-335-5p	2	165	7.8129	[3.4098, 12.2160]	3.05E-02
	miR-132-3p	2	23	5.0466	[2.1656, 7.9277]	3.63E-02
	miR-135a-5p	2	90	6.8317	[2.9193, 10.7441]	3.78E-02
	miR-188-3p	2	26	5.0382	[2.1401, 7.9363]	4.00E-02
Down-regulation	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	3.61E-17
	miR-30c-5p	5	295	7.9181	[6.1442, 9.6919]	1.32E-16
	miR-198	2	850	12.1054	[9.3304, 14.8805]	7.50E-16
	miR-593	4	200	7.8637	[5.8846, 9.8427]	4.17E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	5.41E-13
	miR-197-3p	3	283	8.6733	[6.3905, 10.9560]	5.83E-12
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.09E-07
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	2.71E-07
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	2.71E-07
	miR-378	4	64	5.6664	[3.6496, 7.6832]	2.23E-06
	miR-152-3p	2	100	7.8637	[5.0648, 10.6625]	2.23E-06
	miR-126a	2	93	7.5237	[4.7159, 10.3316]	9.21E-06
	miR-503-5p	2	69	7.1099	[4.2982, 9.9217]	4.39E-05
	miR-182-5p	3	56	5.8221	[3.4929, 8.1512]	5.87E-05
	miR-423-3p	3	57	5.6437	[3.3040, 7.9835]	1.38E-04
	miR-374b-5p	2	42	6.1041	[3.2648, 8.9434]	1.53E-03
	miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	2.64E-03
	miR-660-5p	3	35	4.9138	[2.5467, 7.2809]	2.89E-03
	miR-409-3p	2	37	5.8618	[3.0131, 8.7104]	3.36E-03
	miR-214-3p	2	89	6.9567	[3.4471, 10.4663]	6.22E-03

ESM Table 29. Sensitivity analysis based on human sample size by empirical Bayes estimation (n=90)

Sample size	Direction of regulation	miRNA	No. of sub-studies	Pooled sample size	Overall effect		
					LogOR	[95%CI]	Adjusted *p* values
No less than 25	Up- regulation	miR-93-5p	5	716	9.7747	[8.0145, 11.5348]	7.67E-26
		miR-210-3p	4	540	9.6747	[7.7066, 11.6429]	3.20E-20
		miR-29a-3p	4	295	8.2552	[6.2771, 10.2333]	1.60E-15
		miR-222-3p	4	203	7.7746	[5.7929, 9.7562]	8.29E-13
		miR-30d-5p	3	313	8.7249	[6.4439, 11.0060]	3.67E-12
		miR-148a-3p	2	889	10.5404	[7.7535, 13.3273]	6.94E-12
		miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	6.94E-12
		miR-375	3	292	8.5832	[6.3000, 10.8664]	9.69E-12
		miR-346	3	180	8.2217	[5.9401, 10.5034]	9.13E-11
		miR-1303	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-661	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-892b	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-571	2	246	9.3691	[6.5826, 12.1555]	2.46E-09
		miR-572	2	200	9.2302	[6.4447, 12.0157]	4.66E-09
		miR-9-5p	3	142	7.4373	[5.1390, 9.7355]	1.27E-08
		miR-4463	3	90	6.8025	[4.5007, 9.1044]	3.89E-07
		miR-146b-5p	2	221	8.8849	[5.8523, 11.9175]	5.23E-07
		miR-302a-3p	2	102	7.871	[5.0718, 10.6702]	1.99E-06
		miR-451a	2	119	7.8737	[5.0699, 10.6776]	2.08E-06
		miR-29c-3p	2	95	7.5697	[4.7632, 10.3762]	7.00E-06
		miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	4.03E-05
		miR-4306	2	64	6.9324	[4.1164, 9.7485]	7.84E-05
		miR-19a-3p	2	187	8.4249	[4.9854, 11.8644]	8.85E-05
	Down-regulation	miR-223-3p	5	343	8.16	[6.3904, 9.9296]	8.96E-18
		miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	3.32E-17
		miR-197-3p	4	353	8.6362	[6.6601, 10.6123]	6.05E-16
		miR-198	2	850	12.1054	[9.3304, 14.8805]	6.89E-16
		miR-30c-5p	4	280	8.4854	[6.5111, 10.4596]	2.04E-15
		miR-144-5p	3	746	9.2328	[6.9538, 11.5119]	1.13E-13
		miR-593	4	200	7.8637	[5.8846, 9.8427]	3.82E-13

		miR-103b	3	269	9.0039	[6.7282, 11.2797]	4.97E-13
		miR-23a-3p	4	211	7.7607	[5.7785, 9.7428]	9.35E-13
		miR-26b-5p	4	176	7.54	[5.5565, 9.5234]	5.20E-12
		miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	7.00E-11
		miR-320b	2	200	9.2302	[6.4447, 12.0157]	4.66E-09
		let-7f-5p	3	134	7.4077	[5.1138, 9.7017]	1.38E-08
		miR-130a-3p	3	116	7.3221	[5.0293, 9.6148]	2.17E-08
		miR-96-5p	3	133	7.3394	[5.0404, 9.6385]	2.20E-08
		miR-100-5p	2	175	8.8902	[6.1015, 11.6790]	2.32E-08
		miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	2.32E-08
		miR-98-5p	2	169	8.8885	[6.1004, 11.6766]	2.32E-08
		miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.00E-07
		miR-4477a	2	133	8.3626	[5.5690, 11.1563]	2.49E-07
		miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	2.49E-07
		miR-423-3p	2	129	8.1601	[5.3621, 10.9580]	6.10E-07
		miR-10b-5p	2	128	8.097	[5.2971, 10.8969]	8.06E-07
		miR-342-3p	2	125	8.0642	[5.2646, 10.8637]	9.18E-07
		miR-374b-5p	2	119	7.8737	[5.0699, 10.6776]	2.08E-06
		miR-186-5p	2	88	7.6054	[4.8027, 10.4081]	5.88E-06
		miR-26a-5p	2	162	8.2401	[5.1650, 11.3151]	8.40E-06
		miR-126a	2	93	7.5237	[4.7159, 10.3316]	8.46E-06
		miR-126-3p	24	2748	5.8539	[2.9564, 8.7515]	4.20E-03
No less than 50	Up-regulation	miR-93-5p	5	716	9.7747	[8.0145, 11.5348]	5.34E-26
		miR-221-3p	5	781	9.3868	[7.6232, 11.1503]	6.90E-24
		miR-210-3p	4	540	9.6747	[7.7066, 11.6429]	2.23E-20
		miR-148a-3p	2	889	10.5404	[7.7535, 13.3273]	4.84E-12
		miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	4.84E-12
		miR-27a-3p	3	218	8.5517	[6.2725, 10.8309]	7.49E-12
		miR-99b-5p	3	212	8.4823	[6.2024, 10.7622]	1.19E-11
		miR-346	3	180	8.2217	[5.9401, 10.5034]	6.36E-11
		miR-222-3p	3	175	8.1404	[5.8577, 10.4231]	1.08E-10
		miR-15b-5p	2	275	9.7437	[6.9607, 12.5267]	2.65E-10
		miR-30d-5p	2	276	9.4392	[6.6525, 12.2258]	1.23E-09
		miR-1303	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
		miR-661	2	246	9.3691	[6.5826, 12.1555]	1.72E-09

	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	1.72E-09
	miR-572	2	200	9.2302	[6.4447, 12.0157]	3.24E-09
	miR-375	2	255	9.2294	[6.4389, 12.0199]	3.52E-09
	miR-29a-3p	2	220	9.1972	[6.4098, 11.9846]	3.90E-09
	miR-302a-3p	2	102	7.871	[5.0718, 10.6702]	1.39E-06
	miR-138-5p	2	100	7.8637	[5.0648, 10.6625]	1.43E-06
Down-regulation	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	2.31E-17
	miR-198	2	850	12.1054	[9.3304, 14.8805]	4.80E-16
	miR-30c-5p	4	280	8.4854	[6.5111, 10.4596]	1.42E-15
	miR-197-3p	3	326	9.2808	[7.0061, 11.5554]	4.99E-14
	miR-144-5p	3	746	9.2328	[6.9538, 11.5119]	7.88E-14
	miR-593	4	200	7.8637	[5.8846, 9.8427]	2.66E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	3.46E-13
	miR-223-3p	3	262	8.6563	[6.3763, 10.9364]	3.90E-12
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	4.88E-11
	miR-320b	2	200	9.2302	[6.4447, 12.0157]	3.24E-09
	miR-100-5p	2	175	8.8902	[6.1015, 11.6790]	1.62E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	1.62E-08
	miR-98-5p	2	169	8.8885	[6.1004, 11.6766]	1.62E-08
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	1.73E-07
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	1.73E-07
	miR-26b-5p	2	102	7.8932	[5.0946, 10.6918]	1.26E-06

ESM Table 30. Statistically significant dysregulation of miRNAs in PBMCs by empirical Bayes estimation (n = 12)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-18a-5p	2	413	10.6376	[7.8589, 13.4163]	7.48E-13
	miR-346	3	180	8.2217	[5.9401, 10.5034]	1.96E-11
	miR-29b-3p	2	36	5.8889	[3.0451, 8.7327]	5.93E-04
	miR-222-3p	2	36	5.8889	[3.0451, 8.7327]	5.93E-04
	miR-186-5p	2	36	5.8889	[3.0451, 8.7327]	5.93E-04
	miR-188-3p	2	26	5.0382	[2.1401, 7.9363]	7.87E-03
	miR-20a-5p	2	26	5.0382	[2.1401, 7.9363]	7.87E-03
Down-regulation	miR-146a-5p	3	140	7.6934	[5.4058, 9.9810]	5.22E-10
	miR-144-5p	2	133	8.3626	[5.5690, 11.1563]	5.33E-08
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	5.33E-08
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	5.33E-08
	miR-155-5p	2	80	7.4271	[4.6217, 10.2326]	2.54E-06

ESM Table 31. Statistically significant dysregulation of miRNAs in Whole blood by empirical Bayes estimation (n = 25)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-122-5p	2	889	10.5404	[7.7535, 13.3273]	3.10E-12
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	3.10E-12
	miR-155-5p	3	120	7.4271	[5.1365, 9.7177]	5.20E-09
	miR-103a-3p	2	120	7.8123	[5.0062, 10.6185]	1.22E-06
	miR-15b-5p	2	48	6.4378	[3.6111, 9.2645]	2.01E-04
	miR-26b-5p	2	39	5.9944	[3.1524, 8.8363]	8.90E-04
	miR-151a-5p	2	39	5.9944	[3.1524, 8.8363]	8.90E-04
	miR-150-5p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-192-5p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-27a-3p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-320a	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-148a-3p	3	895	8.3764	[4.0322, 12.7206]	3.93E-03
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	1.00E-02
	miR-151a-3p	2	21	4.7465	[1.8376, 7.6554]	3.45E-02
Down-regulation	miR-24-3p	4	211	7.6194	[5.6304, 9.6085]	1.50E-12
	miR-378	4	64	5.6664	[3.6496, 7.6832]	9.13E-07
	miR-486-5p	2	48	6.4378	[3.6111, 9.2645]	2.01E-04
	miR-342-3p	2	48	6.305	[3.4702, 9.1397]	3.25E-04
	miR-17-5p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	1.08E-03
	miR-210-3p	2	32	5.6664	[2.8143, 8.5186]	2.47E-03
	let-7f-5p	2	89	6.9567	[3.4471, 10.4663]	2.55E-03
	miR-214-3p	2	89	6.9567	[3.4471, 10.4663]	2.55E-03
	miR-20a-5p	2	21	4.7465	[1.8376, 7.6554]	3.45E-02
	miR-660-5p	2	21	4.7465	[1.8376, 7.6554]	3.45E-02

ESM Table 32. Statistically significant dysregulation of miRNAs in serum by empirical Bayes estimation (n = 38)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-210-3p	4	540	9.6747	[7.7066, 11.6429]	2.29E-20
	miR-221-3p	6	793	8.701	[6.7983, 10.6037]	1.27E-17
	miR-29a-3p	3	257	8.5626	[6.2811, 10.8441]	7.60E-12
	miR-15a-5p	4	209	6.8546	[4.8481, 8.8610]	8.60E-10
	miR-125b-5p	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	1.76E-09
	miR-130b-3p	2	194	9.1696	[6.3837, 11.9555]	4.44E-09
	miR-99b-5p	4	162	6.6902	[4.6165, 8.7638]	1.02E-08
	miR-128-3p	2	160	8.7889	[6.0000, 11.5778]	2.62E-08
	miR-302a-3p	3	112	6.8914	[4.5807, 9.2022]	2.02E-07
	miR-9-5p	3	107	6.8083	[4.4964, 9.1202]	3.14E-07
	miR-27b-3p	3	85	6.1699	[3.8419, 8.4978]	8.20E-06
	miR-24-3p	4	200	6.5303	[4.0615, 8.9991]	8.68E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	2.88E-05
	miR-124-3p	2	47	6.0729	[3.2224, 8.9235]	1.19E-03
	miR-194-5p	2	39	5.9049	[3.0577, 8.7521]	1.92E-03
	miR-150-5p	2	49	5.9913	[2.9747, 9.0079]	3.96E-03
	miR-20b-5p	2	49	5.9913	[2.9747, 9.0079]	3.96E-03
	miR-107	2	23	5.0466	[2.1656, 7.9277]	2.39E-02
	miR-132-3p	2	23	5.0466	[2.1656, 7.9277]	2.39E-02
	miR-1304-5p	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
	miR-302d-3p	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
Down-regulation	miR-198	2	850	12.1054	[9.3304, 14.8805]	4.92E-16
	miR-593	4	200	7.8637	[5.8846, 9.8427]	2.73E-13
	miR-1-3p	3	270	9.0217	[6.7461, 11.2973]	3.13E-13
	miR-192-5p	4	381	7.7444	[5.3454, 10.1433]	1.00E-08
	miR-152-3p	2	100	7.8637	[5.0648, 10.6625]	1.46E-06
	miR-186-5p	2	88	7.6054	[4.8027, 10.4081]	4.20E-06
	miR-503-5p	2	69	7.1099	[4.2982, 9.9217]	2.88E-05
	miR-423-3p	3	57	5.6437	[3.3040, 7.9835]	9.08E-05
	let-7i-5p	2	54	6.2461	[3.3984, 9.0939]	6.88E-04
	miR-1246	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
	miR-6131	2	20	4.7958	[1.9007, 7.6908]	4.67E-02
	miR-98-5p	2	20	4.7958	[1.9007, 7.6908]	4.67E-02

ESM Table 33. Statistically significant dysregulation of miRNAs in plasma by empirical Bayes estimation (n = 25)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-144-3p	6	951	9.2373	[7.3972, 11.0775]	1.99E-21
	miR-93-5p	4	564	9.3044	[7.2507, 11.3582]	1.75E-17
	miR-34a-5p	5	183	7.0493	[5.2683, 8.8303]	2.25E-13
	miR-4463	4	112	6.686	[4.6910, 8.6810]	1.32E-09
	miR-572	2	200	9.2302	[6.4447, 12.0157]	2.16E-09
	miR-29c-3p	2	95	7.5697	[4.7632, 10.3762]	3.25E-06
	miR-30b-5p	2	172	8.1724	[4.4843, 11.8604]	3.64E-04
	miR-199a-3p	2	42	6.1802	[3.3460, 9.0144]	4.99E-04
	miR-320c	2	34	5.6717	[2.8136, 8.5298]	2.60E-03
Down-regulation	miR-30c-5p	4	280	8.4854	[6.5111, 10.4596]	9.46E-16
	miR-223-3p	4	309	8.4201	[6.4439, 10.3962]	1.76E-15
	miR-130b-3p	3	140	7.5897	[5.2989, 9.8804]	2.18E-09
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	4.65E-08
	miR-185-5p	2	125	8.2932	[5.4995, 11.0870]	1.55E-07
	miR-126-3p	14	1421	7.5404	[4.8793, 10.2016]	7.28E-07
	miR-26a-5p	2	162	8.2401	[5.1650, 11.3151]	3.90E-06
	miR-126a	2	93	7.5237	[4.7159, 10.3316]	3.93E-06
	miR-125b-5p	2	93	7.5237	[4.7159, 10.3316]	3.93E-06
	miR-26b-5p	2	78	7.2781	[4.4681, 10.0880]	9.98E-06
	miR-195-5p	2	85	7.2492	[4.4345, 10.0639]	1.16E-05
	miR-197-3p	2	187	8.4249	[4.9854, 11.8644]	4.11E-05
	miR-192-5p	2	79	6.8486	[3.7805, 9.9167]	3.15E-04
	miR-15b-5p	2	41	5.9617	[3.1116, 8.8118]	1.08E-03
	miR-182-5p	2	41	5.9617	[3.1116, 8.8118]	1.08E-03
	miR-20a-5p	2	30	5.4271	[2.5589, 8.2953]	5.41E-03

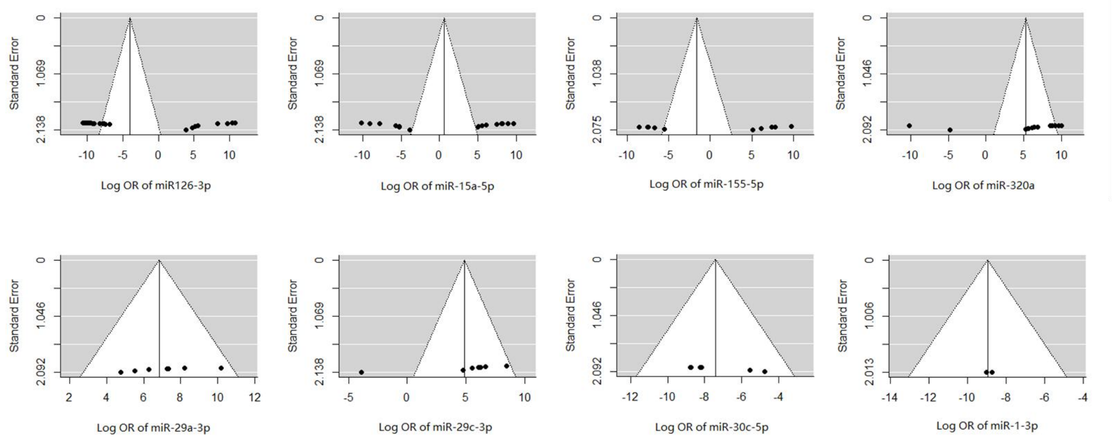
ESM Table 34. Statistically significant dysregulation of miRNAs detected by PCR-based methods and empirical Bayes estimation (n = 61)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-144-3p	12	1105	7.4907	[5.9419, 9.0395]	2.25E-19
	miR-29a-3p	8	352	6.838	[5.4211, 8.2548]	2.74E-19
	miR-29c-3p	7	172	6.1063	[4.5842, 7.6284]	3.30E-13
	miR-375	4	307	7.8447	[5.7837, 9.9057]	7.60E-12
	miR-589-3p	2	889	10.5404	[7.7535, 13.3273]	1.09E-11
	miR-4463	5	138	6.6571	[4.8722, 8.4420]	2.35E-11
	miR-346	3	180	8.2217	[5.9401, 10.5034]	1.43E-10
	miR-1303	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-571	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-661	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-770-5p	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-892b	2	246	9.3691	[6.5826, 12.1555]	3.87E-09
	miR-302a-3p	3	114	6.9902	[4.6842, 9.2962]	2.49E-07
	miR-9-5p	3	107	6.8083	[4.4964, 9.1202]	6.90E-07
	miR-148a-3p	3	907	9.0132	[5.9479, 12.0786]	7.27E-07
	miR-208a	4	70	5.769	[3.7527, 7.7854]	1.80E-06
	miR-376a-3p	2	69	7.1099	[4.2982, 9.9217]	6.34E-05
	miR-142-5p	2	110	7.5032	[4.3913, 10.6150]	2.02E-04
	miR-19b-3p	3	49	5.5337	[3.1943, 7.8730]	3.12E-04
	miR-30b-5p	3	182	7.0631	[3.9827, 10.1436]	6.15E-04
	miR-32-5p	2	45	6.2739	[3.4413, 9.1064]	1.25E-03
	miR-187-3p	2	40	6.0845	[3.2472, 8.9218]	2.31E-03
	miR-589	2	107	7.3325	[3.8801, 10.7850]	2.77E-03
	miR-136-5p	2	37	5.7482	[2.8907, 8.6058]	7.09E-03
	miR-4695-5p	2	32	5.6095	[2.7527, 8.4663]	1.05E-02
	miR-296-5p	2	29	5.4174	[2.5522, 8.2826]	1.85E-02
	miR-483-3p	2	26	5.2619	[2.3911, 8.1327]	2.88E-02
	miR-455-3p	2	28	5.2417	[2.3620, 8.1214]	3.17E-02
	miR-140-3p	2	24	5.1299	[2.2535, 8.0063]	4.16E-02
	miR-320a	14	867	5.2885	[2.2827, 8.2899]	4.87E-02
Down-regulation	miR-30c-5p	6	305	7.4205	[5.7924, 9.0485]	3.63E-17
	miR-1-3p	4	347	8.9444	[6.9732, 10.9155]	5.21E-17
	miR-198	2	850	12.1054	[9.3304, 14.8805]	1.08E-15
	miR-100-5p	6	239	6.7735	[5.1393, 8.4077]	3.98E-14
	miR-593	4	200	7.8637	[5.8846, 9.8427]	6.01E-13
	miR-103b	3	269	9.0039	[6.7282, 11.2797]	7.81E-13
	miR-152-3p	3	192	8.2663	[5.9844, 10.5483]	1.10E-10
	miR-10b-5p	3	150	7.4974	[5.2028, 9.7920]	1.33E-08
	miR-133a-3p	2	169	8.8885	[6.1004,11.6766]	3.65E-08
	miR-374b-5p	3	134	7.1157	[4.8121, 9.4194]	1.24E-07
	miR-200b-3p	2	242	8.5849	[5.7880, 11.3818]	1.58E-07
	miR-423-3p	3	139	7.0846	[4.6737, 9.4955]	7.42E-07
	miR-98-5p	3	179	7.5755	[4.9202, 10.2308]	1.98E-06
	miR-378	4	64	5.6664	[3.6496, 7.6832]	3.21E-06
	miR-126a	2	93	7.5237	[4.7159, 10.3316]	1.33E-05
	miR-363-3p	4	55	5.2327	[3.1969, 7.2685]	4.14E-05
	miR-182-5p	3	56	5.8221	[3.4929, 8.1512]	8.47E-05
	miR-30e-3p	2	49	6.4626	[3.6362, 9.2890]	6.52E-04
	miR-1228-3p	3	37	5.0521	[2.6954, 7.4087]	2.33E-03
	miR-766-3p	3	35	4.9924	[2.6343, 7.3505]	2.93E-03
	miR-652-3p	2	111	7.3736	[3.8398, 10.9074]	3.80E-03
	miR-1281	3	34	4.9235	[2.5616, 7.2853]	3.86E-03

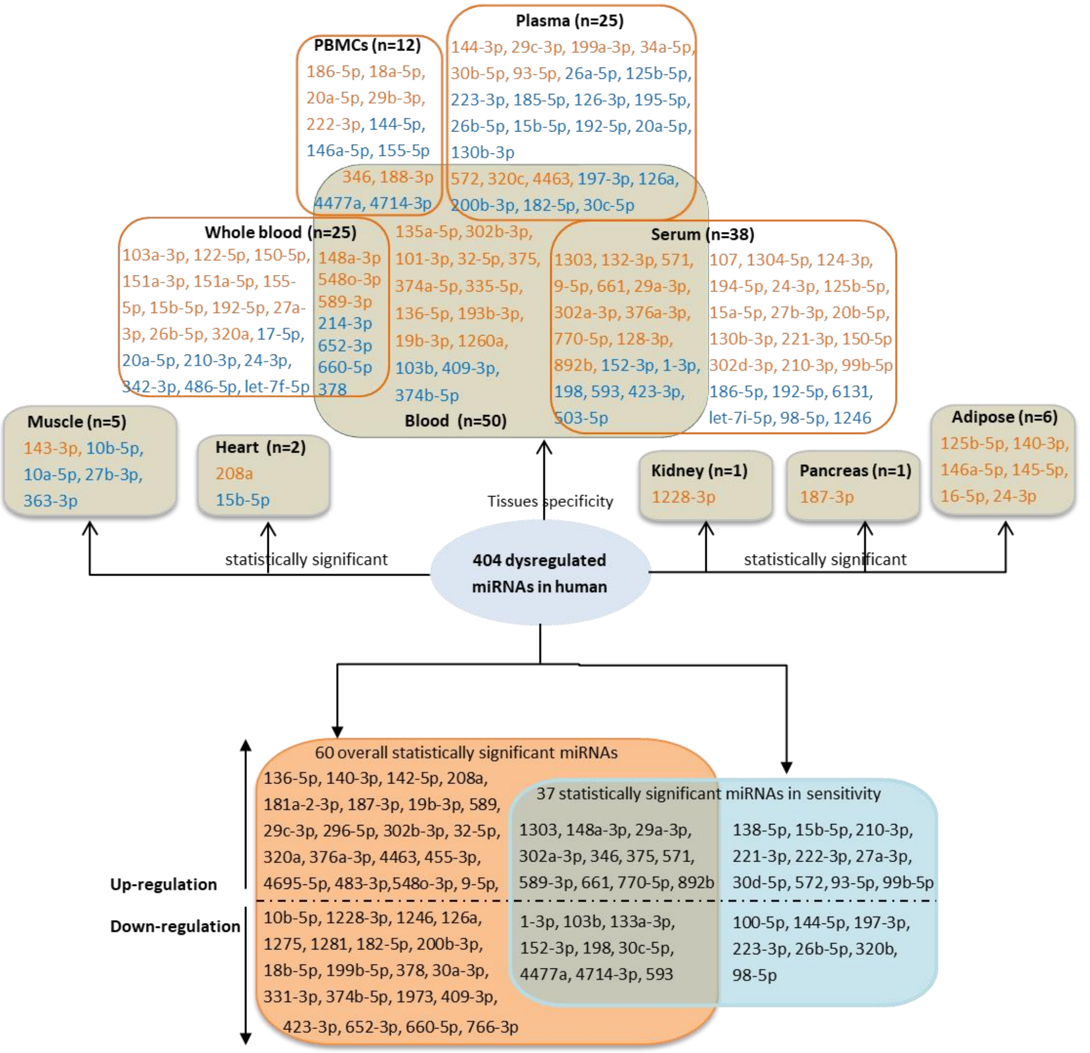
	miR-409-3p	2	37	5.8618	[3.0131, 8.7104]	4.85E-03
	miR-1275	2	30	5.44	[2.5724, 8.3076]	1.76E-02
	miR-1973	2	30	5.44	[2.5724, 8.3076]	1.76E-02
	miR-660-5p	2	29	5.3927	[2.5242, 8.2612]	2.02E-02
	miR-199b-5p	2	104	7.1309	[3.2754, 10.9865]	2.54E-02
	miR-331-3p	2	104	7.1309	[3.2754, 10.9865]	2.54E-02
	miR-223-3p	8	392	5.9464	[2.7181, 9.1748]	2.69E-02
	miR-18b-5p	2	26	5.1858	[2.3077, 8.0638]	3.63E-02
	miR-30a-3p	2	25	5.1408	[2.2614, 8.0203]	4.11E-02

ESM Table 35. Statistically significant dysregulation of miRNAs detected by RNA-Seq and empirical Bayes estimation (n=11)

	miRNA	No. of sub-studies	No. of samples	Overall effect		
				LogOR	[95%CI]	Adjusted p values
Up-regulation	miR-15b-5p	2	48	6.4378	[3.6111, 9.2645]	8.86E-05
	miR-99b-5p	2	34	5.6364	[2.7761, 8.4967]	1.23E-03
	miR-548o-3p	2	30	5.2248	[2.3322, 8.1173]	4.40E-03
Down-regulation	miR-144-3p	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-144-5p	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-4477a	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-4714-3p	2	133	8.3626	[5.5690, 11.1563]	4.88E-08
	miR-486-5p	3	58	5.9077	[3.5816, 8.2339]	7.07E-06
	miR-126-5p	2	16	4.3543	[1.4258, 7.2828]	3.93E-02
	miR-16-5p	2	16	4.3543	[1.4258, 7.2828]	3.93E-02
	miR-30b-5p	2	16	4.3543	[1.4258, 7.2828]	3.93E-02



ESM Fig. 1. Funnel plots of publication bias on different microRNAs



ESM Fig. 2. The Venn diagram of microRNA categories and flow chart of systematic review. “n”, number of statistically significant microRNAs. The prefix “miR-” of microRNA identifiers is omited. microRNAs in red are up-regulated and in blue are down-regulated.

Appendix

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