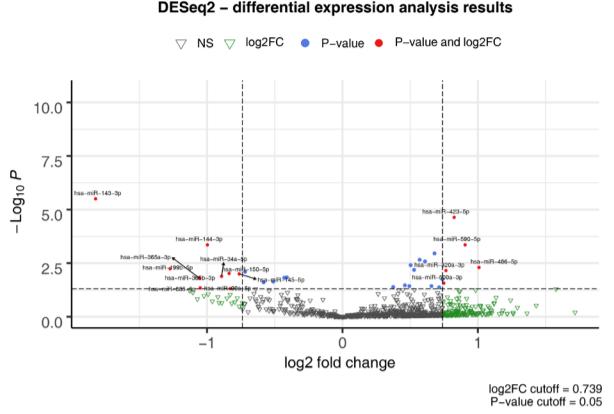
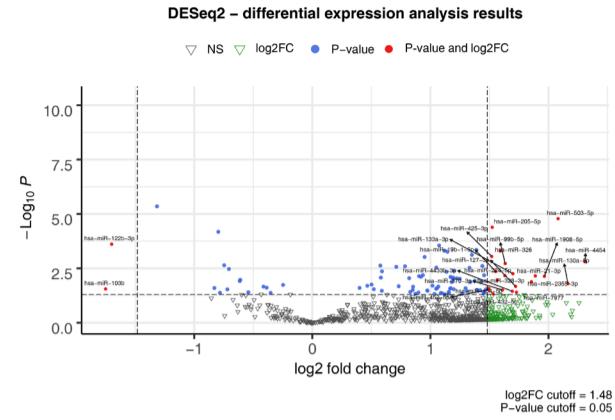


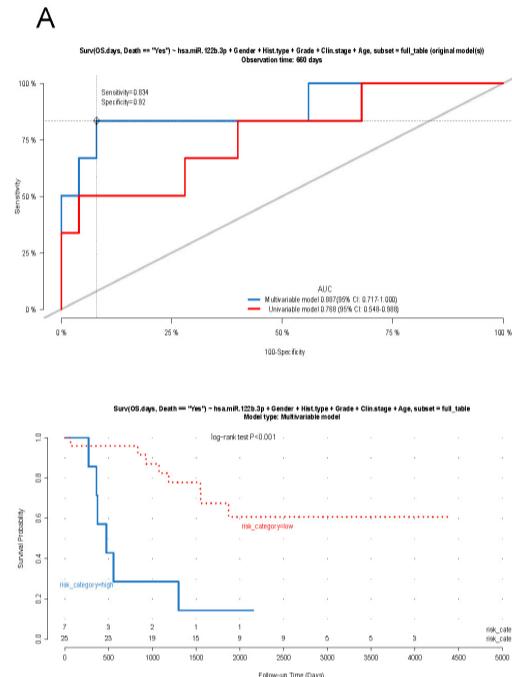
DESeq2 – differential expression analysis results



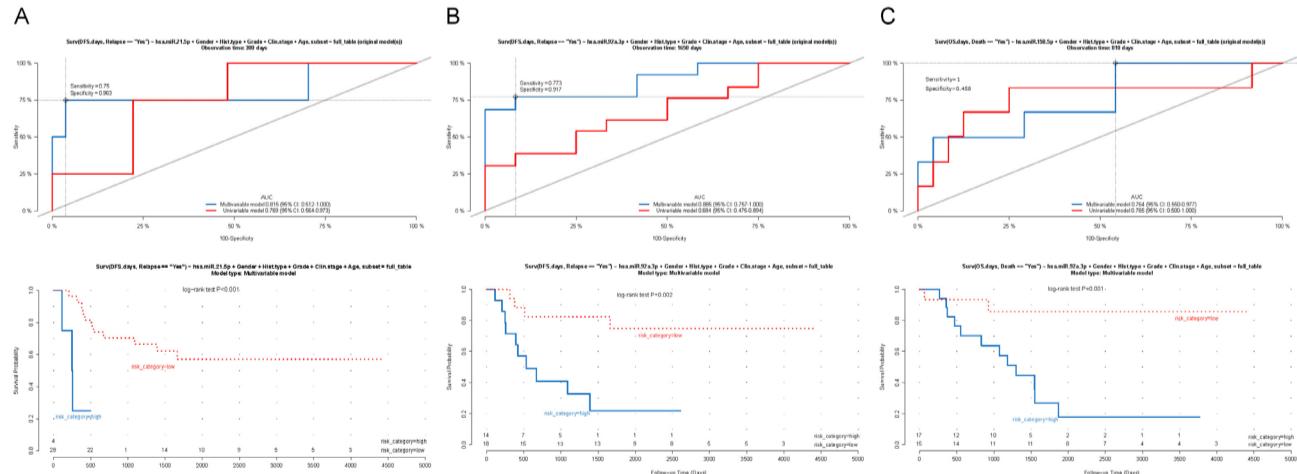
**Figure S1** Volcano plot showing microRNAs (miRs) significantly differentiating non-small cell lung cancer (NSCLC) patients with adenocarcinoma (BS<sub>ADC</sub>, n=18) and controls (C, n=24). The most important miRs, according to P-value and log2FC analysis, are marked with a name. NS, not significant.



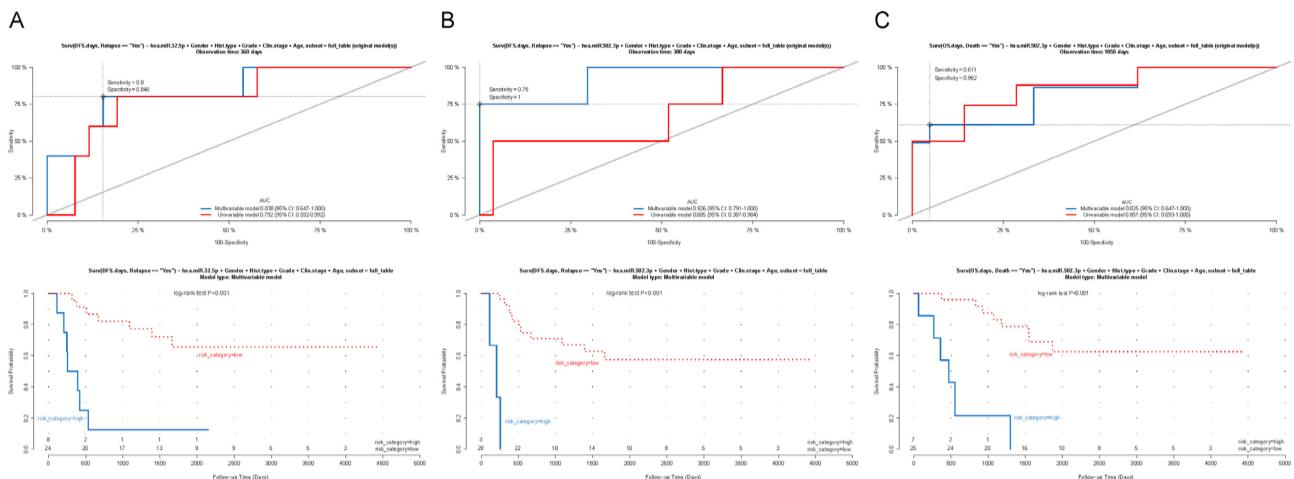
**Figure S2** Volcano plot showing microRNAs (miRs) significantly differentiating non-small cell lung cancer (NSCLC) patients with squamous cell carcinoma (BS<sub>SCC</sub>, n=18) from controls (C, n=24). The most important miRs, according to P-value and log<sub>2</sub>FC analysis, are marked with a name. NS, not significant.



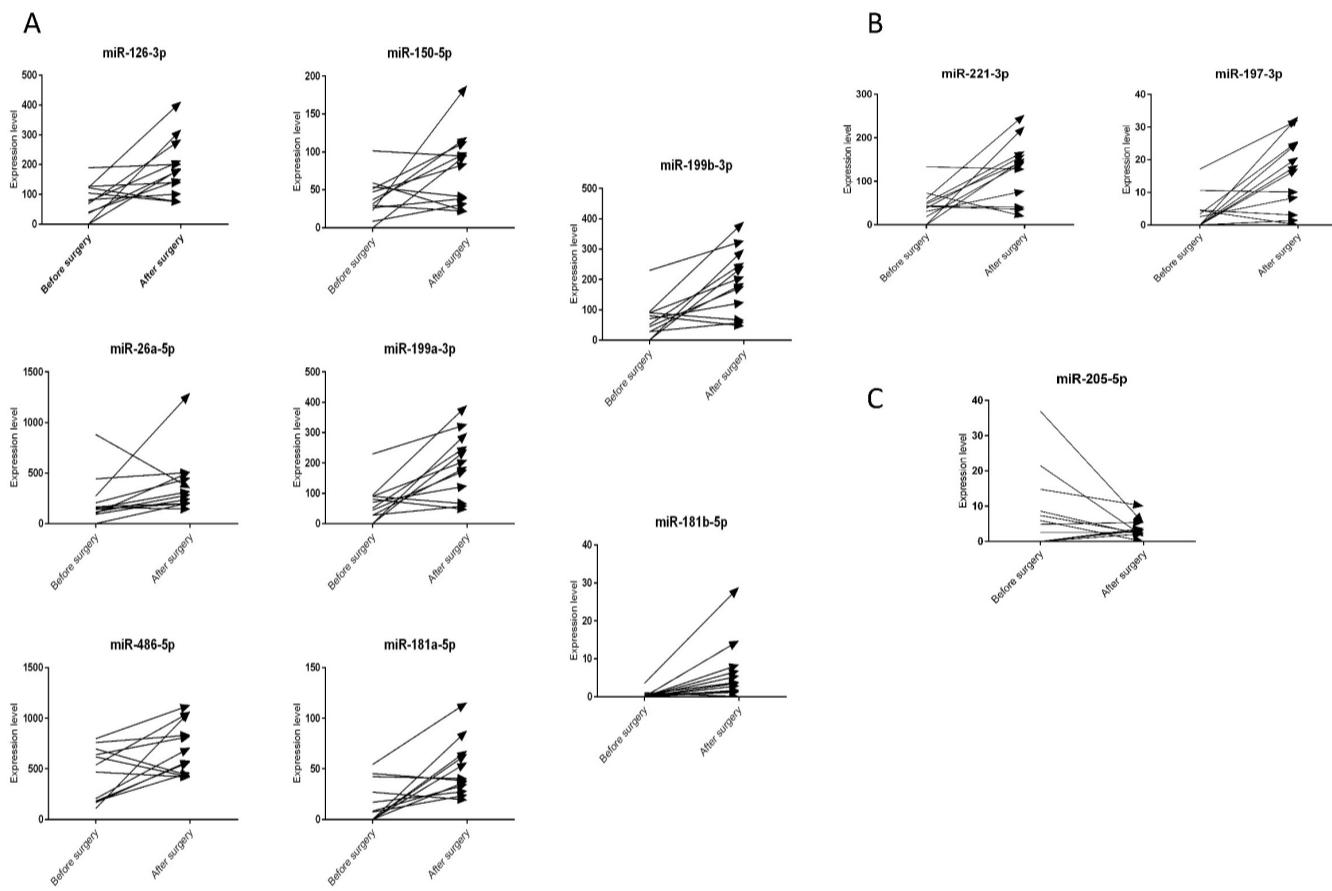
**Figure S3** The receiver operating characteristic (ROC) curves for miR-122b-3p (A), miR-150-5p (B) showing their sensitivity and specificity in differentiating patients in the context of overall survival (OS), and the corresponding Kaplan-Meier survival curves. AUC (areas under ROC curve) values are accompanied by 95% confidence intervals (CI) shown in square brackets. The multivariable analyses included gender, histological type, grade, clinical stage, and age.



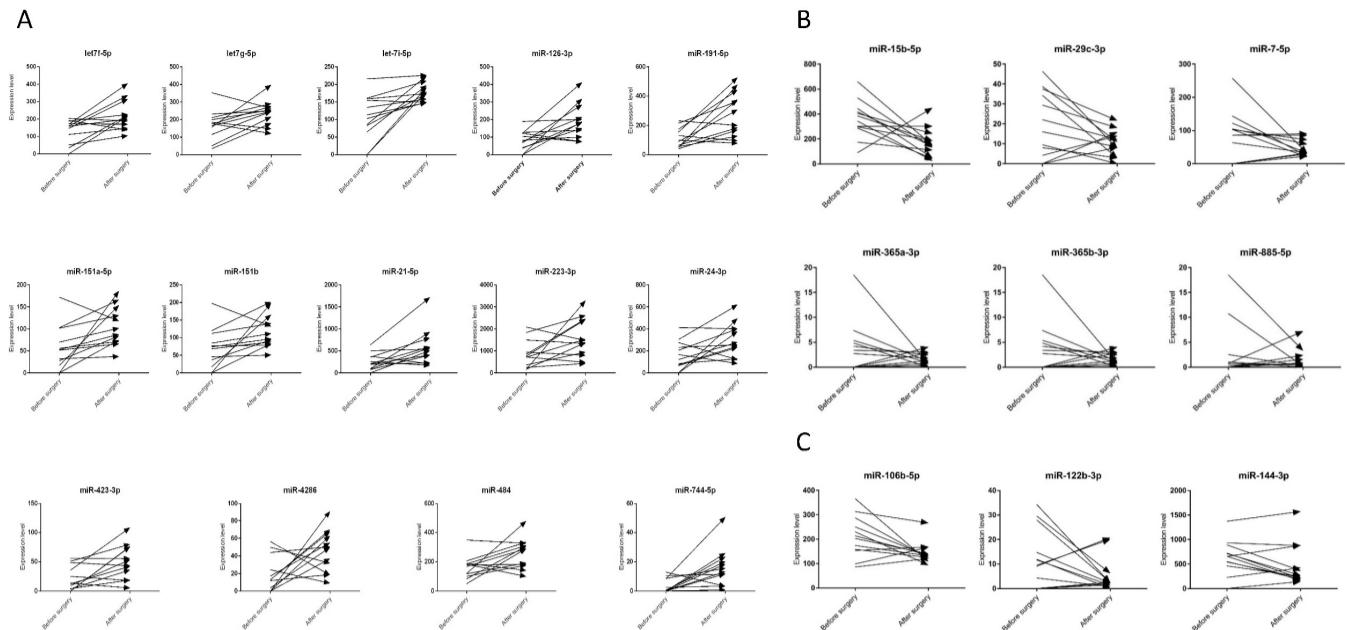
**Figure S4** The receiver operating characteristic (ROC) curves for miR-21-5p (A), miR-92a-3p (B, C) showing their sensitivity and specificity in differentiating patients in the context of disease-free survival (DFS) (A,B) or OS (C) and the corresponding Kaplan-Meier survival curves. AUC (areas under ROC curve) values are accompanied by 95% confidence intervals (CI) shown in square brackets. The multivariable analyses included gender, histological type, grade, clinical stage, and age.



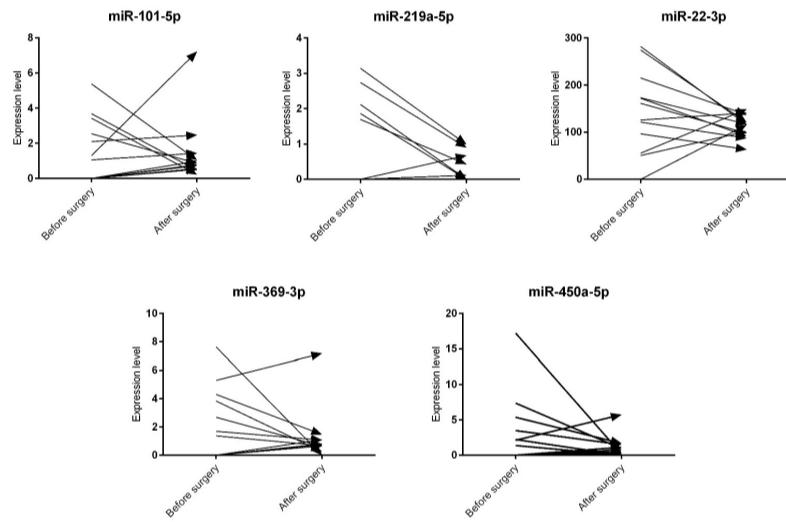
**Figure S5** The receiver operating characteristic (ROC) curves for miR-32-5p (A), miR-502-3p (B, C) showing their sensitivity and specificity in differentiating patients in the context of disease-free survival (DFS) (A,B) or overall survival (OS) (C) and the corresponding Kaplan-Meier survival curves. AUC (areas under ROC curve) values are accompanied by 95% confidence intervals (CI) shown in square brackets. The multivariable analyses included gender, histological type, grade, clinical stage, and age.



**Figure S6** Changes in plasma microRNA (miR) levels in non-small cell lung cancer (NSCLC) patients (n=12) before (BS<sub>Paired</sub>) and after (AS<sub>Paired</sub>) tumour resection in the analysis of paired samples (BS<sub>Paired</sub> vs. AS<sub>Paired</sub>). miRs with increased and normalised plasma levels in NSCLC patients after tumour resection (AS<sub>Paired</sub> vs. C) (A). Two pre-surgery down-regulated miRs (miR-197-3p and miR-221-3p) exceeded normal levels after surgery (AS<sub>Paired</sub> vs. C) (B). miRs -205-5p do not differentiate significantly NSCLC patients before surgery (BS<sub>Paired</sub>) from control group (C) but show a significant downregulation after surgery in the analysis of paired samples (BS<sub>Paired</sub> vs. AS<sub>Paired</sub>)



**Figure S7** Changes in plasma microRNA (miR) levels in non-small cell lung cancer (NSCLC) patients (n=12) before ( $BS_{\text{paired}}$ ) and after ( $AS_{\text{paired}}$ ) tumour resection in the analysis of paired samples ( $BS_{\text{paired}}$  vs.  $AS_{\text{paired}}$ ). Novel miRs with up-regulated (A) and down-regulated (B) plasma levels in NSCLC patients after tumour resection ( $AS_{\text{paired}}$  vs. C). miRs with persisting altered expression levels after surgery by an additional down-regulation ( $AS_{\text{paired}}$  vs. C) (C).



**Figure S8** Changes in plasma microRNA (miR) levels in non-small cell lung cancer (NSCLC) patients (n=12) before ( $BS_{\text{paired}}$ ) and after ( $AS_{\text{paired}}$ ) tumour resection in the analysis of paired samples ( $BS_{\text{paired}}$  vs.  $AS_{\text{paired}}$ ). miRs that do not differentiate NSCLC patients before ( $BS_{\text{paired}}$ ) and after ( $AS_{\text{paired}}$ ) surgery from control group (C) but show a significant down-regulation after surgery in the analysis of paired samples ( $BS_{\text{paired}}$  vs.  $AS_{\text{paired}}$ ).

**Table S1** Pathomorphological characteristics of non-small cell lung cancer (NSCLC) patients (n=36). Adenocarcinoma (ADC) (n=18), squamous cell carcinoma (SCC) (n=18). First sample collection before surgery (BS), second sample collection after surgery (AS). Signature of samples: before surgery (A), after surgery (D). Female (f) (n=13), male (m) (n=23). DFS, Disease Free Survival; OS, Overall Survival.

No	ID	Age (years)			Pathomorph. diagnosis	BS/AS	Time interval between BS and AS (years / month)	Recurrence (Rec)	Tumor grade	Tumor stage	pT	pN	pM	Smoking/ Non- smoking	DFS (months)	OS (months)	Time interval between surgery and the date of last visit or death (years /months)	Death	Other cancers
		Median age 62.5 (43-77)	Sex																
1	25A/D	43	m	ADC	Yes/Yes	1/1	No	2	IB	2a	0	0	smoking	145.1	145.1	11/11	No	lung	
2	34A/D	59	m	ADC	Yes/Yes	1/1	No	2	IB	3	0	0	smoking	143.9	143.9	11/10	No	prostate	
3	44A/D	60	m	ADC	Yes/Yes	1/10	No	2	IB	2a	0	0	ex-smoking	92.9	92.9	7/8	No	bones	
4	52A/D	59	f	ADC	Yes/Yes	1/9	No	2	IIIA	2a	2	0	smoking	121.8	121.8	11/3	No	No	
5	70A/D	68	f	ADC	Yes/Yes	1/3	No	3	IA	1a	0	0	smoking	50.9	50.9	4/1	Yes/cardiac causes	No	
6	80A/D	67	m	ADC	Yes/Yes	3/2	No	2	IIB	3	0	0	smoking	94.9	94.9	8/9	No	No	
7	89A/D	66	f	ADC	Yes/Yes	2/7	No	1	IA	1a	0	0	non- smoking	83.8	83.8	7/10	No	No	
8	54A/D	55	m	SCC	Yes/Yes	1/9	No	2	IA	1b	0	0	smoking	49.3	61.4	4/7	Yes/after gallbladder surgery	No	
9	72A/D	62	m	SCC	Yes/Yes	2/6	No	3	IIB	3	0	0	smoking	70.7	70.7	5/10	No	No	
10	86A/D	62	f	SCC	Yes/Yes	3/0	No	2	IB	2a	0	0	smoking	92.5	92.5	8/8	No	lung	
11	90A/D	76	m	SCC	Yes/Yes	2/7	No	2	IIIA	2b	0	0	smoking	85.7	85.7	8/2	No	No	
12	92A/D	57	m	SCC	Yes/Yes	2/6	No	2	IIIA	2a	1	0	smoking	86.2	86.2	8/1	No	No	
13	5A	63	m	ADC	Yes/No	-	recurrence mediastinal lymph nodes	2	IB	2a	0	0	smoking	17.5	18.2	1/6	Yes	No	
14	9A	56	m	ADC	Yes/No	-	recurrence brain	3	IIIA	2a	1	0	smoking	6.8	11.8	1/0	Yes	No	
15	15A	70	f	ADC	Yes/No	-	recurrence lungs	2	IIIA	4	0	0	smoking	13.8	42.6	3/6	Yes	No	
16	27A	65	f	ADC	Yes/No	-	No	2	IIIA	2a	2	0	smoking	59.7	59.7	4/11	No	No	
17	28A	56	m	ADC	Yes/No	-	recurrence bones	2	IB	2a	0	0	smoking	16.8	30.4	3/6	Yes	No	
18	40A	55	m	ADC	Yes/No	-	No	2	IA	1b	0	0	ex-smoking	55.7	55.7	4/7	No	No	
19	48A	73	m	ADC	Yes/No	-	recurrence mediastinal lymph nodes	2	IA	1b	0	0	smoking	12.4	60.2	4/11	No	No	
20	51A	69	m	ADC	Yes/No	-	recurrence lungs, lymph nodes	2	IIIA	2a	2	0	smoking	22.0	27.3	2/3	Yes	No	
21	67A	60	f	ADC	Yes/No	-	No	3	IA	1a	0	0	smoking	43.6	43.6	3/7	No	No	
22	87A	65	m	ADC	Yes/No	-	No	2	IIIA	3	1	0	smoking	22.6	22.6	1/10	No	No	
23	99A	50	m	ADC	Yes/No	-	No	1	IB	2	0	0	smoking	132.2	132.2	2/0	No	other cancer (2017)	
24	23A	77	f	SCC	Yes/No	-	recurrence mediastinal lymph nodes	2	IIIA	2a	1	0	smoking	10.3	35.3	2/1	Yes	No	
25	32A	56	m	SCC	Yes/No	-	No	3	IIIA	2b	0	0	smoking	123.8	123.8	10/2	No	other cancers: (2014,2020)	
26	36A	56	f	SCC	Yes/No	-	recurrence inguinal lymph nodes	2	IV	2a	0	1	smoking	8.4	30.0	2/5	No	No	
27	43A	76	m	SCC	Yes/No	-	recurrence lungs	2	IB	2a	0	0	smoking	12.9	15.5	1/4	Yes	No	
28	46A	72	m	SCC	Yes/No	-	No	3	IA	1a	0	0	ex-smoking	126.0	126.0	10/4	No	other cancer: (2013)	
29	53A	70	f	SCC	Yes/No	-	recurrence bones	3	IIIA	4	0	0	smoking	3.7	8.8	0/9	Yes	No	
30	55A	58	f	SCC	Yes/No	-	recurrence cervical lymph nodes	2	IB	2a	0	0	smoking	45.7	50.8	5/10	Yes	No	
31	59A	72	m	SCC	Yes/No	-	recurrence thoracic lymph nodes	2	IIB	2b	1	0	smoking	54.6	57.3	4/8	No	No	
32	62A	59	f	SCC	Yes/No	-	No	2	IIB	2b	1	0	smoking	1.6	2.1	0/3	Yes	No	
33	73A	77	m	SCC	Yes/No	-	No	2	IIIA	2b	0	0	smoking	45.9	45.9	4/3	No	No	
34	76A	57	m	SCC	Yes/No	-	recurrence liver	3	IIB	2b	0	0	smoking	35.8	38.9	3/2	Yes	No	
35	84A	63	m	SCC	Yes/No	-	recurrence	3	IIB	3	0	0	smoking	8,1	12.2	1/0	Yes	No	
36	96A	72	f	SCC	Yes/No	-	No	2	IB	2a	0	0	smoking	16,3	16.3	1/4	No	No	

**Table S2** List of samples from healthy donors, control group (C) (n=24), female (f) (n=9), male (m) (n=15).

No	Sample ID	Age (years) Median age 58.5 (36-70)	f/m	Smoking/Non-smoking	Disease status
1	14K	36	f	non-smoker	
2	21K	38	m	non-smoker	not diagnosed with lung disease, cancer or other significant medical conditions
3	22K	62	m	ex-smoker	
4	23K	52	f	smoker	
5	24K	60	f	non-smoker	
6	28K	52	m	ex-smoker	
7	30K	65	f	non-smoker	
8	32K	57	f	smoker	
9	33K	63	m	smoker	
10	34K	60	m	non-smoker	
11	36K	57	f	non-smoker	
12	39K	63	m	smoker	
13	40K	58	f	non-smoker	
14	43K	59	m	ex-smoker	
15	44K	51	m	non-smoker	
16	45K	44	m	smoker	
17	46K	70	m	smoker	
18	49K	66	m	non-smoker	
19	50K	65	m	smoker	
20	51K	56	f	non-smoker	
21	52K	64	m	smoker	
22	53K	38	m	non-smoker	
23	54K	62	f	non-smoker	
24	55K	50	m	ex-smoker	

**Table S3** List of microRNAs (miRs) verified by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) (TaqMan Advanced miRNA Assay).

TaqMan Advanced miRNA Assay	ID number (Applied Biosystems CN A25576)
miR-17-5p	ID 478447_mir
miR-20a-5p	ID 478586_mir
miR-92a-3p	ID 477827_mir
miR-140-3p	ID 477908_mir
miR-143-3p	ID 477912_mir
miR-144-3p	ID 477913_mir
miR-144-5p	ID 477914_mir
miR-150-5p	ID 477918_mir
miR-205-5p	ID 477967_mir
miR-320a-3p	ID 478594_mir
miR-423-5p	ID 478090_mir
miR-425-5p	ID 478094_mir
miR-451a	ID 478107_mir
miR-590-5p	ID 478367_mir
miR-652-3p	ID 478189_mir
Internal controls	
miR-101-3p	ID 477863_mir
miR-361-5p	ID 478056_mir

**Table S4** List of categories used for ontological analyses performed with microRNA (miR) enrichment analysis and annotation tool (miEAA, <https://ccb-compute2.cs.uni-saarland.de/mieaa/>, version 2.1).

Database	Description
GO_Annotations_indirect	Annotations derived over miRTarBase (Gene Ontology)
GO_Annotations	Annotation (Gene Ontology)
KEGG	Pathways (KEGG)
miRandola	exRNA forms (miRandola)
miRBase_Chromosomes	Chromosomal location (miRBase)
miRBase_Conversed_miRNAs_5_organisms	Conservation (miRBase)
miRBase_High_confidence	Confidence (miRBase)
miRBase_Seed_family	Seed family (miRBase)
miRPathDB_GO_Biological_process	GO Biological process (miRPathDB)
miRPathDB_GO_Cellular_component	GO Cellular component (miRPathDB)
miRPathDB_GO_Molecular_function	GO Molecular function (miRPathDB)
miRPathDB_KEGG	KEGG (miRPathDB)
miRPathDB_Reactome	Reactome (miRPathDB)
miRPathDB_WikiPathways	WikiPathways (miRPathDB)
miRTarBase	Target genes (miRTarBase)
miRWalk_Diseases	Diseases (miRWalk)
miRWalk_GO	Gene Ontology (miRWalk)
miRWalk_Organs	Organs (miRWalk)
miRWalk_Pathways	Pathways (miRWalk)
MNDR	Diseases (MNDR)
NPIter	Interactions (NPIter)
Published_Age_gender	Gender/Age
Published_cell_specific	Cell-type specific (Atlas)
Published_Diseases	Published Diseases
Published_Immune_cells	Immune cells
RNAlocate	Localization (RNAlocate)
SM2miR	Drugs (SM2miR)
TissueAtlas	Expressed in tissue (Tissue Atlas)

**Table S5** Plasma microRNAs (miRs) significantly differentiating all non-small cell lung cancer (NSCLC) patients (BS<sub>All</sub>, n=36) and controls (C, n=24). The most important miRs, according to P-value and log2FC analysis, are marked in bold (see Figure 2) (miRs with diagnostic significance confirmed through logistic regression model are marked in red). NA, Not Available.

BS <sub>All</sub> (n=36) vs. C (n=24)				
miRs	BaseMean	Log2FC	P-Value	Padj
Plasma miRs up-regulated in NSCLC patients (BS <sub>All</sub> ) (48 miRs)				
hsa-miR-423-5p	117.49	0.67	<0.001	0.006
hsa-miR-590-5p	10.67	0.85	<0.001	0.006
hsa-miR-185-5p	320.27	0.57	<0.001	0.009
hsa-miR-320a-3p	138.70	0.86	<0.001	0.009
hsa-miR-484	213.57	0.60	<0.001	0.009
<b>hsa-miR-503-5p</b>	3.66	1.56	<0.001	0.009
hsa-miR-130a-3p	56.96	0.90	<0.001	0.01
hsa-miR-1307-5p	8.22	1.08	0.001	0.02
hsa-miR-140-3p	83.51	0.45	0.002	0.03
<b>hsa-miR-425-3p</b>	1.87	1.23	0.002	NA
hsa-miR-191-5p	155.49	0.77	0.002	0.03
<b>hsa-miR-326</b>	14.99	1.18	0.002	0.03
hsa-miR-652-3p	23.29	0.82	0.004	0.046
<b>hsa-miR-4454</b>	0.60	1.81	0.005	NA
<b>hsa-miR-766-3p</b>	5.13	1.12	0.006	0.056
hsa-miR-22-5p	13.99	0.55	0.007	0.05
hsa-miR-92a-3p	479.83	0.48	0.008	0.07

**Table S5 (continued)**

**Table S5 (continued)**

BS <sub>All</sub> (n=36) vs. C (n=24)				
miRs	BaseMean	Log2FC	P-Value	Padj
hsa-miR-423-3p	33.09	0.89	0.01	0.08
<b>hsa-miR-19b-1-5p</b>	0.54	1.18	0.01	NA
<b>hsa-miR-133a-3p</b>	4.70	1.30	0.01	0.09
<b>hsa-miR-328-3p</b>	3.28	1.26	0.01	0.09
hsa-miR-584-5p	8.39	0.93	0.01	0.10
hsa-miR-26b-3p	1.08	0.96	0.01	NA
<b>hsa-miR-4433b-3p</b>	0.45	1.63	0.01	NA
hsa-miR-152-3p	3.37	0.82	0.01	0.11
hsa-miR-30d-5p	211.13	0.41	0.02	0.12
<b>hsa-miR-1908-5p</b>	0.41	1.46	0.02	NA
<b>hsa-miR-130a-5p</b>	0.33	1.74	0.02	NA
hsa-miR-1307-3p	6.55	0.82	0.02	0.12
hsa-miR-99b-5p	2.51	1.08	0.02	NA
hsa-miR-151a-3p	3.38	0.91	0.02	0.12
<b>hsa-miR-224-5p</b>	2.18	1.18	0.02	NA
hsa-miR-151b	101.90	0.58	0.02	0.12
hsa-miR-151a-5p	86.72	0.64	0.02	0.12
hsa-miR-205-5p	17.19	0.80	0.03	0.12
hsa-miR-744-5p	7.73	1.00	0.03	0.12
hsa-miR-425-5p	63.80	0.40	0.03	0.12
hsa-miR-210-3p	5.78	0.49	0.03	0.12
hsa-miR-21-5p	518.42	0.66	0.03	0.12
hsa-miR-130b-5p	1.28	1.01	0.03	NA
hsa-miR-486-5p	1418.87	0.65	0.03	0.13
<b>hsa-miR-21-3p</b>	0.60	1.29	0.03	NA
hsa-miR-296-5p	0.66	0.91	0.03	NA
<b>hsa-miR-877-5p</b>	0.77	1.15	0.04	NA
hsa-miR-629-5p	3.13	0.57	0.04	0.15
hsa-let-7d-3p	7.44	0.68	0.04	0.15
hsa-miR-146a-5p	98.30	0.63	0.04	0.15
<b>hsa-miR-2355-3p</b>	0.52	1.30	0.048	NA
Plasma miRs down-regulated in NSCLC patients (BS <sub>All</sub> ) (17 miRs)				
<b>hsa-miR-144-3p</b>	867.33	-1.14	<0.001	<0.001
<b>hsa-miR-143-3p</b>	16.06	-1.18	<0.001	0.009
hsa-miR-451a	46953.08	-0.54	0.001	0.02
hsa-miR-150-5p	78.83	-0.78	0.004	0.046
hsa-miR-106b-5p	309.34	-0.42	0.004	0.046
hsa-miR-20a-5p	341.01	-0.40	0.004	0.046
hsa-miR-122b-3p	42.76	-1.07	0.006	0.05
hsa-miR-144-5p	49.74	-0.52	0.01	0.08
hsa-miR-106a-5p	35.06	-0.50	0.01	0.08
hsa-miR-20b-5p	20.53	-0.55	0.02	0.12
hsa-miR-18b-5p	10.33	-0.46	0.02	0.12
hsa-miR-19a-3p	509.86	-0.19	0.02	0.12
hsa-miR-17-5p	199.76	-0.48	0.02	0.12
hsa-miR-29a-3p	50.72	-0.50	0.03	0.12
hsa-miR-365a-3p	5.76	-0.78	0.03	0.12
hsa-miR-365b-3p	5.76	-0.78	0.03	0.12
hsa-miR-99a-5p	7.97	-0.68	0.049	0.17

**Table S6** microRNAs (miRs) identified in a logistic regression model in the context of non-small cell lung cancer (NSCLC) occurrence, considering variables such as gender, smoking status, and age. Areas under ROC curve values (AUC); Confidence Intervals (CI); Hazard Ratio/Odds Ratio (HR/OR).

Formula	Factor	HR/OR	95% CI	AUC.Multivariable original model	AUC.Multivariable bootstrapped model
Disease.status ~ hsa.miR.122b.3p + Gender + Smoking.status + Age	hsa.miR.122b.3p	0.456505	[0.229-0.91]	0.924	0.863
Disease.status ~ hsa.miR.144.3p + Gender + Smoking.status + Age	hsa.miR.144.3p	0.195553	[0.048-0.797]	0.940	0.900
Disease.status ~ hsa.miR.185.5p + Gender + Smoking.status + Age	hsa.miR.185.5p	7.534904	[1.595-35.597]	0.953	0.919
Disease.status ~ hsa.miR.20a.5p + Gender + Smoking.status + Age	hsa.miR.20a.5p	0.235476	[0.058-0.956]	0.928	0.886
Disease.status ~ hsa.miR.20b.5p + Gender + Smoking.status + Age	hsa.miR.20b.5p	0.128416	[0.024-0.681]	0.936	0.909
Disease.status ~ hsa.miR.423.5p + Gender + Smoking.status + Age	hsa.miR.423.5p	29.32893	[2.273-378.473]	0.979	0.909
Disease.status ~ hsa.miR.451a + Gender + Smoking.status + Age	hsa.miR.451a	0.200784	[0.049-0.826]	0.938	0.896
Disease.status ~ hsa.miR.590.5p + Gender + Smoking.status + Age	hsa.miR.590.5p	8.205019	[1.572-42.815]	0.952	0.899

**Table S7** microRNAs (miRs) identified in the multivariable Cox regression analysis as independent prognostic factors for overall survival (OS) and disease-free survival (DFS). The analysis included gender, histological type, grade, clinical stage, and age. miRs differentiating before surgery group (BS<sub>ALL</sub>) and control group (C) are marked in blue. Areas under ROC curve values (AUC); Confidence Intervals (CI); Hazard Ratio/Odds Ratio (HR/OR).

Formula	Factor	HR/OR	95% CI	P-value	AUC. Multivariable original_model	AUC. Multivariable bootstrapped model
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.21.5p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.21.5p	17.87	[1.131-282.404]	0.04	0.81	0.88
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.21.5p + Gender + Hist.type + Grade + Clin.stage + Age	Clin.stage:IV	38.37	[1.759-836.98]	0.02	0.81	0.88
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.21.5p + Gender + Hist.type + Grade + Clin.stage + Age	Age	1.11	[1.001-1.222]	0.047	0.81	0.88
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.32.5p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.32.5p	26.50	[3.051-230.229]	0.003	0.84	0.78
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.32.5p + Gender + Hist.type + Grade + Clin.stage + Age	Grade:3	6.51	[1.12-37.879]	0.03	0.84	0.78
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.502.3p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.502.3p	175.55	[7.347-4194.415]	0.001	0.93	0.90
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.502.3p + Gender + Hist.type + Grade + Clin.stage + Age	Grade:3	5.43	[1.015-29.1]	0.048	0.93	0.90
Surv(OS.days, Death == "Yes") ~ hsa.miR.502.3p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.502.3p	369.75	[14.523-9413.804]	<0.001	0.83	0.69
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.92a.3p	448273.14	[254.125-790747312.601]	0.001	0.89	0.68
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	Hist.type:SCC	12.79	[1.362-120.152]	0.02	0.89	0.68
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	Clin.stage:IIA_IIB	0.12	[0.015-0.876]	0.03	0.89	0.68
Surv(DFS.days, Relapse == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	Clin.stage:IV	38.24	[1.548-944.819]	0.02	0.89	0.68
Surv(OS.days, Death == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.92a.3p	194000.00	[188.698-199451220.104]	0.001	0.83	0.67
Surv(OS.days, Death == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	Hist.type:SCC	15.86	[2.168-116.002]	0.006	0.83	0.67
Surv(OS.days, Death == "Yes") ~ hsa.miR.92a.3p + Gender + Hist.type + Grade + Clin.stage + Age	Clin.stage:IIA_IIB	0.12	[0.017-0.919]	0.04	0.83	0.67
Surv(OS.days, Death == "Yes") ~ hsa.miR.122b.3p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.122b.3p	562.65	[7.849-40335.738]	0.003	0.89	0.74
Surv(OS.days, Death == "Yes") ~ hsa.miR.122b.3p + Gender + Hist.type + Grade + Clin.stage + Age	Grade:3	4.49	[1.085-18.584]	0.04	0.89	0.74
Surv(OS.days, Death == "Yes") ~ hsa.miR.150.5p + Gender + Hist.type + Grade + Clin.stage + Age	hsa.miR.150.5p	33800.60	[5.191-220102681.5]	0.02	0.76	0.71

**Table S8** Plasma microRNAs (miRs) significantly differentiating adenocarcinoma (ADC) NSCLC patients (BS<sub>ADC</sub>, n=18) and controls (C, n=24). The most important miRs, according to P-value and log2FC analysis, are marked in bold (Figure S1). NA, Not Available.

BS <sub>ADC</sub> (n=18) vs. C (n=24)				
miRs	BaseMean	Log2FC	P-Value	Padj
Plasma miRs up-regulated in ADC NSCLC (BS <sub>ADC</sub> ) (16miRs)				
<b>hsa-miR-423-5p</b>	117.49	0.82	<0.001	0.001
<b>hsa-miR-590-5p</b>	10.67	0.91	<0.001	0.01
hsa-miR-92a-3p	479.83	0.68	0.001	0.02
hsa-miR-185-5p	320.27	0.57	0.002	0.048
hsa-miR-484	213.57	0.61	0.002	0.050
hsa-miR-140-3p	83.51	0.50	0.003	0.06
<b>hsa-miR-486-5p</b>	1418.87	1.01	0.005	0.07
hsa-let-7i-5p	149.33	0.53	0.006	0.08
<b>hsa-miR-320a-3p</b>	138.70	0.76	0.007	0.08
hsa-miR-502-3p	2.79	0.74	0.01	NA
<b>hsa-miR-500a-3p</b>	4.01	0.75	0.02	NA
hsa-miR-15a-5p	911.24	0.46	0.03	0.22
hsa-miR-130a-3p	56.96	0.66	0.03	0.22
hsa-miR-25-3p	53.29	0.49	0.03	0.22
hsa-miR-107	214.56	0.37	0.04	0.23
hsa-miR-629-5p	3.13	0.71	0.04	NA
Plasma miRs down-regulated in ADC NSCLC (BS <sub>ADC</sub> ) (15 miRs)				
<b>hsa-miR-143-3p</b>	16.06	-1.82	<0.001	<0.001
<b>hsa-miR-144-3p</b>	867.33	-1.00	<0.001	0.01
<b>hsa-miR-199b-5p</b>	1.93	-1.27	0.005	NA
hsa-miR-29a-3p	50.72	-0.72	0.008	0.08
<b>hsa-miR-150-5p</b>	78.83	-0.84	0.009	0.09
<b>hsa-miR-145-5p</b>	73.53	-0.76	0.01	0.09
<b>hsa-miR-34a-5p</b>	6.71	-0.89	0.01	0.11
hsa-miR-20a-5p	341.01	-0.41	0.01	0.11
hsa-miR-106b-5p	309.34	-0.43	0.01	0.11
<b>hsa-miR-365a-3p</b>	5.76	-1.06	0.01	NA
<b>hsa-miR-365b-3p</b>	5.76	-1.06	0.01	NA
hsa-miR-18a-5p	70.44	-0.51	0.02	0.17
hsa-miR-17-5p	199.76	-0.58	0.02	0.17
<b>hsa-miR-885-5p</b>	2.41	-1.05	0.04	NA
<b>hsa-miR-99a-5p</b>	7.97	-0.83	0.049	0.27

**Table S9** Plasma microRNAs (miRs) significantly differentiating squamous cell carcinoma (SCC) NSCLC patients (BS<sub>SCC</sub>, n=18) and controls (C, n=24). The most important miRs, according to P-value and log2FC analysis, are marked in bold (Figure S2). NA, Not Available.

BS <sub>SCC</sub> (n=18) vs. C (n=24)				
miRs	BaseMean	Log2FC	P-Value	Padj
Plasma miRs up-regulated in SCC NSCLC patients (BS <sub>SCC</sub> ) (86 miRs)				
<b>hsa-miR-503-5p</b>	3.66	2.08	<0.001	0.003
<b>hsa-miR-205-5p</b>	17.19	1.52	<0.001	0.004
hsa-miR-191-5p	155.49	1.07	<0.001	0.01
hsa-miR-1307-5p	8.22	1.39	<0.001	0.01
hsa-miR-130a-3p	56.96	1.12	<0.001	0.01
<b>hsa-miR-326</b>	14.99	1.59	<0.001	0.01
hsa-miR-652-3p	23.29	1.14	<0.001	0.01
hsa-miR-423-3p	33.09	1.35	<0.001	0.02
<b>hsa-miR-425-3p</b>	1.87	1.52	<0.001	0.02
hsa-miR-320a-3p	138.70	0.95	0.001	0.02
<b>hsa-miR-4454</b>	0.60	2.31	0.001	0.04
<b>hsa-miR-99b-5p</b>	2.51	1.63	0.001	0.04
hsa-miR-185-5p	320.27	0.58	0.002	0.04
hsa-miR-766-3p	5.13	1.44	0.002	0.04
hsa-miR-590-5p	10.67	0.78	0.002	0.04
hsa-miR-22-5p	13.99	0.71	0.002	0.04
hsa-miR-21-5p	518.42	1.05	0.002	0.04
hsa-miR-26b-3p	1.08	1.33	0.003	0.04
hsa-miR-1307-3p	6.55	1.20	0.004	0.06
hsa-miR-484	213.57	0.59	0.004	0.06
<b>hsa-miR-19b-1-5p</b>	0.54	1.55	0.004	0.06
hsa-miR-152-3p	3.37	1.14	0.004	0.06
<b>hsa-miR-133a-3p</b>	4.70	1.70	0.005	0.07
hsa-miR-23a-3p	380.33	0.94	0.006	0.07
hsa-miR-744-5p	7.73	1.45	0.006	0.07
<b>hsa-miR-224-5p</b>	2.18	1.63	0.006	0.07
<b>hsa-miR-21-3p</b>	0.60	1.89	0.007	0.07
hsa-miR-24-3p	245.45	0.90	0.007	0.07
<b>hsa-miR-1908-5p</b>	0.41	1.97	0.007	0.07
hsa-miR-151a-5p	86.72	0.92	0.007	0.07
hsa-miR-199a-3p	190.16	1.17	0.007	0.07
hsa-miR-199b-3p	190.16	1.17	0.007	0.07
hsa-miR-425-5p	63.80	0.58	0.008	0.07
hsa-miR-584-5p	8.39	1.19	0.008	0.07
hsa-miR-151b	101.90	0.82	0.009	0.08
hsa-miR-151a-3p	3.38	1.22	0.009	0.08
hsa-miR-652-5p	1.63	1.25	0.009	0.08
hsa-miR-28-5p	4.64	1.19	0.009	0.08
<b>hsa-miR-328-3p</b>	3.28	1.57	0.01	0.08
hsa-miR-130b-5p	1.28	1.38	0.01	0.09
<b>hsa-miR-2355-3p</b>	0.52	1.86	0.01	0.09
hsa-miR-421	0.92	1.34	0.01	0.09
hsa-miR-199a-5p	13.40	1.18	0.01	0.09
hsa-miR-1301-3p	1.98	1.43	0.01	0.09
<b>hsa-miR-130a-5p</b>	0.33	2.16	0.01	NA
hsa-miR-30d-5p	211.13	0.50	0.01	0.12
hsa-miR-4286	36.17	1.02	0.01	0.13
hsa-miR-423-5p	117.49	0.47	0.02	0.13
hsa-miR-126-5p	156.34	0.73	0.02	0.13
<b>hsa-miR-127-3p</b>	0.83	1.72	0.02	0.13
hsa-miR-338-3p	2.81	1.07	0.02	0.13

**Table S9 (continued)**

**Table S9 (continued)**

BS <sub>scc</sub> (n=18) vs. C (n=24)				
miRs	BaseMean	Log2FC	P-Value	Padj
hsa-miR-146a-5p	98.30	0.85	0.02	0.13
hsa-miR-140-3p	83.51	0.40	0.02	0.14
hsa-miR-33a-5p	8.97	1.06	0.02	0.14
hsa-miR-505-5p	0.87	1.17	0.02	0.14
hsa-miR-543	2.34	1.30	0.02	0.14
<b>hsa-miR-154-5p</b>	0.86	1.49	0.02	0.14
hsa-miR-409-3p	3.88	1.17	0.02	0.14
hsa-miR-4433b-5p	22.78	1.05	0.02	0.14
hsa-miR-654-3p	0.92	1.47	0.02	0.14
hsa-miR-128-3p	37.33	0.52	0.02	0.14
hsa-miR-28-3p	2.57	1.20	0.02	0.14
<b>hsa-miR-452-5p</b>	0.52	1.49	0.03	0.14
hsa-miR-339-3p	0.57	1.39	0.03	0.14
hsa-miR-93-3p	2.15	0.85	0.03	0.14
<b>hsa-miR-370-3p</b>	0.35	1.61	0.03	0.14
hsa-miR-877-5p	0.77	1.42	0.03	0.14
hsa-miR-376a-3p	19.38	0.97	0.03	0.14
hsa-miR-376c-3p	25.80	0.97	0.03	0.14
hsa-miR-339-5p	24.72	0.59	0.03	0.14
hsa-miR-487b-3p	1.42	1.31	0.03	0.15
<b>hsa-miR-4433b-3p</b>	0.45	1.69	0.03	0.15
hsa-miR-382-5p	2.28	1.16	0.03	0.16
hsa-let-7d-3p	7.44	0.83	0.03	0.16
<b>hsa-miR-7977</b>	0.31	1.73	0.03	NA
hsa-miR-197-3p	12.37	0.90	0.04	0.16
hsa-miR-628-3p	0.37	1.46	0.04	0.16
hsa-miR-7-1-3p	1.04	1.09	0.04	0.16
hsa-miR-329-3p	3.42	1.16	0.04	0.16
hsa-miR-181c-5p	1.61	1.10	0.04	0.16
hsa-miR-1185-1-3p	0.50	1.45	0.04	0.17
hsa-miR-494-3p	1.90	1.27	0.046	0.17
hsa-miR-1260b	22.60	0.87	0.047	0.17
<b>hsa-miR-432-5p</b>	0.49	1.53	0.047	0.17
hsa-let-7e-5p	2.93	1.03	0.048	0.17
hsa-miR-625-3p	3.07	1.12	0.049	0.17
Plasma miRs down-regulated in SCC NSCLC (BS <sub>scc</sub> ) (16 miRs)				
hsa-miR-144-3p	867.33	-1.32	<0.001	0.001
hsa-miR-451a	46953.08	-0.80	<0.001	0.006
<b>hsa-miR-122b-3p</b>	42.76	-1.70	<0.001	0.01
hsa-miR-144-5p	49.74	-0.75	0.002	0.048
hsa-miR-106a-5p	35.06	-0.71	0.003	0.053
hsa-miR-16-2-3p	41.93	-0.61	0.01	0.08
hsa-miR-18b-5p	10.33	-0.61	0.01	0.09
hsa-miR-19a-3p	509.86	-0.25	0.01	0.12
hsa-miR-106b-5p	309.34	-0.41	0.02	0.13
hsa-miR-20a-5p	341.01	-0.39	0.02	0.14
hsa-miR-190a-5p	2.66	-0.83	0.02	0.14
hsa-miR-103b	1.30	-1.75	0.02	0.14
hsa-miR-150-5p	78.83	-0.72	0.02	0.14
hsa-miR-15b-3p	19.26	-0.54	0.03	0.16
hsa-miR-143-3p	16.06	-0.78	0.04	0.16
hsa-miR-16-5p	1990.11	-0.35	0.04	0.16

**Table S10** Plasma microRNAs (miRs) significantly differentiating non-small cell lung cancer (NSCLC) patients with adenocarcinoma (ADC, BS<sub>ADC</sub>, n=18) and squamous cell carcinoma (SCC, BS<sub>SCC</sub>, n=18) subtypes.

BS <sub>ADC</sub> (n=18) vs. BS <sub>SCC</sub> (n=18)						
miRs	BaseMean		Log2FC		P-Value	Padj
Plasma miRs up-regulated in ADC NSCLC vs. SCC NSCLC patients (3 miRs)						
hsa-miR-15a-5p		911.24		0.89	<0.001	0.02
hsa-miR-107		214.55		0.60	0.003	0.08
hsa-miR-32-5p		11.08		1.14	0.003	0.08
Plasma miRs down-regulated in ADC NSCLC vs. SCC NSCLC patients (13 miRs)						
hsa-miR-199a-5p		13.40		-1.81	<0.001	0.051
hsa-miR-376a-3p		19.38		-1.65	<0.001	0.07
hsa-miR-543		2.34		-2.03	0.001	0.07
hsa-miR-199a-3p		190.15		-1.50	0.001	0.07
hsa-miR-199b-3p		190.15		-1.50	0.001	0.07
hsa-miR-376c-3p		25.79		-1.56	0.001	0.07
hsa-miR-34a-5p		6.71		-1.18	0.001	0.07
hsa-miR-126-5p		156.34		-1.02	0.002	0.08
hsa-miR-495-3p		3.94		-1.87	0.003	0.08
hsa-miR-574-3p		4.11		-1.52	0.003	0.08
hsa-miR-381-3p		1.18		-2.26	0.003	0.08
hsa-miR-487b-3p		1.42		-1.92	0.004	0.08
hsa-miR-337-5p		1.16		-2.21	0.004	0.08

**Table S11** Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) verification of selected plasma microRNAs (miRs) identified in the NGS study, significantly differentiating all non-small cell lung cancer (NSCLC) patients (BS<sub>All</sub>, n=36)/ adenocarcinoma ADC NSCLC patients (BS<sub>ADC</sub>, n=18)/ squamous cell carcinoma SCC NSCLC patients (BS<sub>SCC</sub>, n=18) and control group (C, n=24).

miRs	RT-qPCR						NGS				miR significantly differentiating the compared groups in NGS study
	Plasma levels in Controls (median)	Plasma levels in BS <sub>All</sub> (median)	Plasma levels in BS <sub>ADC</sub> (median)	Plasma levels in BS <sub>SCC</sub> (median)	BS <sub>All</sub> vs. C P-Value	BS <sub>ADC</sub> vs. C P-Value	BS <sub>SCC</sub> vs. C P-Value	P-Value (BS <sub>All</sub> vs. C)	P-Value (BS <sub>ADC</sub> vs. C)	P-Value (BS <sub>SCC</sub> vs. C)	
Selected miRs up-regulated in NSCLC											
hsa-miR-205-5p	0.026	0.03	-	0.07	0.37	-	0.006	0.03	-	<0.001	BS <sub>All</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-423-5p	2.344	5.20	6.24	4.21	0.001	0.002	0.01	<0.001	<0.001	0.02	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-425-5p	0.819	0.99	-	0.81	0.16	-	0.72	0.03	-	0.008	BS <sub>All</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-590-5p	0.027	0.02	0.02	0.02	0.048	0.77	0.004	<0.001	<0.001	0.002	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-92a-3p	9.719	13.59	14.89	-	0.02	<0.001	-	0.008	0.004	-	BS <sub>All</sub> /BS <sub>ADC</sub> vs. C
hsa-miR-140-3p	0.234	0.26	0.30	0.25	0.14	0.03	0.71	0.002	0.005	0.02	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-320a-3p	0.894	1.48	1.72	1.21	<0.001	<0.001	0.052	<0.001	0.007	<0.001	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-652-3p	1.077	1.60	-	1.59	0.001	-	0.001	0.004	-	<0.001	BS <sub>All</sub> /BS <sub>SCC</sub> vs. C
Selected miRs down-regulated in NSCLC											
hsa-miR-143-3p	0.183	0.12	0.08	0.12	0.041	0.06	0.10	<0.001	<0.001	0.04	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-144-3p	28.227	24.21	25.24	24.21	0.162	0.62	0.11	<0.001	<0.001	<0.001	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-144-5p	0.055	0.02	-	0.02	0.003	-	0.001	0.01	-	0.002	BS <sub>All</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-150-5p	1.663	1.16	1.25	0.91	0.015	0.08	0.01	0.004	0.01	0.02	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-451a	304.861	310.04	-	305.32	0.704	-	0.48	0.001	-	<0.001	BS <sub>All</sub> /BS <sub>SCC</sub> vs. C
hsa-miR-17-5p	10.385	8.01	8.95	-	0.042	0.56	-	0.02	0.02	-	BS <sub>All</sub> /BS <sub>ADC</sub> vs. C
hsa-miR-20a-5p	4.595	3.54	4.12	3.14	0.031	0.40	0.005	0.004	0.01	0.02	BS <sub>All</sub> /BS <sub>ADC</sub> /BS <sub>SCC</sub> vs. C

**Table S12** Ontological analysis of selected up-regulated plasma microRNAs (miRs) (n=8) in non-small cell lung cancer (NSCLC) patients (BS<sub>All</sub>, n=36), verified by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) method.

No	Subcategory	q-value*	miRs observed	hsa-miRs/precursors
GO Annotations indirect				
1	Extrinsic component of neuronal dense core vesicle membrane GO0098674	0.004	3	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-652-3p
2	Positive regulation of TRAIL-activated apoptotic signaling pathway GO1903984	0.004	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
3	Postsynaptic density assembly GO0097107	0.004	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p
4	Electron transport coupled proton transport GO0015990	0.007	4	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
5	Negative regulation of intrinsic apoptotic signaling pathway in response to osmotic stress GO1902219	0.007	4	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
6	NADP biosynthetic process GO0006741	0.009	2	hsa-miR-425-5p; hsa-miR-92a-3p
7	Cytoplasmic side of rough endoplasmic reticulum membrane GO0098556	0.009	4	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
8	Angiostatin binding GO0043532	0.01	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
9	Glutamate-tRNA ligase activity GO0004818	0.01	3	hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p
GO Annotations				
1	Extracellular space GO0005615	0.04	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
2	Negative regulation of endothelial cell proliferation GO0001937	0.04	2	hsa-miR-205-5p; hsa-miR-92a-3p
3	Positive regulation of metalloendopeptidase activity GO1904685	0.04	2	hsa-miR-205-5p; hsa-miR-92a-3p
miRPath DB Biological process				
1	Cytoplasmic translation	0.01	3	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-652-3p
2	Protein localization to membrane	0.02	4	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-652-3p
3	Nuclear envelope disassembly	0.03	2	hsa-miR-205-5p; hsa-miR-92a-3p
miRPath DB Cellular component				
1	Cytoplasmic side of endoplasmic reticulum membrane	0.002	2	hsa-miR-425-5p; hsa-miR-652-3p
2	Cytosolic ribosome	0.01	3	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-652-3p
3	Organelle membrane	0.01	3	hsa-miR-205-5p; hsa-miR-92a-3p; hsa-miR-652-3p
4	Sin3 complex	0.0144891	2	hsa-miR-205-5p; hsa-miR-652-3p
miRPath DB Molecular function				
1	Clathrin binding	0.006	2	hsa-miR-205-5p; hsa-miR-92a-3p
2	Inositol phosphate phosphatase activity	0.006	2	hsa-miR-205-5p; hsa-miR-425-5p
3	Transcription coregulator activity	0.01	4	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-590-5p; hsa-miR-92a-3p
4	Double-stranded RNA binding	0.01	3	hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-652-3p
5	Transcription coactivator activity	0.01	3	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-92a-3p
miRPath DB KEGG				
1	Cell cycle	0.02	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p
miRPath DB Reactome				
1	Activation of the mRNA upon binding of the cap-binding complex and eIFs and subsequent binding to 43S	0.01	3	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-652-3p
2	Formation of the ternary complex and subsequently the 43S complex	0.01	3	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-652-3p
3	Ribosomal scanning and start codon recognition	0.01	3	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-652-3p
4	Translation initiation complex formation	0.01	3	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-652-3p
5	Mitotic G1-G1S phases	0.01	4	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p
miRPath DB WikiPathways				
1	Cell Cycle	0.03	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p

**Table S12 (continued)**

**Table S12 (continued)**

No	Subcategory	q-value*	miRs observed	hsa-miRs/precursors
miRTarBase				
1	ATP5B	<0.001	4	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
2	EPM2AIP1	<0.001	5	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
3	RPL27	<0.001	3	hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
4	KIF1A	0.001	3	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-652-3p
5	CCNI	0.002	3	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
6	HIST1H1E	0.002	4	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
7	NADK	0.003	2	hsa-miR-425-5p; hsa-miR-92a-3p
8	POM121	0.006	3	hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
9	RAB11A	0.007	2	hsa-miR-92a-3p; hsa-miR-320a-3p
10	EIF3C	0.007	3	hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
11	CARS	0.007	2	hsa-miR-92a-3p; hsa-miR-652-3p
12	COX1	0.007	3	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
13	EIF3G	0.007	2	hsa-miR-425-5p; hsa-miR-92a-3p
14	FAM3A	0.007	2	hsa-miR-423-5p; hsa-miR-92a-3p
15	FAU	0.007	2	hsa-miR-92a-3p; hsa-miR-140-3p
16	PDLIM1	0.007	2	hsa-miR-92a-3p; hsa-miR-320a-3p
17	PFDN6	0.007	2	hsa-miR-92a-3p; hsa-miR-320a-3p
18	GAPDH	0.008	3	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
miRWalk GO				
1	GO0007017 Microtubule based process	0.04	6	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
2	GO0007243 Intracellular protein kinase cascade	0.04	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
3	GO0007507 Heart development	0.04	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
4	GO0009749 Response to glucose stimulus	0.04	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
5	GO0010506 Regulation of autophagy	0.04	5	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
6	GO0035162 Embryonic hemopoiesis	0.04	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
7	GO0060021 Palate development	0.04	7	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
miRWalk Pathways				
1	P02721 ATP synthesis	0.03	4	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
2	P04374 5HT2 Type receptor mediated signaling pathway	0.03	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
3	P04385 Histamine H1 receptor mediated signaling pathway	0.03	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
4	P04391 Oxytocin receptor mediated signaling pathway	0.03	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
5	P04394 Thyrotropin releasing hormone receptor signaling pathway	0.03	5	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p
6	WP2018 RANKL RANK Signaling Pathway	0.03	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
7	WP366 TGF beta Signaling Pathway1	0.03	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
8	WP404 Nucleotide Metabolism	0.03	5	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
9	hsa00480 Glutathione metabolism	0.03	5	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
10	hsa04350 TGF beta Signaling pathway	0.03	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p

**Table S12 (continued)**

**Table S12 (continued)**

No	Subcategory	q-value*	miRs observed	hsa-miRs/precursors
11	hsa05212 Pancreatic cancer	0.03	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
12	hsa00970 Aminoacyl tRNA biosynthesis	0.04	5	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
13	hsa04930 Type II diabetes mellitus	0.04	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
14	P00021 FGF Signaling pathway	0.04	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
15	P00018 EGF Receptor signaling pathway	0.04	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
16	WP313 Signaling of Hepatocyte Growth Factor Receptor	0.04	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p
17	hsa04140 Regulation of autophagy	0.04	4	hsa-miR-423-5p; hsa-miR-92a-3p; hsa-miR-320a-3p; hsa-miR-652-3p
MNDR				
1	Multiple myeloma	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
2	Retinoblastoma	<0.001	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p
3	Osteosarcoma	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
4	Amyotrophic lateral sclerosis	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
5	Cardiovascular disease	<0.001	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-652-3p
6	Cervical squamous cell carcinoma	<0.001	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-652-3p
7	Prostate cancer	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
8	Bladder urothelial carcinoma	<0.001	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-652-3p
9	Breast cancer luminal	<0.001	6	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p
10	Dysautonomia familial	<0.001	6	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-652-3p
11	Lung cancer	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
RNALocate				
1	Cytoplasm	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
2	Nucleus	<0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
3	Circulating	0.001	8	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
4	Microvesicle	0.001	7	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
5	Mitochondrion	0.001	7	hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-590-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p; hsa-miR-652-3p
6	Exosome	0.002	6	hsa-miR-205-5p; hsa-miR-423-5p; hsa-miR-425-5p; hsa-miR-92a-3p; hsa-miR-140-3p; hsa-miR-320a-3p
isomiRdb Tissue specific				
1	Blood specific	<0.001	2	hsa-miR-425-5p; hsa-miR-92a-3p

\* p-value after the Benjamini-Hochberg adjustment

**Table S13** Ontological analysis of selected down-regulated plasma micro RNAs (miRs) (n=7) in non-small cell lung cancer (NSCLC) patients (BS<sub>All</sub>, n=36), verified by the reverse transcription-quantitative polymerase chain reaction (RT-qPCR) method.

No	Subcategory	*q-value	miRs observed	hsa-miRs/precursors
GO Annotations indirect				
1	Rhombomere 3 structural organization GO0021659	0.005	3	hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
2	Rhombomere 5 structural organization GO0021665	0.005	3	hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
3	BAD-BCL-2 complex GO0097138	0.008	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
4	G protein-coupled GABA receptor complex GO1902712	0.008	3	hsa-miR-144-5p; hsa-miR-17-5p; hsa-miR-20a-5p
5	Schwann cell differentiation GO0014037	0.008	4	hsa-miR-143-3p; hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
6	Brush border assembly GO1904970	0.008	4	hsa-miR-143-3p; hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
7	Channel inhibitor activity GO0016248	0.008	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
8	Histone H3-K27 trimethylation GO0098532	0.008	4	hsa-miR-144-3p; hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
9	Negative regulation of bicellular tight junction assembly GO1903347	0.008	4	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p
10	Negative regulation of cellular pH reduction GO0032848	0.008	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
11	Negative regulation of fatty acid beta-oxidation GO0031999	0.008	5	hsa-miR-143-3p; hsa-miR-150-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
12	Neuron-glial cell signaling GO0150099	0.008	3	hsa-miR-144-5p; hsa-miR-17-5p; hsa-miR-20a-5p
13	Prostaglandin biosynthetic process GO0001516	0.008	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-150-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
14	Protein localization to microvillus GO1904106	0.008	4	hsa-miR-143-3p; hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
15	Regulation of miRNA transcription GO1902893	0.008	4	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-17-5p; hsa-miR-20a-5p
16	Slit diaphragm assembly GO0036060	0.008	3	hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
17	Muscle alpha-actinin binding GO0051371	0.008	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-150-5p; hsa-miR-17-5p; hsa-miR-20a-5p
GO Annotations				
1	Positive regulation of pulmonary blood vessel remodeling GO1905111	<0.001	3	hsa-miR-143-3p; hsa-miR-17-5p; hsa-miR-20a-5p
2	Outflow tract morphogenesis GO0003151	0.007	2	hsa-miR-17-5p; hsa-miR-20a-5p
3	Positive regulation of vascular associated smooth muscle cell migration GO1904754	0.007	3	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-20a-5p
4	Negative regulation of amyloid precursor protein biosynthetic process GO0042985	0.009	3	hsa-miR-144-3p; hsa-miR-17-5p; hsa-miR-20a-5p
5	Positive regulation of phagocytosis GO0050766	0.009	2	hsa-miR-17-5p; hsa-miR-20a-5p
6	Extracellular space GO0005615	0.048	7	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-150-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
7	Positive regulation of cardiac muscle hypertrophy in response to stress GO1903244	0.048	2	hsa-miR-17-5p; hsa-miR-20a-5p
8	Cellular response to hypoxia GO0071456	0.048	2	hsa-miR-17-5p; hsa-miR-20a-5p
9	Cellular response to lipopolysaccharide GO0071222	0.048	2	hsa-miR-17-5p; hsa-miR-20a-5p
10	Negative regulation of BMP signaling pathway GO0030514	0.048	2	hsa-miR-17-5p; hsa-miR-20a-5p
11	Negative regulation of gene expression GO0010629	0.048	4	hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
12	Negative regulation of transforming growth factor beta receptor signaling pathway GO0030512	0.048	2	hsa-miR-17-5p; hsa-miR-20a-5p
miRPathDB GO Biological process				
1	Protein localization	0.007	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
2	Actin filament-based process	0.009	4	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-17-5p; hsa-miR-20a-5p
3	Cytosolic transport	0.009	3	hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
4	Muscle cell proliferation	0.009	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
5	Muscle structure development	0.009	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
6	pri-miRNA transcription by RNA polymerase II	0.01	4	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-17-5p; hsa-miR-20a-5p
7	Biosynthetic process	0.01	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
8	Nitrogen compound metabolic process	0.01	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
9	Positive regulation of gene expression	0.01	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
10	I-kappaB phosphorylation	0.01	2	hsa-miR-143-3p; hsa-miR-451a
11	Chemical synaptic transmission	0.01	2	hsa-miR-143-3p; hsa-miR-451a
12	Muscle cell differentiation	0.01	4	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p

**Table S13 (continued)**

**Table S13 (continued)**

No	Subcategory	*q-value	miRs observed	hsa-miRs/precursors
13	Positive regulation of brown fat cell differentiation	0.01	2	hsa-miR-143-3p; hsa-miR-144-3p
14	Positive regulation of vascular smooth muscle cell proliferation	0.01	3	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p
15	Regulation of cell differentiation	0.01	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
16	Regulation of cellular component organization	0.01	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
17	Regulation of cellular response to stress	0.01	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
18	Regulation of immune system process	0.01	4	hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
19	Regulation of protein stability	0.01	4	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p
miRPathDB GO Molecular function				
1	Metalloendopeptidase activity	0.005	2	hsa-miR-143-3p; hsa-miR-451a
2	Metallopeptidase activity	0.005	2	hsa-miR-143-3p; hsa-miR-451a
miRPathDB GO KEGG				
1	Small cell lung cancer	0.01	5	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
2	MicroRNAs in cancer	0.01	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
3	TGF-beta signaling pathway	0.01	4	hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
4	Chronic myeloid leukemia	0.01	5	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
5	Hepatitis B	0.01	5	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
6	Leukocyte transendothelial migration	0.01	3	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a
7	Measles	0.01	4	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p
8	Prostate cancer	0.02	5	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
9	Influenza A	0.02	3	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p
10	Toxoplasmosis	0.02	3	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p
11	Apoptosis	0.02	3	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p
12	Pathways in cancer	0.02	5	hsa-miR-143-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
13	Amoebiasis	0.02	2	hsa-miR-143-3p; hsa-miR-451a
14	Bladder cancer	0.02	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
miRPathDB GO Reactome				
1	BH3-only proteins associate with and inactivate anti-apoptotic BCL-2 members	0.01	3	hsa-miR-143-3p; hsa-miR-17-5p; hsa-miR-20a-5p
2	DDX58IFIH1-mediated induction of interferon-alpha/beta	0.01	3	hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
3	Intrinsic Pathway for Apoptosis	0.01	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
4	Negative regulation of the PI3KAKT network	0.01	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
5	PTEN Regulation	0.01	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
6	TP53 Regulates Metabolic Genes	0.01	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
7	Activation of Matrix Metalloproteinases	0.02	2	hsa-miR-143-3p; hsa-miR-451a
8	Collagen degradation	0.02	2	hsa-miR-143-3p; hsa-miR-451a
9	Degradation of the extracellular matrix	0.02	2	hsa-miR-143-3p; hsa-miR-451a
10	Immune System	0.02	4	hsa-miR-143-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
11	Sphingolipid de novo biosynthesis	0.02	2	hsa-miR-143-3p; hsa-miR-20a-5p
12	Extracellular matrix organization	0.04	2	hsa-miR-143-3p; hsa-miR-451a
13	Vesicle-mediated transport	0.04	3	hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
miRPathDB GO Wiki Pathways				
1	TGF-beta Receptor Signaling	<0.001	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-17-5p; hsa-miR-20a-5p
2	TGF-beta Signaling Pathway	<0.001	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
3	DNA Damage Response only ATM dependent	<0.001	6	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
4	Nanoparticle triggered autophagic cell death	<0.001	3	hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
5	Hepatitis C and Hepatocellular Carcinoma	0.002	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-451a; hsa-miR-17-5p; hsa-miR-20a-5p
6	PI3K-Akt Signaling Pathway	0.002	5	hsa-miR-143-3p; hsa-miR-144-3p; hsa-miR-144-5p; hsa-miR-451a; hsa-miR-17-5p

**Table S13 (continued)**