

# **BAL-miRNAs are potential novel biomarkers of outcome after lung transplantation**

## **SUPPLEMENTAL DIGITAL CONTENT**

Supplementary Material includes Suppl. Methods, Figures with corresponding Legend and 13 Suppl. Tables

### **Supplemental Methods**

#### *Lung Transplantation protocol*

Donor lung selection. Donor lung suitability is determined according to usual criteria, including clinical history, chest X-ray, arterial blood gas analysis, bronchoscopy, duration of mechanical ventilation and visual inspection. Anthropometric characteristics, cause of death and Oto score were also recorded. Questionable grafts or from extended criteria donors, including donors after cardiac death, were evaluated with ex-vivo lung perfusion (EVLP) before transplantation. Lung procurement technique. We usually perform bi-pulmonary block retrieval. Before anterograde flush of Perfadex, prostaglandin E1 is injected into the pulmonary artery. We are also using retrograde flush with Perfadex at the time of the back-table. Lung transplantation technique. The surgical approach for BLTx is 2 separate anterolateral thoracotomies. A bilateral trans-sternal anterior thoracotomy (clamshell incision) is used for providing added exposure when a relatively small chest cavity makes hilar exposure difficult or if central extracorporeal support is instituted. Close attention is paid to continuous topical cooling of the donor lung during the implantation; the

donor lung is placed in a bed of ice slush into the thoracic cavity. First, the bronchial anastomoses are carried out with absorbable suture materials in 2 continuous sutures. Then we perform the vascular anastomoses, pulmonary artery and atrium, with non-absorbable suture materials in 2 continuous sutures. The pleural spaces are drained with 2 drains (no. 28 and 32) in each pleural space. The sternum is reapproximated using the sternal wires. The ribs are reapproximated with heavy interrupted figure-of-eight multifilament absorbable suture. The pectoralis muscle, fascia and the subcutaneous tissue are approximated with monofilament absorbable suture. Skin is reapproximated with staples.

Recipient selection and care after transplantation. Recipient selection, donor/recipient matching, care after LuTx, antibiotic prophylaxis, immunosuppression regimens, and surveillance bronchoscopy are carried out according to current standard practice at our Institution. Briefly, standard immunosuppression consisted of prednisone, tacrolimus, azathioprine, without specific induction therapy. Episodes of rejection were treated with intravenous methylprednisolone at a dose of 1 g/d for 3 days followed by steroid taper. Perioperative antibiotics consisting of a third-generation cephalosporin or target therapy if specific colonization. Prophylaxis against *Pneumocystis carinii* (Bactrim) is standard, whereas cytomegalovirus (CMV) prophylaxis is determined by preoperative serologic status of both donor and recipient and postoperative monitoring (Ganciclovir/Valganciclovir). Patients receive an initial routine bronchoscopic surveillance before hospital discharge. Routine surveillance bronchoscopic examinations is planned for 4 to 8 weeks postoperatively and then every 3 months during the first postoperative year. Results of pulmonary function test, radiographic findings and clinical symptoms determine the need for additional bronchoscopic evaluations. Pulmonary trans-bronchial biopsies (TBB) are scheduled at 3, 6, 12 months after transplantation.

Recipient data recorded included: lung allocation score (LAS), diagnosis, type of

transplantation, intraoperative warm ischemia time, need of cardiopulmonary support during surgery (extracorporeal membrane oxygenation, ECMO). Short-term outcome for recipients included days to extubation, highest primary graft dysfunction (PGD) grade within 72 hours, onset of bronchial anastomotic complications and 6 months survival.

All patients undergo bronchoscopic surveillance with BAL 7 and 15 days after surgery. Pulmonary trans-bronchial biopsies (TBB) were scheduled at 3, 6 and 12 months after transplantation, and in case of lung function decline or other clinical suspect of ALAD.

For histological AR (h-AR), the most severe grade A or B detected during the follow-up is indicated (Table 1).

As ALAD we intended all cases with acute decline of FEV1 (>20% drop compared with the posttransplant baseline) due to acute infections, pneumonia or acute cellular or antibody-mediated rejection. For acute clinical rejection (c-AR), we intended all symptomatic cases for which the pulmonary function tests showed a decline in FEV1, serological testing on BAL excluded pneumonia but TBB histology of was either missing or negative.

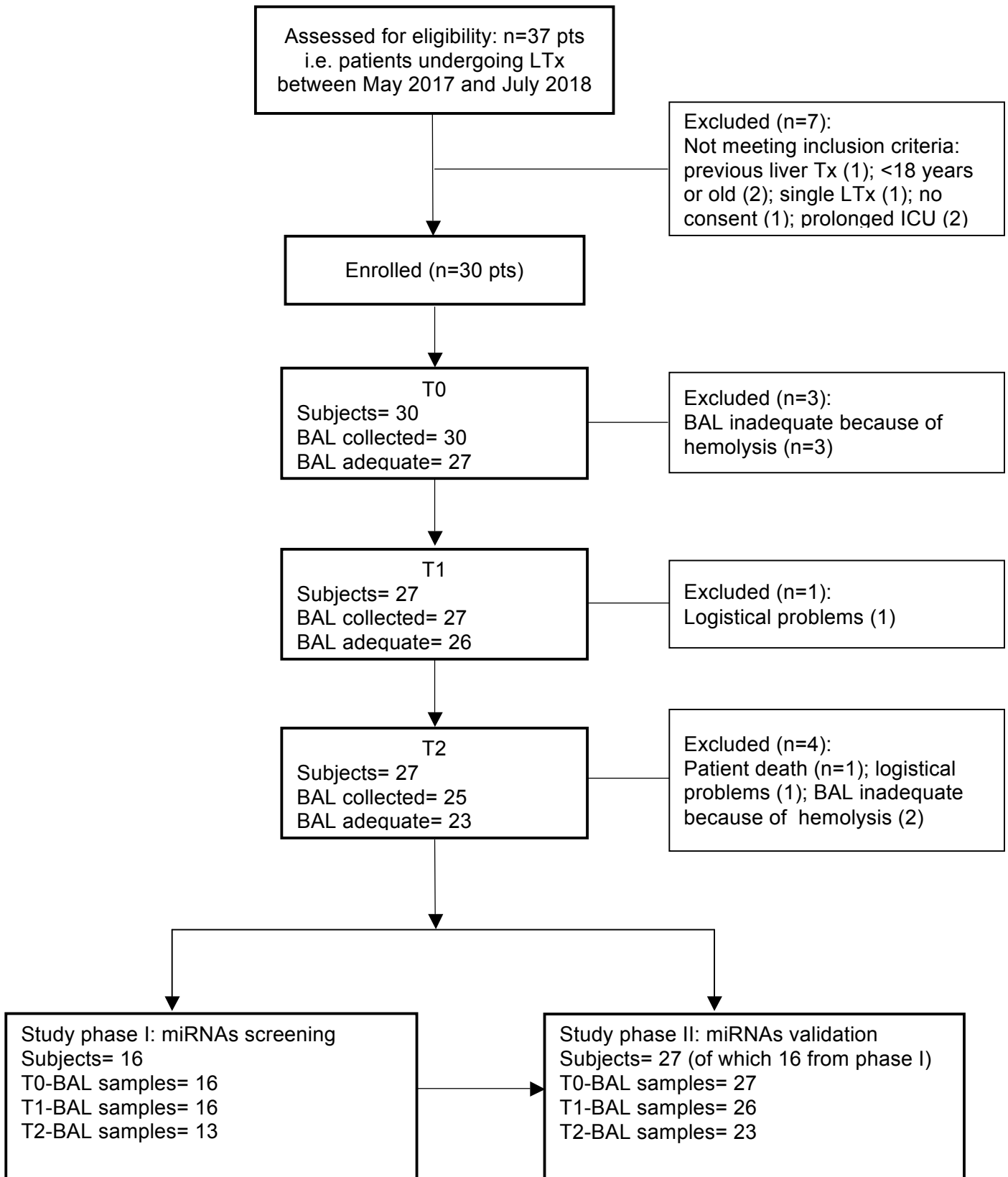
### *miRNAs profiling*

An exogenous spike-in RNA (cel-miR-39) was added to all BALs to monitor RNA purification procedures as described.[5] Total RNA was purified using the RNeasy serum/plasma kit (Qiagen) and 90 ng of total RNA per sample were reverse transcribed and preamplified using the Megaplex Primers Pools A and B. Then cDNA was loaded on the TaqMan Array Human MicroRNA Card Set v3.0 and analyzed on an ABI PRISM 7900HT Sequence Detection System as previously described.[6]

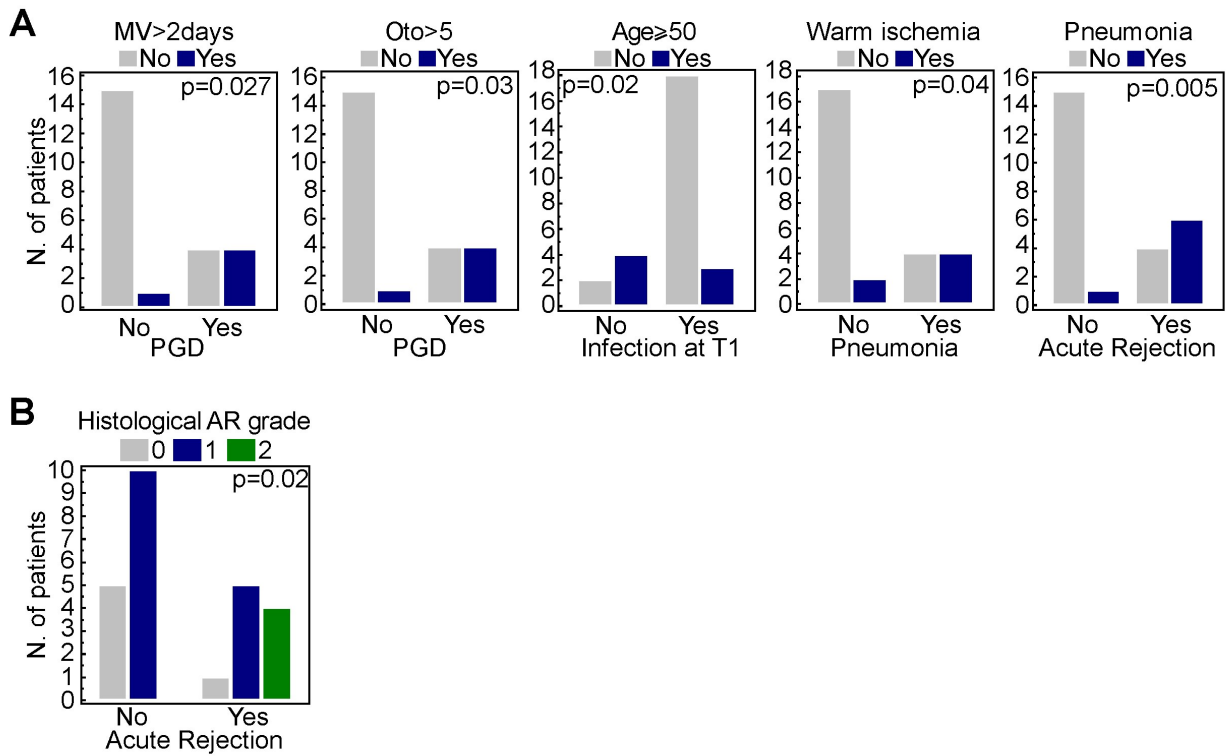
MiRNA profiles were then obtained using the TLDA miRNA Human A and B Cards (all from Thermo Fischer Scientific). Only miRNAs present in the miRBASE v21 were considered for the analyses. miRNAs whose mean raw data (Ct) less 1 standard

deviation was above 35 (mean miRNA Ct – sd>35) were considered undetermined and excluded from further analysis. For the remaining miRNAs, Cts were converted into relative quantities (RQ) using the global mean method. For statistical purposes, miRNAs RQ were median-normalized and log2-transformed.

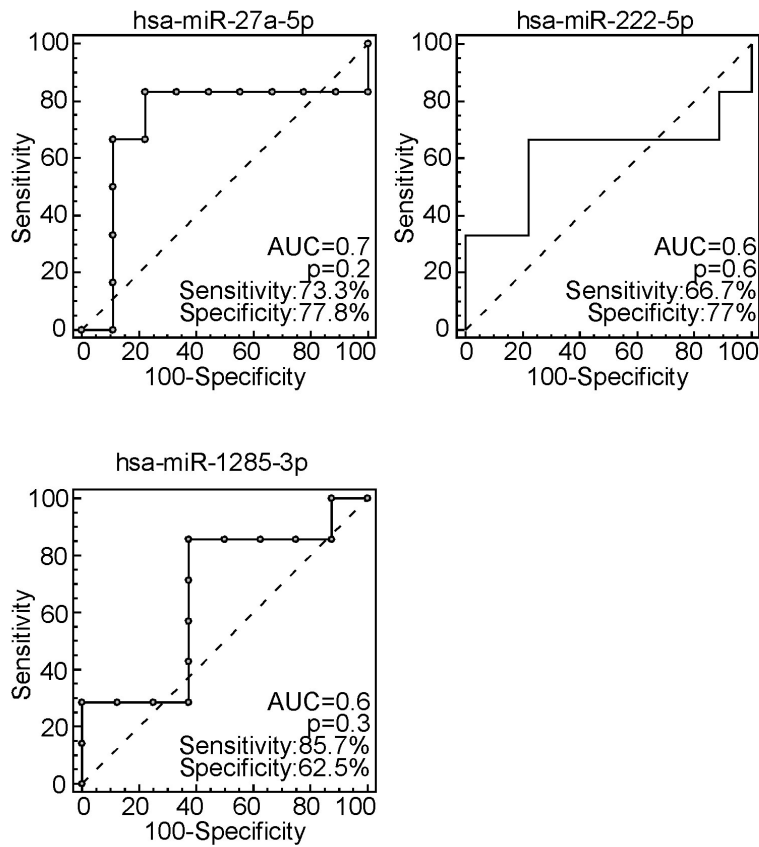
## Supplementary Figures



**FIGURE S1** Consort chart.



**FIGURE S2** Clinical variables provide marginal information about early graft dysfunction. **(A)** The correlations between recipient-, donor-, and surgery-related variables or pneumonia with PGD, infections, pneumonia or acute rejection (clinical AR within the first year after LTx) were evaluated by Fisher's exact test. **(B)** Concordance between AR detected by histological examination of TBB and clinical AR. P value is from chi-square test. For both analyses the complete patients series was used (n=27).



**FIGURE S3** ROC curves were generated to test the accuracy of the indicated T0-miRNAs (miR-27a-5p, miR-222-5p) or T1-miR-1285-3p in classifying patients according to clinical AR in first year after LTx. The cut-off for miRNA expression was calculated using Youden's J statistic. AUC, area under curve; 95% CI, 95% confidence interval.

**Table S1.** Additional patients details are provided

Patient code	Study phase	Microbial colonization of recipient			Mismatch	Surgery-related features			posttransplantation– associated features			
		P. aeruginos:	Bacteria	Aspergillus spp	Age(D/R_ratio)	Mechanical_ventilation (days)	ECMO_pre	ECMO_post	Neoplasia	Infection_BAI	Infection_BAL_T1	Infection_BAL_T2
LTx_1	miR screening+validation	Y	Y	N	1,615	1	N	N	N	1	1	1
LTx_2	miR screening+validation	N	N	N	0,65625	2	N	N	N	0	0	0
LTx_3	miR screening+validation	Y	Y	N	1,3	1	Y	Y	N	1	1	1
LTx_4	miR screening+validation	Y	Y	N	1,113636364	0	N	N	N	1	1	1
LTx_5	miR screening+validation	N	Y	N	2,380952381	1	N	N	Y	1	1	0
LTx_6	miR screening+validation	N	Y	N	0,722222222	0	N	N	N	0	1	0
LTx_7	miR screening+validation	N	Y	Y	1,454545455	1	N	N	N	1	1	0
LTx_8	miR screening+validation	Y	Y	N	0,65625	0	N	N	N	1	1	1
LTx_9	miR screening+validation	N	N	N	0,935483871	1	N	N	N	0	0	0
LTx_10	miR screening+validation	N	N	N	1,046511628	6	N	N	N	1	1	0
LTx_11	miR screening+validation	N	N	N	0,962962963	7	N	N	N	1	1	0
LTx_12	miR screening+validation	Y	Y	N	2,125	3	N	N	N	1	0	1
LTx_13	miR screening+validation	Y	Y	N	1,702702703	1	N	Y	N	1	1	1
LTx_14	miR screening+validation	Y	Y	Y	2,214285714	2	N	N	N	1	1	0
LTx_15	miR screening+validation	Y	Y	Y	2,095238095	1	N	N	N	1	1	0
LTx_16	miR screening+validation	N	N	N	1	4	N	N	N	0	0	1
LTx_17	miR validation	Y	Y	Y	1,04	1	N	N	N	1	1	1
LTx_18	miR validation	N	N	N	0,98	0	N	N	N	1	0	0
LTx_19	miR validation	Y	Y	Y	1,46	1	N	N	N	1	0	0
LTx_20	miR validation	Y	Y	Y	2,65	2	N	N	Y	1	1	1
LTx_21	miR validation	Y	Y	N	1,32	1	N	N	N	1	1	1
LTx_22	miR validation	N	N	N	0,67	7	N	Y	N	0	1	0
LTx_23	miR validation	Y	Y	Y	1,08	0	N	N	N	1	1	1
LTx_24	miR validation	Y	Y	Y	0,473	1	N	N	N	1	1	0
LTx_25	miR validation	N	N	N	0,92	4	N	Y	N	1	1	1
LTx_26	miR validation	Y	Y	N	0,5588	1	N	N	N	0	1	1
LTx_27	miR validation	Y	Y	Y	1,8	0	N	N	N	1	1	1



**Table S2.** Biological processes (GO terms) predicted to be targeted by k-means cluster 1 and 2 miRNA (more expressed at T0,1). Only signaling with a q-value =0 are reported.

geneSet	description	link	size	overlap	expect	enrichmentRatio	pValue	FDR	overlapId	database	userid
GO:1902531	regulation of intracellular signal transduction	<a href="http://amigo.geneontology.org/amigo/term/GO:1902531">http://amigo.geneontology.org/amigo/term/GO:1902531</a>	1824	117	39,15544927	2,988089837	0	0	19;100;142;20	geneontology_Biological_Process	GF;RASA1;CRK;MAPK1;IRAK4;KRAS;MAPK7;PTGS2;AKT1;MDM2;BCL2;CD44;BRAF;IGF1R;TNF;SOX2;KLF4;IRS1;MYC;IRS2;ESR1;PAK4;ILK;MAP2K6;TMEM98;TSPAN6;MYO5A;SOX9;CD28;FOXO1;KDR;RAF1;CDC42;CHUK;BCL2L2;BTRC;MET;MAPK14;CAV2;MTOR;STK11;IGF1;PTEN;ERBB4;SOCS1;PRMT5;BCL2L1;KIT;ABCA1;PSAP;PHLPP1;SOCS3;DDIT4;TBK1;TIMP3;TNFSF10;ICAM1;
GO:0010629	negative regulation of gene expression	<a href="http://amigo.geneontology.org/amigo/term/GO:0010629">http://amigo.geneontology.org/amigo/term/GO:0010629</a>	1733	107	37,20197016	2,876191759	0	0	91;142;207;33	geneontology_Biological_Process	1;AKT1;MDM2;RREB1;KLF5;TNF;DDX6;SOX2;KLF4;MYC;PPM1D;CPEB4;EIF4E;ITGB8;ESR1;SOX9;SMAD3;HMG2;E2F3;CD28;CCNE1;CCND1;AXIN2;PURA;SMAD7;FOXO1;KDR;RUNX2;CCND3;MBD1;DICER1;BIRC5;MYB;BTRC;MAPK14;SMARCA2;MTOR;IGF1;MECP2;ATXN1;MYCN;MXD1;ZBTB4;DNMT1;CDKN1B;FOXO3;CDKN1C;TBK1;CREBZF;TCEAL1;TRPS1;ZEB2;CTCF;MXI1;HDAC4
GO:0044093	positive regulation of molecular function	<a href="http://amigo.geneontology.org/amigo/term/GO:0044093">http://amigo.geneontology.org/amigo/term/GO:0044093</a>	1717	100	36,85850131	2,713078298	0	0	142;207;317;3	geneontology_Biological_Process	ASA1;CRK;CCNB1;BDNF;MAPK1;IRAK4;KRAS;AKT1;BCL2;BRAF;TNF;KLF4;IRS1;MYC;ESR1;PAK4;ILK;ADAM17;GMFB;SERINC5;MAP2K6;APH1A;SMAD3;TGFB2;HMG2;CFTR;CCND1;RAF1;CCND3;CDC42;CAB39;CHUK;ATG14;MET;MAPK8;MAPK14;CAV2;MTOR;STK11;IGF1;PTEN;SOCS1;BCL2L1;KIT;PSAP;CDKN1B;BBC3;TNFSF10;ICAM1;SELE;DVL2;ZEB2;APAF1;RAB1A;FGFR3;GIT1;
GO:0048585	negative regulation of response to stimulus	<a href="http://amigo.geneontology.org/amigo/term/GO:0048585">http://amigo.geneontology.org/amigo/term/GO:0048585</a>	1545	101	33,16621114	3,045267956	0	0	100;207;596;5	geneontology_Biological_Process	K7;SERPINE1;PTGS2;AKT1;MDM2;BCL2;CD44;IGF1R;TNF;SOX2;KLF4;IRS1;MYC;ESR1;SOCS7;ADAM17;KREMEN1;MMP14;TSPAN6;ETS1;SOX9;SMAD3;TGFB2;CTNND1;CDK6;HMG2;RPS6KB1;AXIN2;SMAD7;FOXO1;SMURF1;KDR;RAF1;RUNX2;CDC42;BCL2L2;BTRC;MET;MAPK14;CAV2;MTOR;STK11;IGF1;PTEN;ERBB4;SOCS1;KIT;PSAP;PHLPP1;SOCS3;CDKN1B;FOXO3;DDIT4;DKK2;
GO:0002682	regulation of immune system process	<a href="http://amigo.geneontology.org/amigo/term/GO:0002682">http://amigo.geneontology.org/amigo/term/GO:0002682</a>	1400	87	30,05352466	2,894835165	0	0	60;91;92;100;	geneontology_Biological_Process	E1;JAG1;AKT1;BCL2;BRAF;TNF;YES1;HOXA9;MYC;IRS2;ESR1;NRAS;ADAM17;MAP2K6;AP1G1;MMP14;MIXL1;TSPAN6;ETS1;ACTB;SOX9;SMAD3;TGFB2;CDK6;CD28;RAF1;CDC42;CHUK;MYB;MAPK9;MAPK8;MAPK14;MTOR;STK11;IGF1;HOXA5;KAT2B;SOCS1;KIT;PHLPP1;SOCS3;FOXO3;TBK1;ICAM1;FOS;CORO1A;PIK3R1;MAFB;ADA;P2RX7;IGF2;MUC4;EP300;CCR6;ACV2A;
GO:0043085	positive regulation of catalytic activity	<a href="http://amigo.geneontology.org/amigo/term/GO:0043085">http://amigo.geneontology.org/amigo/term/GO:0043085</a>	1380	88	29,62418859	2,970545496	0	0	207;317;396;5	geneontology_Biological_Process	CCNB1;BDNF;MAPK1;KRAS;AKT1;BCL2;BRAF;TNF;KLF4;IRS1;MYC;ESR1;PAK4;ILK;ADAM17;GMFB;SERINC5;MAP2K6;APH1A;SMAD3;TGFB2;HMG2;CCND1;RAF1;CCND3;CDC42;CAB39;ATG14;MAPK8;MAPK14;CAV2;MTOR;STK11;IGF1;PTEN;SOCS1;BCL2L1;KIT;PSAP;CDKN1B;BBC3;TNFSF10;ICAM1;SELE;DVL2;ZEB2;APAF1;RAB1A;FGFR3;GIT1;PDGFRA;P2RX7;IGF2;SRCIN1;ZNF6
GO:0080134	regulation of response to stress	<a href="http://amigo.geneontology.org/amigo/term/GO:0080134">http://amigo.geneontology.org/amigo/term/GO:0080134</a>	1361	95	29,21631933	3,251607396	0	0	100;142;164;2	geneontology_Biological_Process	1;IRAK4;KRAS;MAPK7;SERPINE1;PTGS2;AKT1;MDM2;BCL2;RREB1;CD44;BRAF;IGF1R;TNF;KLF4;MYC;ESR1;NRAS;MAP2K6;AP1G1;TSPAN6;ETS1;SMAD3;TGFB2;CDK6;HMG2;CD28;AXIN2;FOXO1;RAF1;CDC42;CHUK;MET;MAPK14;MTOR;PTEN;SOCS1;BCL2L1;PSAP;PHLPP1;SOCS3;CDKN1B;FOXO3;TBK1;SELE;CERS2;DVL2;ZEB2;PIK3R1;MGMT;RAD51;BCL2L1;PDGFRA;ADA;MUC
GO:0001944	vasculature development	<a href="http://amigo.geneontology.org/amigo/term/GO:0001944">http://amigo.geneontology.org/amigo/term/GO:0001944</a>	682	60	14,64035987	4,098259916	0	0	182;207;388;5	geneontology_Biological_Process	AKT1;MDM2;KLF5;KLF4;ITGB8;PAK4;MMP14;ETS1;COL5A1;TGFB2;SP1;HMG2;RECK;SMAD7;FOXO1;KDR;CDC42;MAPK14;STK11;HOXA5;MECP2;PTEN;BMP2;KIT;SOCS3;DNMT1;MMP2;PDGFRA;PAX6;NOTCH3;LUZP1;HMOX1;FGF2;BRCA1;AKT3;WNT4;SOX4;NDST1;RHOB;FBXW7;LIF;PRDM1;E2F2;NOTCH1;TGFB1;MAP2K1
GO:0001568	blood vessel development	<a href="http://amigo.geneontology.org/amigo/term/GO:0001568">http://amigo.geneontology.org/amigo/term/GO:0001568</a>	654	55	14,03928937	3,917577203	0	0	182;207;388;5	geneontology_Biological_Process	AKT1;MDM2;KLF5;KLF4;ITGB8;PAK4;MMP14;ETS1;COL5A1;TGFB2;SP1;HMG2;RECK;SMAD7;FOXO1;KDR;CDC42;MAPK14;HOXA5;MECP2;PTEN;BMP2;SOCS3;MMP2;PDGFRA;PAX6;NOTCH3;LUZP1;HMOX1;FGF2;BRCA1;AKT3;WNT4;SOX4;NDST1;RHOB;FBXW7;PRDM1;E2F2;NOTCH1;TGFB1;MAP2K1
GO:0009611	response to wounding	<a href="http://amigo.geneontology.org/amigo/term/GO:0009611">http://amigo.geneontology.org/amigo/term/GO:0009611</a>	642	54	13,78168773	3,918242891	0	0	60;596;673;89	geneontology_Biological_Process	L2;RREB1;CD44;BRAF;HNF4A;SOX2;KLF4;ILK;ADAM17;ETS1;COL5A1;ACTB;SMAD3;TGFB2;RPS6KB1;RAF1;CDC42;MTOR;IGF1;PTEN;ERBB4;CDKN1B;CERS2;PIK3R1;PDGFRA;PAX6;P2RX7;TNXN2;ITGA2;HMOX1;FGF2;WNT3A;WNT4;NOTCH1;DHFR;TGFB1;CDK1;PTPRF;EZH2;HDAC1;ITPR1;MAP2K1

**Table S3.** Biological processes (GO terms) predicted to be targeted by k-means cluster 3 miRNA (more expressed at T2).

geneSet	description	link	size	overlap	expect	enrichmentRatio	pValue	FDR	overlapId	database	userId
GO:0008637	apoptotic mitochondrial changes	<a href="http://amigo.geneontology.org/amigo/term/GO:0008637">http://amigo.geneontology.org/amigo/term/GO:0008637</a>	116	3	0,184944767	16,22105911	8,15E-04	1	6648;27113;84883	geneontology_Biological_Process	AIFM2;BBC3;SOD2
GO:0001836	release of cytochrome c from mitochondria	<a href="http://amigo.geneontology.org/amigo/term/GO:0001836">http://amigo.geneontology.org/amigo/term/GO:0001836</a>	59	2	0,094066735	21,26150121	0,003965128	1	6648;27113	geneontology_Biological_Process	BBC3;SOD2
GO:0048306	calcium-dependent protein binding	<a href="http://amigo.geneontology.org/amigo/term/GO:0048306">http://amigo.geneontology.org/amigo/term/GO:0048306</a>	60	2	0,095661086	20,90714286	0,004097826	1	55696;79720	geneontology_Molecular_Function	RBM22;VPS37B
GO:0050660	flavin adenine dinucleotide binding	<a href="http://amigo.geneontology.org/amigo/term/GO:0050660">http://amigo.geneontology.org/amigo/term/GO:0050660</a>	77	2	0,122765061	16,29128015	0,006661974	1	27034;84883	geneontology_Molecular_Function	ACAD8;AIFM2
GO:0051289	protein homotetramerization	<a href="http://amigo.geneontology.org/amigo/term/GO:0051289">http://amigo.geneontology.org/amigo/term/GO:0051289</a>	79	2	0,125953764	15,87884268	0,007001126	1	226;6648	geneontology_Biological_Process	SOD2;ALDOA
GO:0032803	regulation of low-density lipoprotein particle receptor catabolic process	<a href="http://amigo.geneontology.org/amigo/term/GO:0032803">http://amigo.geneontology.org/amigo/term/GO:0032803</a>	5	1	0,007971757	125,4428571	0,00794728	1	29116	geneontology_Biological_Process	MYLIP
GO:0090677	reversible differentiation	<a href="http://amigo.geneontology.org/amigo/term/GO:0090677">http://amigo.geneontology.org/amigo/term/GO:0090677</a>	5	1	0,007971757	125,4428571	0,00794728	1	6648	geneontology_Biological_Process	SOD2
GO:0035279	mRNA cleavage involved in gene silencing by miRNA	<a href="http://amigo.geneontology.org/amigo/term/GO:0035279">http://amigo.geneontology.org/amigo/term/GO:0035279</a>	5	1	0,007971757	125,4428571	0,00794728	1	192669	geneontology_Biological_Process	AGO3
GO:0098795	mRNA cleavage involved in gene silencing	<a href="http://amigo.geneontology.org/amigo/term/GO:0098795">http://amigo.geneontology.org/amigo/term/GO:0098795</a>	5	1	0,007971757	125,4428571	0,00794728	1	192669	geneontology_Biological_Process	AGO3
GO:0070061	fructose binding	<a href="http://amigo.geneontology.org/amigo/term/GO:0070061">http://amigo.geneontology.org/amigo/term/GO:0070061</a>	5	1	0,007971757	125,4428571	0,00794728	1	226	geneontology_Molecular_Function	ALDOA







Machine P	hsa_miR_339_3p	-2,40	0,030	0,129								
	hsa_miR_342_3p	-2,84	0,004	0,065								
	<b>hsa_miR_345_5p</b>	<b>-1,96</b>	<b>0,010</b>	<b>0,079</b>								
	hsa_miR_34b_3p	-2,74	0,026	0,124								
	<b>hsa_miR_363_3p</b>	<b>1,40</b>	<b>0,003</b>	<b>0,065</b>								
	<b>hsa_miR_374b_5p</b>	<b>-2,73</b>	<b>0,005</b>	<b>0,067</b>								
	<b>hsa_miR_376c_3p</b>	<b>1,39</b>	<b>0,014</b>	<b>0,089</b>								
	<b>hsa_miR_380_5p</b>	<b>3,61</b>	<b>0,002</b>	<b>0,062</b>								
	<b>hsa_miR_381_3p</b>	<b>1,81</b>	<b>0,001</b>	<b>0,053</b>								
	<b>hsa_miR_409_3p</b>	<b>1,23</b>	<b>0,018</b>	<b>0,100</b>								
	<b>hsa_miR_423_5p</b>	<b>-3,46</b>	<b>0,007</b>	<b>0,071</b>								
	<b>hsa_miR_425_5p</b>	<b>-3,32</b>	<b>0,011</b>	<b>0,081</b>								
	<b>hsa_miR_449a</b>	<b>-2,59</b>	<b>0,015</b>	<b>0,092</b>								
	<b>hsa_miR_454_3p</b>	<b>-3,18</b>	<b>0,009</b>	<b>0,073</b>								
	<b>hsa_miR_484</b>	<b>-1,99</b>	<b>0,007</b>	<b>0,071</b>								
	hsa_miR_485_3p	1,20	0,031	0,130								
	<b>hsa_miR_491_5p</b>	<b>-1,47</b>	<b>0,016</b>	<b>0,096</b>								
	<b>hsa_miR_505_5p</b>	<b>-2,42</b>	<b>0,004</b>	<b>0,065</b>								
	<b>hsa_miR_512_3p</b>	<b>2,47</b>	<b>0,004</b>	<b>0,065</b>								
	<b>hsa_miR_516b_3p</b>	<b>3,03</b>	<b>0,008</b>	<b>0,071</b>								
	<b>hsa_miR_517c_3p</b>	<b>1,50</b>	<b>0,004</b>	<b>0,065</b>								
	<b>hsa_miR_518f_3p</b>	<b>1,36</b>	<b>0,005</b>	<b>0,067</b>								
	<b>hsa_miR_520c_3p</b>	<b>1,59</b>	<b>0,003</b>	<b>0,065</b>								
	hsa_miR_520d_3p	2,02	0,032	0,134								
	hsa_miR_523_3p	1,02	0,036	0,140								
	<b>hsa_miR_532_3p</b>	<b>-1,67</b>	<b>0,006</b>	<b>0,067</b>								
	hsa_miR_532_5p	-2,79	0,027	0,124								
	<b>hsa_miR_548b_5p</b>	<b>2,86</b>	<b>0,017</b>	<b>0,098</b>								
	<b>hsa_miR_548c_5p</b>	<b>3,62</b>	<b>0,007</b>	<b>0,071</b>								
	<b>hsa_miR_548d_5p</b>	<b>3,28</b>	<b>0,011</b>	<b>0,081</b>								
	<b>hsa_miR_550a_5p</b>	<b>1,14</b>	<b>0,011</b>	<b>0,081</b>								
	<b>hsa_miR_551b_5p</b>	<b>1,22</b>	<b>0,011</b>	<b>0,081</b>								
	hsa_miR_572	1,51	0,037	0,141								
	<b>hsa_miR_574_3p</b>	<b>-2,62</b>	<b>0,002</b>	<b>0,062</b>								
	<b>hsa_miR_589_5p</b>	<b>1,27</b>	<b>0,001</b>	<b>0,053</b>								
	<b>hsa_miR_591</b>	<b>2,52</b>	<b>0,004</b>	<b>0,065</b>								
	hsa_miR_605_5p	2,52	0,033	0,134								
	hsa_miR_660_5p	-3,31	0,029	0,125								
	<b>hsa_miR_744_5p</b>	<b>-2,18</b>	<b>0,016</b>	<b>0,097</b>								
	<b>hsa_miR_769_5p</b>	<b>-2,64</b>	<b>0,011</b>	<b>0,081</b>								
	<b>hsa_miR_770_5p</b>	<b>1,93</b>	<b>0,000</b>	<b>0,040</b>								
	<b>hsa_miR_93_3p</b>	<b>-2,67</b>	<b>0,008</b>	<b>0,071</b>								
	ECMO	hsa_let_7f_5p	-2,30	0,030	0,997	hsa_let_7a_5p	-4,199	0,034	0,978	hsa_miR_1180_3p	2,446	0,042
hsa_miR_1825		-2,23	0,029	0,997	hsa_miR_146b_5p	-2,052	0,020	0,822	hsa_miR_1226_5p	-1,041	0,025	0,443
hsa_miR_671_3p		-1,77	0,032	0,997	hsa_miR_155_5p	-1,644	0,014	0,822	hsa_miR_1244	-1,080	0,036	0,443
					hsa_miR_181a_2_3p	-1,864	0,023	0,822	hsa_miR_125a_5p	2,054	0,008	0,443
					hsa_miR_181a_3p	-1,943	0,023	0,822	hsa_miR_15a_5p	-1,285	0,045	0,443
					hsa_miR_21_3p	-2,701	0,010	0,822	hsa_miR_18a_5p	-1,228	0,045	0,443
					hsa_miR_22_5p	-1,780	0,027	0,842	hsa_miR_191_3p	-1,125	0,011	0,443
					hsa_miR_27a_5p	-1,823	0,045	0,978	hsa_miR_200b_3p	2,164	0,031	0,443
					hsa_miR_30e_3p	-1,695	0,007	0,822	hsa_miR_205_5p	2,113	0,045	0,443
					hsa_miR_34a_3p	-2,859	0,002	0,581	hsa_miR_20b_5p	2,702	0,045	0,443
					hsa_miR_378a_5p	-1,541	0,022	0,822	hsa_miR_21_3p	-2,035	0,042	0,443
					hsa_miR_616_3p	1,993	0,023	0,822	hsa_miR_23a_3p	-1,033	0,045	0,443
									hsa_miR_296_5p	1,821	0,039	0,443
									hsa_miR_30d_3p	-1,003	0,045	0,443
									hsa_miR_335_5p	2,364	0,020	0,443
									hsa_miR_339_5p	-1,191	0,045	0,443
									hsa_miR_342_5p	-1,061	0,045	0,443
									hsa_miR_424_5p	-1,021	0,045	0,443
									hsa_miR_425_5p	-1,633	0,011	0,443
									hsa_miR_489_3p	-1,319	0,048	0,443
								hsa_miR_548i	-1,066	0,036	0,443	
								hsa_miR_622	-1,158	0,039	0,443	
								hsa_miR_661	3,716	0,039	0,443	
								hsa_miR_98_5p	-1,526	0,045	0,443	
								hsa_miR_99b_3p	-2,893	0,008	0,443	
								hsa_miR_99b_5p	2,113	0,028	0,443	

**Table S7.** Univariate analysis was conducted to explore differences of BAL-miRNAs according to posttransplant-related clinical variable (binary variables) at the 3 time-points. P values and log2ratios (l2r) are from Kolmogorov-Smirnov test whereas adjusted p values (adj\_p\_value) is from FDR correction.

clin var	MIR-BAL T0				MIR-BAL T1				MIR-BAL T2				
	Symbol	l2r	p_value	adj_p_value	Symbol	l2r	p_value	adj_p_value	Symbol	l2r	p_value	adj_p_value	
PGD grade 0-1 versus grade 2					hsa_miR_15a_3p	1,46	0,046	0,94	hsa_let_7a_5p	-3,84	0,01	0,88	
					hsa_miR_18a_5p	1,96	0,04	0,94	hsa_miR_101_3p	-1,48	0,046	0,88	
					hsa_miR_192_5p	1,57	0,037	0,94	hsa_miR_135a_5p	-1,48	0,037	0,88	
					hsa_miR_194_5p	2,16	0,0012	0,39	hsa_miR_146b_3p	-1,64	0,018	0,88	
					hsa_miR_29c_5p	1,69	0,045	0,94	hsa_miR_190b	-5,93	0,048	0,88	
					hsa_miR_424_5p	1,61	0,047	0,94	hsa_miR_19a_3p	-1,71	0,032	0,88	
					hsa_miR_505_3p	2,30	0,0054	0,87	hsa_miR_204_5p	-1,30	0,038	0,88	
					hsa_miR_590_3p	1,51	0,023	0,94	hsa_miR_362_5p	-1,90	0,0015	0,88	
								hsa_miR_374a_5p	-1,90	0,038	0,88		
								hsa_miR_623	1,13	0,024	0,88		
								hsa_miR_628_5p	-1,20	0,048	0,88		
best FEV1>80%	hsa_let_7b_5p	-1,46	0,0385	0,8792	hsa_let_7a_5p	4,66	0,0308	0,3484	hsa_miR_1260a	4,82	0,042	0,955	
	hsa_miR_1226_5p	-2,48	0,0440	0,8792	hsa_let_7d_5p	2,04	0,0308	0,3484	hsa_miR_30d_5p	-1,64	0,028	0,955	
	hsa_miR_125a_3p	-2,13	0,0253	0,8792	hsa_let_7g_5p	1,60	0,0110	0,3484	hsa_miR_489_3p	-1,86	0,021	0,955	
	hsa_miR_126_5p	1,75	0,0429	0,8792	hsa_miR_103a_3p	3,11	0,0286	0,3484	hsa_miR_502_3p	-1,62	0,028	0,955	
	hsa_miR_29c_5p	-2,08	0,0396	0,8792	hsa_miR_10a_5p	2,60	0,0044	0,3484					
	hsa_miR_381_3p	1,40	0,0418	0,8792	hsa_miR_130a_3p	2,14	0,0407	0,3484					
	hsa_miR_505_5p	-2,36	0,0220	0,8792	hsa_miR_146b_3p	2,76	0,0385	0,3484					
	hsa_miR_629_3p	-2,49	0,0099	0,8792	hsa_miR_146b_5p	2,45	0,0132	0,3484					
	hsa_miR_886_3p	-3,26	0,0407	0,8792	hsa_miR_151a_3p	2,99	0,0011	0,1161					
	hsa_miR_886_5p	-3,71	0,0165	0,8792	hsa_miR_151a_5p	2,54	0,0121	0,3484					
	hsa_miR_92a_1_5p	-1,60	0,0319	0,8792	hsa_miR_181a_5p	2,70	0,0462	0,3484					
	hsa_miR_942_5p	-2,02	0,0165	0,8792	hsa_miR_193b_3p	2,07	0,0440	0,3484					
					hsa_miR_203a_3p	2,94	0,0374	0,3484					
					hsa_miR_224_5p	3,45	0,0220	0,3484					
					hsa_miR_26a_5p	1,52	0,0495	0,3484					
					hsa_miR_27b_3p	3,43	0,0077	0,3484					
					hsa_miR_29b_3p	2,26	0,0165	0,3484					
					hsa_miR_30a_3p	2,09	0,0011	0,1161					
					hsa_miR_30a_5p	2,80	0,0088	0,3484					
					hsa_miR_30b_5p	2,07	0,0275	0,3484					
					hsa_miR_30d_5p	3,37	0,0099	0,3484					
					hsa_miR_30e_3p	1,45	0,0462	0,3484					
					hsa_miR_31_3p	3,31	0,0253	0,3484					
					hsa_miR_320a	1,39	0,0440	0,3484					
					hsa_miR_324_3p	2,77	0,0286	0,3484					
					hsa_miR_324_5p	2,62	0,0341	0,3484					
					hsa_miR_342_3p	2,05	0,0264	0,3484					
					hsa_miR_362_5p	1,83	0,0396	0,3484					
					hsa_miR_429	2,23	0,0275	0,3484					
					hsa_miR_500a_5p	2,83	0,0011	0,1161					
					hsa_miR_518f_3p	-2,33	0,0374	0,3484					
					hsa_miR_520d_3p	-2,43	0,0495	0,3484					
					hsa_miR_523_3p	-2,51	0,0330	0,3484					
					hsa_miR_532_3p	2,42	0,0165	0,3484					
					hsa_miR_532_5p	3,21	0,0363	0,3484					
					hsa_miR_591	-2,73	0,0418	0,3484					
					hsa_miR_636	-2,71	0,0429	0,3484					
					hsa_miR_660_5p	2,50	0,0473	0,3484					
					hsa_miR_770_5p	-2,84	0,0363	0,3484					
					hsa_miR_95_3p	2,23	0,0231	0,3484					
	Clinical AR	hsa_miR_126_3p	-3,01	0,0176	0,6193	hsa_miR_145_3p	1,24	0,0249	0,9953	hsa_miR_449a	-2,77	0,030	0,952
		hsa_miR_146a_5p	-2,06	0,0322	0,6193	hsa_miR_155_5p	-1,52	0,0484	0,9953	hsa_miR_520d_3p	2,37	0,030	0,952
hsa_miR_16_1_3p		1,71	0,0308	0,6193	hsa_miR_330_3p	-1,20	0,0322	0,9953					
hsa_miR_183_5p		1,52	0,0029	0,4645									
hsa_miR_193b_3p		-3,05	0,0059	0,4645									
hsa_miR_200c_3p		-2,41	0,0322	0,6193									
hsa_miR_23a_5p		1,93	0,0059	0,4645									
hsa_miR_30a_5p		-2,55	0,0410	0,6298									
hsa_miR_30d_5p		-3,11	0,0293	0,6193									
hsa_miR_31_5p		-3,39	0,0352	0,6193									
hsa_miR_345_5p		-1,95	0,0425	0,6298									
hsa_miR_450a_5p		1,77	0,0029	0,4645									
hsa_miR_520c_3p		1,59	0,0249	0,6193									
hsa_miR_523_3p		1,29	0,0103	0,5419									
hsa_miR_532_3p		-1,65	0,0147	0,6193									
hsa_miR_551b_5p		1,24	0,0176	0,6193									
hsa_miR_574_3p	-2,57	0,0088	0,5419										
hsa_miR_629_5p	1,67	0,0337	0,6193										
pneumonia	hsa_miR_145_3p	1,39	0,0396	0,9554	hsa_miR_10a_5p	-2,03	0,033	0,928	hsa_miR_137	1,72	0,04196	0,72471759	
	hsa_miR_22_3p	2,55	0,0154	0,9554	hsa_miR_125a_3p	-1,62	0,010	0,928	hsa_miR_1825	6,85	0,04895	0,72471759	
	hsa_miR_452_5p	2,35	0,0022	0,3484	hsa_miR_1270	2,08	0,032	0,928	hsa_miR_200a_3p	-4,30	0,04895	0,72471759	
	hsa_miR_505_3p	1,92	0,0429	0,9554	hsa_miR_141_5p	1,33	0,046	0,928	hsa_miR_301a_3p	-1,50	0,02098	0,72471759	
	hsa_miR_548i	2,05	0,0022	0,3484	hsa_miR_148b_5p	1,65	0,022	0,928	hsa_miR_34a_3p	-2,06	0,04196	0,72471759	
	hsa_miR_590_5p	2,47	0,0484	0,9554	hsa_miR_155_5p	-1,61	0,027	0,928	hsa_miR_451a	-4,35	0,04196	0,72471759	
	hsa_miR_7_5p	2,21	0,0330	0,9554	hsa_miR_16_1_3p	1,41	0,047	0,928	hsa_miR_484	-1,47	0,03497	0,72471759	
					hsa_miR_539_5p	2,27	0,010	0,928	hsa_miR_590_5p	-1,51	0,01399	0,72471759	
					hsa_miR_550a_5p	1,45	0,037	0,928	hsa_miR_597_5p	1,48	0,00699	0,72471759	
					hsa_miR_886_5p	-2,74	0,031	0,928	hsa_miR_875_5p	1,40	0,02797	0,72471759	
					hsa_miR_9_3p	1,39	0,018	0,928					

presence of INFECTION @BAL withdrawal	hsa_miR_628_5p	2,06	0,0286	0,9390
	hsa_miR_629_5p	-1,80	0,0319	0,9390
	hsa_miR_92a_3p	-1,39	0,0385	0,9390

hsa_miR_1233_3p	4,87	0,038	0,557
hsa_miR_126_3p	1,86	0,048	0,557
hsa_miR_132_3p	3,39	0,034	0,557
hsa_miR_140_5p	2,15	0,041	0,557
hsa_miR_146a_5p	3,05	0,020	0,557
hsa_miR_148b_5p	-1,53	0,036	0,557
hsa_miR_211_5p	-2,11	0,001	0,348
hsa_miR_223_3p	3,96	0,029	0,557
hsa_miR_337_5p	-2,16	0,045	0,557
hsa_miR_449b_5p	2,18	0,047	0,557
hsa_miR_551b_3p	-1,96	0,027	0,557
hsa_miR_576_3p	-1,18	0,026	0,557
hsa_miR_604	-2,31	0,034	0,557
hsa_miR_708_5p	1,93	0,018	0,557
hsa_miR_875_5p	-2,19	0,013	0,557
hsa_miR_9_5p	-1,31	0,029	0,557

hsa_miR_1226_5p	-1,23	0,00311	0,246309246
hsa_miR_1244	-1,18	0,00777	0,328412328
hsa_miR_135b_5p	1,35	0,04662	0,388909336
hsa_miR_140_3p	-1,06	0,00311	0,246309246
hsa_miR_142_5p	-1,24	0,00622	0,328412328
hsa_miR_152_3p	1,81	0,03574	0,377674178
hsa_miR_15a_5p	-1,32	0,02176	0,328412328
hsa_miR_16_1_3p	-1,16	0,01865	0,328412328
hsa_miR_1825	-3,87	0,03108	0,351870352
hsa_miR_18a_5p	-1,26	0,02176	0,328412328
hsa_miR_191_3p	-1,14	0,00311	0,246309246
hsa_miR_193b_3p	2,22	0,04662	0,388909336
hsa_miR_20b_5p	2,50	0,04351	0,388909336
hsa_miR_21_3p	-2,24	0,00622	0,328412328
hsa_miR_212_3p	-2,00	0,01709	0,328412328
hsa_miR_23a_3p	-1,04	0,02176	0,328412328
hsa_miR_30d_3p	-1,01	0,02176	0,328412328
hsa_miR_339_5p	-1,22	0,02176	0,328412328
hsa_miR_342_5p	-1,07	0,02176	0,328412328
hsa_miR_424_5p	-1,03	0,02176	0,328412328
hsa_miR_425_5p	-1,72	0,00311	0,246309246
hsa_miR_494_3p	-1,54	0,01709	0,328412328
hsa_miR_618	-1,16	0,03263	0,356723736
hsa_miR_622	-1,09	0,03108	0,351870352
hsa_miR_629_5p	-1,14	0,02797	0,351870352
hsa_miR_98_5p	-1,60	0,02176	0,328412328
hsa_miR_99b_5p	1,99	0,04507	0,388909336



**Table S8.** Repeated measures nonparametric ANOVA corrected for multiple comparison was used to identify BAL-miRNAs whose variation over times (T0-T1-T2) was significantly different in patients who experienced (yes) or not (no) pneumonia or clinical AR (c-AR). Data are reported as median with interquartile range (IQR). The columns labeled with "Yes" identify the miRNAs values in patients who experienced the event. The

	Mirna NAME	adj_p.value	median with IQR					
			NO-T0	YES-T0	NO-T1	YES-T1	NO-T2	YES-T2
<b>PNEUMONIA</b>	hsa_miR_23b_3p	1,61E+07	-2.0691; 2.1371	-3.4341; 0.379975	-1.1711; 4.7412	-3.4532; 0.8794	-1.42385; 1.0084	-0.63495; 0.867725
<b>c-AR</b>	hsa_miR_22_5p	2,911E+02	-1.150775; 0.70265	0.91445; 0.3496	0.08075; 2.21075	-2.14435; 1.2608	-1.42385; 1.0084	-0.4481; 0.3737
	hsa_miR_29c_5p	4,357E+07	-1.370475; 0.9614	1.45025; 4.1192	-0.17475; 2.0429	-1.8832; 0.7385	-1.0447; 0.4063	0.0716; 1.4131
	hsa_miR_181a_3p	3,111E+08	-2.0691; 1.24865	0.7368; 2.9741	-0.19385; 2.5639	-2.14435; 1.2608	-1.574925; 1.0386	-0.50295; 0.264
	hsa_miR_362_3p	5,557E+09	-1.156725; 1.2083	-1.64165; 0.6788	-0.731675; 1.41875	-1.98475; 0.9416	-1.22765; 0.70845	-0.0438; 1.1823
	hsa_let_7f_5p	0,00199	-1.9354; 1.5966	1.71015; 1.7962	-1.3754; 5.2741	-2.14435; 1.2608	-1.42385; 1.0084	2.48815; 6.2462
	hsa_miR_339_3p	0,00490	0.3258; 2.21845	3.0407; 6.0611	1.008225; 3.17765	-1.12155; 3.3064	-1.02965; 0.9668	0.4698; 2.2095
	hsa_miR_146b_3p	0,00612	-0.35875; 3.1401	2.3386; 2.0845	-0.190225; 3.82575	-1.5523; 0.0767	-0.9913; 1.7339	1.2057; 3.6813
	hsa_miR_452_5p	0,02073	-1.370475; 1.9507	-3.4126; 0.5379	-0.9892; 2.9546	-2.14435; 1.2608	-1.42385; 1.0084	-0.12475; 1.0204
	hsa_miR_571	0,02073	-1.023525; 2.3406	-0.47815; 3.0604	-1.642525; 3.14585	0.55415; 4.1362	0.667425; 2.3447	-0.57525; 5.0576

**Table S9.** Previously validate targets of c-AR-associated BAL-miRNAs (see Suppl. Table 8) were searched using the miRTargetlink Human web tool.

<b>miRNA</b>	<b>Target_Gene</b>	<b>Evidence</b>
hsa-let-7f-5p	MEF2D	weak
hsa-let-7f-5p	SP1	weak
hsa-let-7f-5p	ZNF280B	weak
hsa-let-7f-5p	ATP2A2	weak
hsa-let-7f-5p	PDGFB	weak
hsa-let-7f-5p	DYRK2	strong
hsa-let-7f-5p	IGF1R	weak
hsa-let-7f-5p	BACH1	weak
hsa-let-7f-5p	GRPEL2	weak
hsa-let-7f-5p	NCOA3	weak
hsa-let-7f-5p	MAPK6	weak
hsa-let-7f-5p	C5ORF51	weak
hsa-let-7f-5p	ZNF264	weak
hsa-let-7f-5p	YAE1D1	weak
hsa-let-7f-5p	TSC22D2	weak
hsa-let-7f-5p	SMCR7L	weak
hsa-let-7f-5p	KLHDC8B	weak
hsa-let-7f-5p	KCTD21	weak
hsa-let-7f-5p	ATXN7L3B	weak
hsa-let-7f-5p	PMAIP1	weak
hsa-let-7f-5p	SEMA4C	weak
hsa-let-7f-5p	CEP135	weak
hsa-let-7f-5p	RDX	weak
hsa-let-7f-5p	SOD2	weak
hsa-let-7f-5p	WASL	weak
hsa-let-7f-5p	EPHA4	weak
hsa-let-7f-5p	DUSP1	weak
hsa-let-7f-5p	DNAL1	weak
hsa-let-7f-5p	CCNT2	weak
hsa-let-7f-5p	PLEKHA3	weak
hsa-let-7f-5p	BRI3BP	weak
hsa-let-7f-5p	MTX3	weak
hsa-let-7f-5p	CPA4	weak
hsa-let-7f-5p	ZNF799	weak
hsa-miR-146b-3p	PDGFB	weak
hsa-miR-146b-3p	C5ORF51	weak
hsa-miR-146b-3p	TSC22D2	weak
hsa-miR-146b-3p	NUFIP2	weak
hsa-miR-146b-3p	KLHDC8B	weak
hsa-miR-146b-3p	KCTD21	weak
hsa-miR-146b-3p	ATXN1	weak
hsa-miR-146b-3p	ZNF551	weak
hsa-miR-146b-3p	CBX2	weak
hsa-miR-22-5p	SMCR7L	weak
hsa-miR-22-5p	PMAIP1	weak
hsa-miR-22-5p	CCNT2	weak
hsa-miR-22-5p	EPHA4	weak
hsa-miR-22-5p	DUSP1	weak

hsa-miR-22-5p	GRPEL2	weak
hsa-miR-22-5p	GDNF	weak
hsa-miR-22-5p	B3GALT5	weak
hsa-miR-22-5p	TAS2R30	weak
hsa-miR-22-5p	CPA4	weak
hsa-miR-22-5p	SYNRG	weak
hsa-miR-362-3p	REST	weak
hsa-miR-362-3p	CASD1	weak
hsa-miR-362-3p	BRI3BP	weak
hsa-miR-362-3p	BACH1	weak
hsa-miR-362-3p	DYRK2	weak
hsa-miR-362-3p	IRS1	weak
hsa-miR-362-3p	PLEKHA3	weak
hsa-miR-362-3p	ZNF551	weak
hsa-miR-362-3p	NOTCH2NL	weak
hsa-miR-362-3p	DNAL1	weak
hsa-miR-362-3p	TAS2R30	weak
hsa-miR-362-3p	SOD2	weak
hsa-miR-362-3p	MTX3	weak
hsa-miR-362-3p	RDX	weak
hsa-miR-362-3p	CBX2	weak
hsa-miR-362-3p	MAPK6	weak
hsa-miR-362-3p	CEP135	weak
hsa-miR-362-3p	NUFIP2	weak
hsa-miR-362-3p	NCOA3	weak
hsa-miR-362-3p	IGF1R	weak
hsa-miR-362-3p	CDK6	weak
hsa-miR-362-3p	YAE1D1	weak
hsa-miR-362-3p	SEMA4C	weak
hsa-miR-362-3p	ATXN1	weak
hsa-miR-362-3p	B3GALT5	weak
hsa-miR-362-3p	MEF2D	weak
hsa-miR-362-3p	ATP2A2	weak
hsa-miR-362-3p	ATXN7L3B	weak
hsa-miR-362-3p	ZNF280B	weak
hsa-miR-362-3p	GDNF	weak
hsa-miR-362-3p	SP1	weak
hsa-miR-362-3p	PDK3	weak
hsa-miR-362-3p	WASL	weak
hsa-miR-362-3p	FAM26E	weak
hsa-miR-362-3p	ZNF264	weak
hsa-miR-362-3p	SYNRG	weak
hsa-miR-452-5p	CDK6	weak
hsa-miR-452-5p	NOTCH2NL	weak
hsa-miR-452-5p	CASD1	weak
hsa-miR-452-5p	PDK3	weak
hsa-miR-452-5p	FAM26E	weak
hsa-miR-452-5p	REST	weak
hsa-miR-452-5p	ZNF799	weak
hsa-miR-452-5p	IRS1	weak

**Table S10.** Biological processes (GO terms) predicted to be modulated by c-AR-associated miRNAs. Target genes were imported into WebGestalt tool and the GeneOntology-Biological Process functional database was chosen. As reference set, the human protein coding genome was used. Only data with a FDR<0.05 are reported.

geneSet	description	link	size	overlap	expect	enrichmen	pValue	FDR	overlapId	database
GO:0036166	phenotypic switching	<a href="http://amigo.geneontology.org/amigo/term/GO:0036166">http://amigo.geneontology.org/amigo/term/GO:0036166</a>	7	3	0,01534	195,56757	3,37E-07	0,0012676	5155;6648	geneontology_Biological_Process
GO:1900239	regulation of phenotypic switching	<a href="http://amigo.geneontology.org/amigo/term/GO:1900239">http://amigo.geneontology.org/amigo/term/GO:1900239</a>	7	3	0,01534	195,56757	3,37E-07	0,0012676	5155;6648	geneontology_Biological_Process
GO:0043696	dedifferentiation	<a href="http://amigo.geneontology.org/amigo/term/GO:0043696">http://amigo.geneontology.org/amigo/term/GO:0043696</a>	8	3	0,0175314	171,12162	5,38E-07	0,0012676	1021;5155	geneontology_Biological_Process
GO:0043697	cell dedifferentiation	<a href="http://amigo.geneontology.org/amigo/term/GO:0043697">http://amigo.geneontology.org/amigo/term/GO:0043697</a>	8	3	0,0175314	171,12162	5,38E-07	0,0012676	1021;5155	geneontology_Biological_Process
GO:0062012	regulation of small molecule metabolic process	<a href="http://amigo.geneontology.org/amigo/term/GO:0062012">http://amigo.geneontology.org/amigo/term/GO:0062012</a>	344	7	0,7538498	9,2856694	8,34E-06	0,0157101	3667;5155	geneontology_Biological_Process
GO:0045913	positive regulation of carbohydrate metabolic process	<a href="http://amigo.geneontology.org/amigo/term/GO:0045913">http://amigo.geneontology.org/amigo/term/GO:0045913</a>	77	4	0,1687396	23,70516	2,36E-05	0,029705	3667;5155	geneontology_Biological_Process
GO:0051270	regulation of cellular component movement	<a href="http://amigo.geneontology.org/amigo/term/GO:0051270">http://amigo.geneontology.org/amigo/term/GO:0051270</a>	942	10	2,0643213	4,8442073	2,44E-05	0,029705	488;1021;1	geneontology_Biological_Process
GO:0006109	regulation of carbohydrate metabolic process	<a href="http://amigo.geneontology.org/amigo/term/GO:0006109">http://amigo.geneontology.org/amigo/term/GO:0006109</a>	161	5	0,3528192	14,171563	2,52E-05	0,029705	3667;5155	geneontology_Biological_Process
GO:0090677	reversible differentiation	<a href="http://amigo.geneontology.org/amigo/term/GO:0090677">http://amigo.geneontology.org/amigo/term/GO:0090677</a>	5	2	0,0109571	182,52973	4,65E-05	0,0486909	5155;6648	geneontology_Biological_Process
GO:0032885	regulation of polysaccharide biosynthetic process	<a href="http://amigo.geneontology.org/amigo/term/GO:0032885">http://amigo.geneontology.org/amigo/term/GO:0032885</a>	35	3	0,0766998	39,113514	6,04E-05	0,0568924	3667;5155	geneontology_Biological_Process

**Table S13.** The correlation among clinical variables was analyzed with Fisher's exact test. Only significant association are shown.

<b>VARIABLE 1</b>	<b>VARIABLE 2</b>	<b>P VAL</b>	<b>Statistical test</b>
LAS>40	ECMO	0,018	Fisher's exact
MP	DCD	0,028	Fisher's exact
Oto score>5	MP	0,0015	Fisher's exact
Disease	Histological AR max	0,04	chi square
Mechanical ventilation >2d	Age >50y	0,024	Fisher's exact

LAS, Lung allocation score; MP, machine perfusion; PGD, primary graft dysfunction

**Table S12.** Cox-regression analysis was performed to identify T0-BAL or T1-BAL miRNAs associated with clinical AR risk. P values were corrected for multiple comparison applying the FDR method (pv.adj).

T0-BAL				T1-BAL			
miRNA	pval (Cox)	pv.adj	HR	miRNA	pval (Cox)	pv.adj	HR
<b>hsa_miR_744_3p</b>	<b>0,020</b>	<b>0,998</b>	2,743	<b>hsa_miR_1285_3p</b>	<b>0,048</b>	<b>0,998</b>	1,541
<b>hsa_miR_222_5p</b>	<b>0,032</b>	<b>0,998</b>	1,677	hsa_miR_342_5p	0,069	0,998	0,485
<b>hsa_miR_148b_5p</b>	<b>0,035</b>	<b>0,998</b>	0,312	hsa_miR_505_3p	0,075	0,998	0,616
<b>hsa_miR_27a_5p</b>	<b>0,047</b>	<b>0,998</b>	1,869	hsa_miR_335_5p	0,092	0,998	0,576
hsa_miR_455_5p	0,064	0,998	0,315	hsa_miR_590_3p	0,095	0,998	0,551
hsa_miR_375	0,065	0,998	0,640	hsa_miR_1233_3p	0,099	0,998	1,262
hsa_miR_138_5p	0,066	0,998	0,628	hsa_miR_886_5p	0,103	0,998	1,495
hsa_miR_187_3p	0,072	0,998	1,478	hsa_miR_605_5p	0,103	0,998	1,334
hsa_miR_664a_3p	0,080	0,998	1,279	hsa_miR_362_3p	0,104	0,998	0,508
hsa_miR_628_5p	0,080	0,998	1,577	hsa_miR_576_3p	0,104	0,998	0,555
hsa_miR_181a_3p	0,081	0,998	1,763	hsa_miR_1247_5p	0,116	0,998	1,242
hsa_miR_29c_5p	0,084	0,998	1,576	hsa_miR_31_3p	0,122	0,998	0,744
hsa_miR_548i	0,087	0,998	0,381	hsa_miR_330_3p	0,126	0,998	0,546
hsa_miR_1254	0,090	0,998	1,623	hsa_miR_511_5p	0,128	0,998	0,730
hsa_miR_452_5p	0,092	0,998	0,400	hsa_miR_19b_1_5p	0,133	0,998	2,017
hsa_miR_523_3p	0,093	0,998	0,327	hsa_miR_380_5p	0,133	0,998	1,450
hsa_miR_485_3p	0,097	0,998	0,361	hsa_miR_551b_3p	0,134	0,998	0,582
hsa_miR_22_3p	0,097	0,998	0,342	hsa_miR_1271_5p	0,135	0,998	0,618
hsa_miR_579_3p	0,098	0,998	0,489	hsa_miR_1276	0,136	0,998	1,454
hsa_miR_16_1_3p	0,100	0,998	0,496	hsa_let_7e_5p	0,137	0,998	0,790
hsa_miR_671_3p	0,103	0,998	1,584	hsa_miR_638	0,139	0,998	1,413
hsa_miR_520c_3p	0,104	0,998	0,363	hsa_miR_502_3p	0,149	0,998	0,654
hsa_let_7c_5p	0,106	0,998	0,537	hsa_miR_520d_3p	0,152	0,998	1,436
hsa_miR_190a_5p	0,109	0,998	0,380	hsa_miR_1255b_5p	0,161	0,998	1,379
hsa_miR_628_3p	0,110	0,998	1,421	hsa_miR_1227_3p	0,162	0,998	1,303
hsa_let_7f_5p	0,116	0,998	1,455	hsa_miR_190b	0,167	0,998	0,737
hsa_miR_942_5p	0,117	0,998	1,559	hsa_miR_708_5p	0,171	0,998	1,930
hsa_miR_337_5p	0,121	0,998	0,379	hsa_miR_181a_3p	0,176	0,998	0,680
hsa_miR_210_3p	0,123	0,998	1,315	hsa_miR_454_3p	0,179	0,998	1,495
hsa_miR_141_3p	0,126	0,998	0,789	hsa_miR_1290	0,183	0,998	1,578
hsa_miR_576_3p	0,127	0,998	0,466	hsa_miR_151a_5p	0,184	0,998	0,703
hsa_miR_106b_3p	0,134	0,998	1,365	hsa_miR_1262	0,190	0,998	1,553
hsa_miR_34c_5p	0,136	0,998	0,798	hsa_miR_362_5p	0,191	0,998	0,617
hsa_miR_10a_5p	0,137	0,998	1,396	hsa_miR_1303	0,195	0,998	1,280
hsa_miR_450a_5p	0,139	0,998	0,346	hsa_miR_15a_5p	0,196	0,998	1,303
hsa_miR_551b_5p	0,144	0,998	0,393	hsa_miR_146b_3p	0,198	0,998	0,760
hsa_miR_133a_3p	0,155	0,998	1,517	hsa_miR_452_5p	0,199	0,998	0,660
hsa_miR_1226_5p	0,161	0,998	1,405	hsa_miR_516b_3p	0,204	0,998	1,345
hsa_miR_21_3p	0,163	0,998	1,251	hsa_miR_23a_3p	0,208	0,998	0,760
hsa_miR_604	0,163	0,998	1,971	hsa_miR_1226_5p	0,215	0,998	0,657
hsa_miR_141_5p	0,164	0,998	0,562	hsa_miR_628_5p	0,218	0,998	1,858
hsa_miR_206	0,167	0,998	0,615	hsa_miR_30d_3p	0,219	0,998	1,559
hsa_miR_135a_5p	0,173	0,998	0,463	hsa_miR_194_5p	0,220	0,998	0,613
hsa_miR_770_5p	0,177	0,998	0,401	hsa_miR_766_3p	0,221	0,998	0,831
hsa_miR_638	0,177	0,998	1,464	hsa_miR_133a_3p	0,222	0,998	0,804
hsa_miR_1285_3p	0,177	0,998	1,286	hsa_miR_512_3p	0,223	0,998	1,238
hsa_miR_29a_5p	0,178	0,998	0,432	hsa_miR_200a_3p	0,224	0,998	0,816
hsa_miR_500a_5p	0,179	0,998	1,520	hsa_miR_148b_3p	0,228	0,998	0,690
hsa_miR_320a	0,179	0,998	1,602	hsa_miR_671_3p	0,229	0,998	0,641
hsa_miR_449b_5p	0,182	0,998	0,752	hsa_miR_664a_3p	0,240	0,998	0,825
hsa_miR_331_5p	0,188	0,998	1,636	hsa_miR_34b_5p	0,249	0,998	0,750
hsa_miR_202_3p	0,190	0,998	0,646	hsa_miR_146a_5p	0,257	0,998	1,311
hsa_miR_197_3p	0,194	0,998	0,578	hsa_miR_29c_5p	0,259	0,998	0,722
hsa_miR_629_5p	0,197	0,998	0,564	hsa_miR_1180_3p	0,260	0,998	0,801
hsa_miR_184	0,208	0,998	1,567	hsa_miR_34c_5p	0,268	0,998	0,835
hsa_miR_29b_2_5p	0,211	0,998	2,240	hsa_miR_18a_5p	0,275	0,998	0,759
hsa_miR_23a_5p	0,216	0,998	0,529	hsa_miR_1183	0,278	0,998	1,256
hsa_miR_204_5p	0,216	0,998	0,549	hsa_miR_223_5p	0,280	0,998	1,243
hsa_miR_512_3p	0,217	0,998	0,601	hsa_miR_601	0,284	0,998	1,377
hsa_miR_340_3p	0,230	0,998	1,437	hsa_let_7g_5p	0,285	0,998	0,589
hsa_miR_200a_3p	0,237	0,998	0,849	hsa_miR_449b_5p	0,288	0,998	1,331
hsa_miR_15a_5p	0,239	0,998	1,385	hsa_miR_1254	0,292	0,998	1,215
hsa_miR_1291	0,243	0,998	1,265	hsa_miR_125a_3p	0,300	0,998	0,721
hsa_miR_601	0,244	0,998	1,457	hsa_miR_27b_3p	0,300	0,998	0,828
hsa_miR_1271_5p	0,244	0,998	1,452	hsa_miR_449a	0,302	0,998	1,226
hsa_miR_429	0,245	0,998	0,747	hsa_miR_181c_5p	0,310	0,998	0,658
hsa_miR_589_5p	0,249	0,998	0,436	hsa_miR_197_3p	0,310	0,998	1,265
hsa_miR_323a_3p	0,251	0,998	0,572	hsa_miR_7_1_3p	0,317	0,998	0,828
hsa_miR_34a_5p	0,256	0,998	0,839	hsa_miR_222_3p	0,317	0,998	1,219
hsa_miR_1290	0,263	0,998	1,346	hsa_miR_204_5p	0,317	0,998	0,691
hsa_miR_93_3p	0,266	0,998	1,363	hsa_miR_24_3p	0,321	0,998	1,259
hsa_miR_886_3p	0,268	0,998	1,177	hsa_miR_185_5p	0,322	0,998	0,833
hsa_miR_598_3p	0,270	0,998	1,420	hsa_miR_130a_3p	0,325	0,998	0,771
hsa_miR_342_5p	0,271	0,998	1,422	hsa_miR_485_3p	0,328	0,998	1,532

hsa_miR_203a_3p	0,273	0,998	0,857	hsa_miR_338_5p	0,333	0,998	1,164
hsa_miR_545_3p	0,276	0,998	0,647	hsa_miR_17_5p	0,335	0,998	1,330
hsa_miR_205_5p	0,287	0,998	0,809	hsa_miR_650	0,338	0,998	1,216
hsa_miR_140_3p	0,287	0,998	1,431	hsa_miR_181a_2_3p	0,340	0,998	0,755
hsa_miR_183_5p	0,290	0,998	0,517	hsa_miR_422a	0,346	0,998	0,807
hsa_miR_148b_3p	0,295	0,998	1,313	hsa_miR_191_3p	0,349	0,998	0,732
hsa_let_7e_5p	0,300	0,998	0,848	hsa_miR_16_5p	0,350	0,998	1,263
hsa_miR_223_5p	0,303	0,998	1,296	hsa_miR_296_5p	0,351	0,998	0,736
hsa_miR_886_5p	0,308	0,998	1,189	hsa_miR_125a_5p	0,355	0,998	1,196
hsa_miR_29b_3p	0,309	0,998	0,793	hsa_miR_152_3p	0,358	0,998	0,790
hsa_miR_629_3p	0,310	0,998	1,312	hsa_miR_770_5p	0,358	0,998	1,173
hsa_miR_9_5p	0,314	0,998	0,649	hsa_miR_20b_5p	0,361	0,998	1,257
hsa_miR_296_5p	0,317	0,998	0,566	hsa_miR_591	0,363	0,998	1,193
hsa_miR_422a	0,319	0,998	0,778	hsa_miR_423_5p	0,366	0,998	0,885
hsa_miR_92a_3p	0,324	0,998	0,791	hsa_miR_93_5p	0,368	0,998	1,243
hsa_miR_363_3p	0,328	0,998	0,567	hsa_miR_1267	0,380	0,998	1,228
hsa_miR_590_3p	0,331	0,998	1,327	hsa_miR_505_5p	0,382	0,998	0,839
hsa_miR_338_5p	0,336	0,998	0,721	hsa_miR_28_3p	0,388	0,998	1,265
hsa_miR_1260a	0,340	0,998	1,179	hsa_miR_106a_5p	0,395	0,998	1,252
hsa_miR_7_1_3p	0,341	0,998	1,206	hsa_miR_518f_3p	0,399	0,998	1,214
hsa_miR_484	0,346	0,998	1,310	hsa_miR_18a_3p	0,401	0,998	0,678
hsa_miR_1233_3p	0,347	0,998	1,086	hsa_miR_1208	0,403	0,998	1,207
hsa_miR_145_3p	0,350	0,998	0,610	hsa_let_7d_5p	0,405	0,998	0,782
hsa_miR_744_5p	0,351	0,998	0,791	hsa_miR_579_3p	0,406	0,998	0,750
hsa_miR_642a_5p	0,354	0,998	0,833	hsa_miR_130b_3p	0,408	0,998	0,830
hsa_miR_130a_3p	0,355	0,998	0,695	hsa_miR_598_3p	0,411	0,998	0,803
hsa_miR_185_5p	0,361	0,998	1,224	hsa_miR_7_5p	0,412	0,998	1,294
hsa_miR_30b_5p	0,365	0,998	0,804	hsa_miR_140_5p	0,417	0,998	1,208
hsa_miR_1255b_5p	0,366	0,998	1,222	hsa_miR_223_3p	0,421	0,998	1,129
hsa_miR_424_3p	0,366	0,998	1,295	hsa_miR_195_5p	0,421	0,998	1,230
hsa_miR_875_5p	0,367	0,998	0,729	hsa_miR_625_5p	0,421	0,998	0,666
hsa_miR_142_5p	0,368	0,998	0,793	hsa_miR_155_5p	0,426	0,998	1,315
hsa_miR_1256	0,373	0,998	0,708	hsa_let_7f_5p	0,432	0,998	0,887
hsa_miR_550a_5p	0,373	0,998	1,715	hsa_miR_1275	0,435	0,998	1,073
hsa_miR_125b_5p	0,374	0,998	0,861	hsa_miR_744_3p	0,436	0,998	1,209
hsa_miR_1275	0,382	0,998	1,126	hsa_miR_339_5p	0,437	0,998	0,834
hsa_let_7b_5p	0,389	0,998	0,806	hsa_miR_1256	0,438	0,998	1,215
hsa_miR_362_3p	0,389	0,998	0,635	hsa_miR_517c_3p	0,438	0,998	1,267
hsa_miR_591	0,393	0,998	0,756	hsa_miR_629_5p	0,441	0,998	0,792
hsa_miR_30e_3p	0,399	0,998	1,328	hsa_miR_142_5p	0,441	0,998	0,832
hsa_miR_551b_3p	0,402	0,998	0,720	hsa_miR_450a_5p	0,455	0,998	0,754
hsa_miR_99b_5p	0,402	0,998	0,818	hsa_miR_571	0,457	0,998	1,135
hsa_miR_196b_5p	0,405	0,998	0,756	hsa_miR_374b_5p	0,462	0,998	1,161
hsa_let_7a_5p	0,405	0,998	1,119	hsa_miR_10a_5p	0,463	0,998	0,809
hsa_miR_223_3p	0,406	0,998	1,273	hsa_miR_30b_5p	0,463	0,998	0,835
hsa_miR_193a_5p	0,409	0,998	0,856	hsa_miR_34b_3p	0,465	0,998	0,877
hsa_miR_517c_3p	0,424	0,998	0,709	hsa_miR_636	0,468	0,998	1,145
hsa_miR_330_3p	0,429	0,998	1,520	hsa_miR_523_3p	0,474	0,998	1,158
hsa_miR_195_5p	0,430	0,998	1,351	hsa_miR_33a_3p	0,474	0,998	0,758
hsa_miR_1247_5p	0,431	0,998	1,121	hsa_miR_424_5p	0,476	0,998	0,825
hsa_miR_212_3p	0,432	0,998	1,153	hsa_miR_211_5p	0,476	0,998	0,809
hsa_miR_142_3p	0,432	0,998	0,867	hsa_miR_589_3p	0,477	0,998	1,342
hsa_miR_381_3p	0,444	0,998	0,713	hsa_miR_491_5p	0,479	0,998	1,220
hsa_miR_190b	0,444	0,998	0,838	hsa_miR_15a_3p	0,480	0,998	0,797
hsa_miR_93_5p	0,445	0,998	0,812	hsa_miR_186_5p	0,482	0,998	1,232
hsa_miR_1303	0,448	0,998	1,121	hsa_miR_26b_3p	0,482	0,998	0,850
hsa_miR_27a_3p	0,449	0,998	1,169	hsa_miR_191_5p	0,482	0,998	1,268
hsa_miR_100_5p	0,463	0,998	0,878	hsa_miR_20a_5p	0,488	0,998	1,165
hsa_miR_24_3p	0,467	0,998	1,340	hsa_miR_26b_5p	0,488	0,998	1,198
hsa_miR_99b_3p	0,469	0,998	1,229	hsa_miR_21_3p	0,494	0,998	1,168
hsa_miR_378a_5p	0,469	0,998	1,337	hsa_miR_126_3p	0,499	0,998	1,197
hsa_miR_361_5p	0,471	0,998	1,204	hsa_miR_484	0,500	0,998	1,149
hsa_miR_34a_3p	0,471	0,998	0,748	hsa_miR_34a_3p	0,501	0,998	1,175
hsa_miR_532_3p	0,486	0,998	1,341	hsa_miR_663b	0,503	0,998	0,863
hsa_miR_95_3p	0,486	0,998	1,263	hsa_miR_224_5p	0,508	0,998	0,904
hsa_miR_151a_5p	0,489	0,998	1,154	hsa_miR_361_5p	0,511	0,998	0,873
hsa_miR_143_3p	0,491	0,998	0,889	hsa_miR_199a_3p	0,514	0,998	1,164
hsa_miR_186_5p	0,493	0,998	1,223	hsa_miR_1305	0,515	0,998	1,207
hsa_let_7d_5p	0,493	0,998	0,816	hsa_miR_661	0,518	0,998	1,074
hsa_miR_224_5p	0,496	0,998	0,854	hsa_miR_99b_3p	0,518	0,998	0,843
hsa_miR_339_5p	0,502	0,998	1,356	hsa_miR_520c_3p	0,520	0,998	1,173
hsa_miR_511_5p	0,503	0,998	0,851	hsa_miR_483_5p	0,523	0,998	1,148
hsa_miR_20b_5p	0,504	0,998	0,790	hsa_miR_15b_5p	0,523	0,998	1,108
hsa_miR_140_5p	0,508	0,998	1,308	hsa_miR_92a_1_5p	0,524	0,998	0,803
hsa_miR_338_3p	0,511	0,998	0,850	hsa_miR_616_5p	0,526	0,998	1,205
hsa_miR_23a_3p	0,521	0,998	1,319	hsa_miR_455_5p	0,529	0,998	0,787
hsa_miR_211_5p	0,524	0,998	0,783	hsa_miR_29b_3p	0,530	0,998	0,833
hsa_miR_572	0,531	0,998	1,180	hsa_miR_218_5p	0,530	0,998	1,199
hsa_miR_449a	0,532	0,998	0,889	hsa_miR_27a_3p	0,531	0,998	1,188
hsa_miR_339_3p	0,534	0,998	1,131	hsa_miR_22_5p	0,533	0,998	0,835
hsa_miR_494_3p	0,537	0,998	0,862	hsa_miR_25_3p	0,535	0,998	1,139
hsa_miR_660_5p	0,537	0,998	1,110	hsa_miR_885_5p	0,535	0,998	1,209

hsa_miR_16_5p	0,539	0,998	1,238	hsa_miR_545_3p	0,539	0,998	1,274
hsa_miR_182_5p	0,541	0,998	0,737	hsa_miR_365a_3p	0,547	0,998	0,904
hsa_miR_331_3p	0,543	0,998	0,897	hsa_miR_744_5p	0,554	0,998	1,129
hsa_miR_424_5p	0,544	0,998	0,824	hsa_miR_339_3p	0,554	0,998	0,881
hsa_miR_34b_5p	0,545	0,998	0,914	hsa_miR_574_3p	0,555	0,998	1,132
hsa_miR_708_5p	0,546	0,998	0,859	hsa_miR_138_5p	0,556	0,998	1,157
hsa_miR_624_5p	0,553	0,998	0,809	hsa_miR_622	0,557	0,998	1,138
hsa_miR_652_3p	0,559	0,998	1,098	hsa_miR_550a_5p	0,558	0,998	1,207
hsa_miR_663b	0,561	0,998	1,036	hsa_miR_212_3p	0,558	0,998	1,157
hsa_miR_454_3p	0,564	0,998	1,131	hsa_miR_92a_3p	0,561	0,998	1,145
hsa_miR_589_3p	0,566	0,998	1,303	hsa_miR_31_5p	0,563	0,998	1,101
hsa_miR_505_3p	0,570	0,998	0,800	hsa_miR_363_3p	0,565	0,998	0,832
hsa_miR_30d_5p	0,576	0,998	0,916	hsa_miR_21_5p	0,565	0,998	1,099
hsa_miR_126_3p	0,578	0,998	1,102	hsa_miR_132_3p	0,568	0,998	1,086
hsa_miR_183_3p	0,578	0,998	0,828	hsa_miR_145_5p	0,568	0,998	1,082
hsa_miR_622	0,581	0,998	0,672	hsa_miR_20a_3p	0,569	0,998	1,239
hsa_miR_425_5p	0,587	0,998	1,122	hsa_miR_192_5p	0,572	0,998	0,847
hsa_miR_200a_5p	0,587	0,998	0,878	hsa_let_7a_5p	0,577	0,998	0,935
hsa_miR_125a_3p	0,589	0,998	1,143	hsa_miR_1825	0,581	0,998	1,091
hsa_miR_99a_5p	0,595	0,998	0,912	hsa_miR_429	0,587	0,998	0,885
hsa_miR_148a_3p	0,596	0,998	0,902	hsa_miR_200a_5p	0,592	0,998	0,895
hsa_miR_590_5p	0,601	0,998	1,117	hsa_miR_500a_5p	0,593	0,998	0,876
hsa_miR_374a_5p	0,602	0,998	0,880	hsa_miR_320a	0,600	0,998	1,215
hsa_miR_483_3p	0,604	0,998	0,832	hsa_miR_193a_5p	0,601	0,998	1,087
hsa_miR_92a_1_5p	0,605	0,998	1,217	hsa_miR_29a_3p	0,603	0,998	1,117
hsa_miR_26b_3p	0,607	0,998	1,139	hsa_miR_9_5p	0,604	0,998	0,823
hsa_miR_130b_3p	0,610	0,998	0,912	hsa_miR_128_3p	0,618	0,998	0,902
hsa_miR_21_5p	0,610	0,998	0,909	hsa_miR_22_3p	0,625	0,998	0,916
hsa_miR_30d_3p	0,611	0,998	0,750	hsa_miR_378a_5p	0,625	0,998	0,855
hsa_miR_101_3p	0,615	0,998	0,901	hsa_miR_182_5p	0,626	0,998	0,848
hsa_miR_1302	0,618	0,998	0,837	hsa_miR_141_3p	0,651	0,998	0,910
hsa_miR_23b_3p	0,618	0,998	0,837	hsa_miR_26a_5p	0,651	0,998	0,865
hsa_miR_191_5p	0,619	0,998	1,174	hsa_miR_101_3p	0,652	0,998	0,861
hsa_miR_20a_3p	0,630	0,998	0,767	hsa_miR_106b_5p	0,653	0,998	1,107
hsa_miR_15b_5p	0,632	0,998	1,074	hsa_miR_1291	0,653	0,998	1,112
hsa_miR_135b_5p	0,636	0,998	0,892	hsa_miR_340_3p	0,655	0,998	0,885
hsa_miR_34b_3p	0,637	0,998	0,925	hsa_miR_29c_3p	0,656	0,998	0,909
hsa_miR_516b_3p	0,640	0,998	1,086	hsa_miR_184	0,656	0,998	0,924
hsa_miR_22_5p	0,640	0,998	1,150	hsa_miR_345_5p	0,662	0,998	1,120
hsa_miR_200c_3p	0,642	0,998	0,906	hsa_miR_539_5p	0,666	0,998	1,140
hsa_miR_30c_5p	0,645	0,998	0,881	hsa_miR_551b_5p	0,673	0,998	1,110
hsa_miR_328_3p	0,646	0,998	0,911	hsa_miR_590_5p	0,674	0,998	1,135
hsa_miR_376c_3p	0,646	0,998	0,790	hsa_miR_30a_3p	0,679	0,998	0,893
hsa_miR_616_3p	0,648	0,998	1,183	hsa_miR_135b_5p	0,685	0,998	1,102
hsa_miR_625_3p	0,651	0,998	1,150	hsa_miR_532_5p	0,690	0,998	1,062
hsa_miR_200b_3p	0,656	0,998	0,920	hsa_miR_769_5p	0,691	0,998	0,928
hsa_miR_146a_5p	0,666	0,998	1,128	hsa_miR_29a_5p	0,692	0,998	1,149
hsa_miR_1276	0,667	0,998	1,127	hsa_miR_193a_3p	0,697	0,998	0,853
hsa_miR_518f_3p	0,675	0,998	1,264	hsa_miR_328_3p	0,699	0,998	1,082
hsa_miR_340_5p	0,683	0,998	1,099	hsa_miR_28_5p	0,699	0,998	1,090
hsa_miR_1183	0,688	0,998	1,092	hsa_miR_23b_3p	0,700	0,998	0,935
hsa_miR_636	0,689	0,998	1,128	hsa_miR_203a_3p	0,703	0,998	0,944
hsa_miR_409_3p	0,689	0,998	1,236	hsa_let_7b_5p	0,704	0,998	1,116
hsa_miR_625_5p	0,690	0,998	1,183	hsa_miR_604	0,708	0,998	1,071
hsa_miR_146b_3p	0,694	0,998	1,082	hsa_miR_618	0,708	0,998	1,131
hsa_miR_192_5p	0,697	0,998	1,116	hsa_miR_628_3p	0,709	0,998	0,937
hsa_miR_548b_5p	0,703	0,998	1,069	hsa_miR_126_5p	0,713	0,998	1,090
hsa_miR_155_5p	0,711	0,998	1,092	hsa_miR_323a_3p	0,714	0,998	1,120
hsa_miR_425_3p	0,714	0,998	1,126	hsa_miR_127_3p	0,715	0,998	0,882
hsa_miR_324_5p	0,717	0,998	0,923	hsa_miR_645	0,718	0,998	1,087
hsa_miR_505_5p	0,718	0,998	1,104	hsa_miR_483_3p	0,719	0,998	1,065
hsa_miR_486_5p	0,718	0,998	0,954	hsa_miR_106b_3p	0,723	0,998	0,925
hsa_miR_374b_3p	0,718	0,998	0,877	hsa_miR_135a_5p	0,725	0,998	0,905
hsa_miR_29c_3p	0,723	0,998	0,873	hsa_miR_572	0,725	0,998	1,084
hsa_miR_1180_3p	0,724	0,998	1,077	hsa_miR_409_3p	0,725	0,998	1,067
hsa_miR_222_3p	0,735	0,998	0,889	hsa_miR_629_3p	0,728	0,998	1,088
hsa_miR_345_5p	0,746	0,998	1,095	hsa_miR_494_3p	0,733	0,998	1,097
hsa_miR_145_5p	0,747	0,998	1,092	hsa_miR_99a_3p	0,734	0,998	0,926
hsa_miR_1267	0,749	0,998	0,895	hsa_miR_99b_5p	0,737	0,998	1,064
hsa_miR_25_3p	0,750	0,998	0,933	hsa_miR_150_5p	0,737	0,998	1,068
hsa_miR_98_5p	0,750	0,998	1,082	hsa_miR_331_5p	0,737	0,998	1,085
hsa_miR_1262	0,752	0,998	1,122	hsa_miR_324_3p	0,738	0,998	0,937
hsa_miR_99a_3p	0,752	0,998	0,887	hsa_miR_589_5p	0,744	0,998	1,105
hsa_miR_483_5p	0,755	0,998	1,061	hsa_miR_301a_3p	0,748	0,998	1,138
hsa_miR_152_3p	0,762	0,998	0,927	hsa_miR_99a_5p	0,749	0,998	0,950
hsa_miR_618	0,766	0,998	0,916	hsa_miR_331_3p	0,755	0,998	1,064
hsa_miR_30a_5p	0,770	0,998	0,945	hsa_miR_187_3p	0,760	0,998	0,923
hsa_miR_532_5p	0,773	0,998	0,942	hsa_miR_145_3p	0,762	0,998	1,134
hsa_miR_491_5p	0,776	0,998	1,119	hsa_miR_193b_3p	0,767	0,998	1,067
hsa_miR_27b_3p	0,777	0,998	0,950	hsa_miR_338_3p	0,767	0,998	1,085
hsa_miR_518d_3p	0,778	0,998	0,947	hsa_miR_425_5p	0,768	0,998	1,058
hsa_miR_1825	0,780	0,998	1,068	hsa_miR_103a_3p	0,769	0,998	0,950



hsa_miR_571	0,790	0,998	0,900	hsa_miR_381_3p	0,771	0,998	1,055
hsa_miR_20a_5p	0,791	0,998	0,941	hsa_miR_424_3p	0,772	0,998	0,925
hsa_miR_623	0,795	0,998	0,904	hsa_miR_29b_2_5p	0,777	0,998	0,898
hsa_let_7g_5p	0,798	0,998	1,085	hsa_miR_30c_5p	0,779	0,998	1,058
hsa_miR_103a_3p	0,803	0,998	1,047	hsa_miR_19b_3p	0,779	0,998	1,052
hsa_miR_28_5p	0,803	0,998	0,952	hsa_miR_1244	0,780	0,998	1,074
hsa_miR_15a_3p	0,804	0,998	0,910	hsa_miR_623	0,786	0,998	1,063
hsa_miR_181c_5p	0,807	0,998	1,168	hsa_miR_205_5p	0,786	0,998	0,961
hsa_miR_520d_3p	0,810	0,998	1,052	hsa_miR_625_3p	0,786	0,998	0,947
hsa_miR_423_5p	0,812	0,998	0,960	hsa_miR_639	0,786	0,998	1,065
hsa_miR_193a_3p	0,815	0,998	1,101	hsa_miR_652_3p	0,788	0,998	1,053
hsa_miR_30a_3p	0,818	0,998	0,951	hsa_miR_548b_5p	0,793	0,998	1,052
hsa_miR_502_3p	0,821	0,998	0,891	hsa_miR_16_1_3p	0,797	0,998	1,085
hsa_miR_1227_3p	0,825	0,998	1,044	hsa_miR_148a_3p	0,800	0,998	1,050
hsa_miR_301a_3p	0,825	0,998	0,944	hsa_miR_144_5p	0,811	0,998	0,916
hsa_miR_193b_3p	0,833	0,998	0,961	hsa_miR_324_5p	0,817	0,998	1,050
hsa_miR_127_3p	0,833	0,998	1,080	hsa_miR_143_3p	0,818	0,998	0,957
hsa_miR_320b	0,834	0,998	0,957	hsa_miR_616_3p	0,821	0,998	1,060
hsa_miR_149_5p	0,835	0,998	1,039	hsa_miR_518d_3p	0,823	0,998	0,963
hsa_miR_33a_3p	0,841	0,998	1,128	hsa_miR_376c_3p	0,828	0,998	0,916
hsa_miR_539_5p	0,847	0,998	1,149	hsa_miR_489_3p	0,828	0,998	1,067
hsa_miR_362_5p	0,848	0,998	1,057	hsa_miR_597_5p	0,830	0,998	0,949
hsa_miR_29a_3p	0,851	0,998	1,054	hsa_miR_125b_5p	0,840	0,998	0,977
hsa_miR_661	0,852	0,998	0,975	hsa_miR_30a_5p	0,840	0,998	0,965
hsa_miR_221_3p	0,854	0,998	1,044	hsa_miR_95_3p	0,850	0,998	0,953
hsa_miR_28_3p	0,858	0,998	0,925	hsa_miR_19a_3p	0,854	0,998	1,040
hsa_miR_574_3p	0,865	0,998	1,040	hsa_miR_146b_5p	0,860	0,998	0,954
hsa_miR_885_5p	0,868	0,998	1,054	hsa_miR_149_5p	0,863	0,998	0,970
hsa_miR_766_3p	0,868	0,998	0,976	hsa_miR_320b	0,868	0,998	1,032
hsa_miR_150_5p	0,869	0,998	0,960	hsa_miR_221_3p	0,871	0,998	0,971
hsa_miR_19b_3p	0,869	0,998	0,963	hsa_miR_548i	0,875	0,998	0,934
hsa_miR_126_5p	0,870	0,998	0,955	hsa_miR_30e_3p	0,875	0,998	0,957
hsa_miR_548c_5p	0,871	0,998	0,974	hsa_miR_340_5p	0,876	0,998	1,035
hsa_miR_106b_5p	0,872	0,998	1,035	hsa_miR_210_3p	0,877	0,998	0,980
hsa_miR_650	0,874	0,998	1,028	hsa_miR_875_5p	0,877	0,998	0,969
hsa_miR_365a_3p	0,876	0,998	0,962	hsa_miR_548d_5p	0,878	0,998	0,974
hsa_miR_9_3p	0,884	0,998	1,074	hsa_miR_9_3p	0,880	0,998	1,057
hsa_miR_137	0,886	0,998	1,051	hsa_miR_642a_5p	0,893	0,998	0,978
hsa_miR_31_3p	0,887	0,998	1,033	hsa_miR_200c_3p	0,893	0,998	0,971
hsa_miR_125a_5p	0,894	0,998	0,964	hsa_miR_451a	0,895	0,998	0,984
hsa_miR_605_5p	0,895	0,998	1,025	hsa_miR_374b_3p	0,897	0,998	0,969
hsa_miR_1244	0,897	0,998	1,033	hsa_miR_942_5p	0,908	0,998	1,026
hsa_miR_106a_5p	0,897	0,998	1,049	hsa_miR_1260a	0,910	0,998	1,015
hsa_miR_17_5p	0,898	0,998	0,959	hsa_miR_206	0,912	0,998	0,965
hsa_miR_128_3p	0,901	0,998	1,027	hsa_miR_660_5p	0,912	0,998	1,021
hsa_miR_1208	0,913	0,998	1,056	hsa_miR_181a_5p	0,913	0,998	1,021
hsa_miR_380_5p	0,915	0,998	1,018	hsa_miR_196b_5p	0,915	0,998	0,968
hsa_miR_199a_3p	0,917	0,998	1,021	hsa_miR_30d_5p	0,917	0,998	1,016
hsa_miR_548d_5p	0,919	0,998	0,983	hsa_miR_375	0,917	0,998	1,014
hsa_miR_597_5p	0,924	0,998	1,023	hsa_miR_886_3p	0,919	0,998	0,981
hsa_miR_645	0,924	0,998	1,033	hsa_miR_548c_5p	0,921	0,998	0,980
hsa_miR_26a_5p	0,924	0,998	1,030	hsa_miR_151a_3p	0,922	0,998	0,983
hsa_miR_19b_1_5p	0,926	0,998	0,972	hsa_miR_98_5p	0,924	0,998	0,981
hsa_miR_181a_2_3p	0,927	0,998	1,043	hsa_miR_137	0,927	0,998	1,022
hsa_miR_7_5p	0,935	0,998	1,021	hsa_miR_342_3p	0,927	0,998	1,023
hsa_miR_144_5p	0,937	0,998	0,984	hsa_miR_200b_3p	0,932	0,998	0,986
hsa_miR_489_3p	0,939	0,998	1,020	hsa_miR_27a_5p	0,935	0,998	1,021
hsa_miR_146b_5p	0,942	0,998	0,986	hsa_miR_425_3p	0,947	0,998	1,014
hsa_miR_374b_5p	0,944	0,998	1,014	hsa_miR_148b_5p	0,954	0,998	0,980
hsa_miR_151a_3p	0,948	0,998	1,021	hsa_miR_1270	0,954	0,998	0,987
hsa_miR_181a_5p	0,950	0,998	1,016	hsa_miR_624_5p	0,961	0,998	1,012
hsa_miR_335_5p	0,955	0,998	1,011	hsa_miR_183_3p	0,970	0,998	0,992
hsa_miR_639	0,957	0,998	0,975	hsa_miR_141_5p	0,970	0,998	1,013
hsa_miR_194_5p	0,959	0,998	0,984	hsa_miR_34a_5p	0,970	0,998	1,008
hsa_miR_31_5p	0,960	0,998	1,008	hsa_miR_183_5p	0,971	0,998	0,986
hsa_miR_26b_5p	0,966	0,998	0,987	hsa_miR_142_3p	0,971	0,998	1,008
hsa_miR_342_3p	0,974	0,998	0,994	hsa_miR_222_5p	0,972	0,998	0,993
hsa_miR_451a	0,975	0,998	0,996	hsa_miR_486_5p	0,976	0,998	0,993
hsa_miR_218_5p	0,976	0,998	1,007	hsa_miR_202_3p	0,976	0,998	1,009
hsa_miR_1305	0,977	0,998	1,011	hsa_miR_1302	0,981	0,998	0,994
hsa_miR_191_3p	0,979	0,998	1,008	hsa_miR_23a_5p	0,983	0,998	0,993
hsa_miR_19a_3p	0,982	0,998	1,006	hsa_miR_100_5p	0,984	0,998	1,003
hsa_miR_18a_5p	0,982	0,998	1,005	hsa_miR_93_3p	0,986	0,998	0,997
hsa_miR_1270	0,983	0,998	1,007	hsa_miR_532_3p	0,987	0,998	0,996
hsa_miR_18a_3p	0,988	0,998	1,008	hsa_let_7c_5p	0,991	0,998	1,002
hsa_miR_324_3p	0,988	0,998	0,996	hsa_miR_337_5p	0,995	0,998	0,999
hsa_miR_769_5p	0,997	0,999	1,001	hsa_miR_190a_5p	0,995	0,998	1,002
hsa_miR_616_5p	0,998	0,999	0,999	hsa_miR_140_3p	0,996	0,998	0,998
hsa_miR_132_3p	0,999	0,999	1,000	hsa_miR_374a_5p	0,998	0,998	1,000

**TABLE S13.** Multivariate logistic regression analysis

<b>Dependent Y</b>	c-AR within_1st_year_after_Tx
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<b>Method</b>	Stepwise
<b>Enter variable if P&lt;</b>	0,06
<b>Remove variable if P&gt;</b>	0,1

<b>Sample size</b>	22
<b>Cases with Y=0</b>	17 (77.27%)
<b>Cases with Y=1</b>	5 (22.73%)

**Overall Model Fit**

<b>Null model -2 Log Likelihood</b>	23,582
<b>Full model -2 Log Likelihood</b>	15,12
<b>Chi-square</b>	8,463
<b>DF</b>	1
<b>Significance level</b>	P = 0.0036

**Coefficients and Standard Errors**

<b>Variable</b>	<b>Coefficient</b>	<b>Std. Error</b>	<b>P</b>
miRNA_classes=bad	3,4012	1,34784	0,0116
Constant	-2,7081		

**Variables not included in the model**

miR-148b-5p=LOW
miR-744-3p=HIGH
Age mismatch ≥1.2
Warm ischemia
BEST FEV1≥80%
CMV mismatch
DBD vs DCD=DCD
Disease
ECMO
LAS≥40
Mechanical_ventilation >2 days
MP
Oto>5
Pneumonia
Sex_mismatch
smoking_habit
PGDmax

**Odds Ratios and 95% Confidence Intervals**

<b>Variable</b>	<b>Odds ratio</b>	<b>95% CI</b>
miRNA_classes=bad	30	2.1371 to 421.1375

**Classification table (cut-off value p=0.5)**

<b>Actual group</b>	<b>Predicted group</b>		<b>Percent correct</b>
	<b>0</b>	<b>1</b>	
<b>Y = 0</b>	15	2	88,24%
<b>Y = 1</b>	1	4	80,00%
<b>Percent of cases correctly classified</b>			86,36%

**ROC curve analysis**

<b>Area under the ROC curve (AUC)</b>	0,841
<b>Standard Error</b>	0,116
<b>95% Confidence interval</b>	0.624 to 0.960