

Plasma microRNA signature in presymptomatic and symptomatic subjects with C9orf72-associated frontotemporal dementia and amyotrophic lateral sclerosis

Virgilio Kmetzsch, Vincent Anquetil, Dario Saracino, Daisy Rinaldi, Agnès Camuzat, Thomas Gareau, Ludmila Jornea, Sylvie Forlani, Philippe Couratier, David Wallon, et al.

► **To cite this version:**

Virgilio Kmetzsch, Vincent Anquetil, Dario Saracino, Daisy Rinaldi, Agnès Camuzat, et al.. Plasma microRNA signature in presymptomatic and symptomatic subjects with C9orf72-associated frontotemporal dementia and amyotrophic lateral sclerosis. *Journal of Neurology, Neurosurgery and Psychiatry*, BMJ Publishing Group, 2020, 92 (5), pp.485-493. 10.1136/jnnp-2020-324647 . hal-03046771

HAL Id: hal-03046771

<https://hal.inria.fr/hal-03046771>

Submitted on 8 Dec 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.


L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



OPEN ACCESS

Original research

Plasma microRNA signature in presymptomatic and symptomatic subjects with *C9orf72*-associated frontotemporal dementia and amyotrophic lateral sclerosis

Virgilio Kmetzsch ^{1,2}, Vincent Anquetil,² Dario Saracino,^{1,2,3,4} Daisy Rinaldi,^{2,3,4} Agnès Camuzat,^{2,5} Thomas Gareau,² Ludmila Jornea,² Sylvie Forlani,² Philippe Couratier,⁶ David Wallon,⁷ Florence Pasquier,⁸ Noémie Robil,⁹ Pierre de la Grange,⁹ Ivan Moszer,² Isabelle Le Ber,^{2,3,4,10} Olivier Colliot,^{1,2} Emmanuelle Becker,¹¹ The PREV-DEMALS study group

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/jnnp-2020-324647>).

For numbered affiliations see end of article.

Correspondence to

Dr Emmanuelle Becker, Dyliss team, Irlisa / Inria Rennes-Bretagne Atlantique, Campus de Beaulieu, 35042 Rennes Cedex, France; emmanuelle.becker@univ-rennes1.fr

Received 20 July 2020

Revised 30 September 2020

Accepted 27 October 2020



© Author(s) (or their employer(s)) 2020. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Kmetzsch V, Anquetil V, Saracino D, et al. *J Neurol Neurosurg Psychiatry* Epub ahead of print: [please include Day Month Year]. doi:10.1136/jnnp-2020-324647

ABSTRACT

Objective To identify potential biomarkers of preclinical and clinical progression in chromosome 9 open reading frame 72 gene (*C9orf72*)-associated disease by assessing the expression levels of plasma microRNAs (miRNAs) in *C9orf72* patients and presymptomatic carriers.

Methods The PREV-DEMALS study is a prospective study including 22 *C9orf72* patients, 45 presymptomatic *C9orf72* mutation carriers and 43 controls. We assessed the expression levels of 2576 miRNAs, among which 589 were above noise level, in plasma samples of all participants using RNA sequencing. The expression levels of the differentially expressed miRNAs between patients, presymptomatic carriers and controls were further used to build logistic regression classifiers.

Results Four miRNAs were differentially expressed between patients and controls: miR-34a-5p and miR-345-5p were overexpressed, while miR-200c-3p and miR-10a-3p were underexpressed in patients. MiR-34a-5p was also overexpressed in presymptomatic carriers compared with healthy controls, suggesting that miR-34a-5p expression is deregulated in cases with *C9orf72* mutation. Moreover, miR-345-5p was also overexpressed in patients compared with presymptomatic carriers, which supports the correlation of miR-345-5p expression with the progression of *C9orf72*-associated disease. Together, miR-200c-3p and miR-10a-3p underexpression might be associated with full-blown disease. Four presymptomatic subjects in transitional/prodromal stage, close to the disease conversion, exhibited a stronger similarity with the expression levels of patients.

Conclusions We identified a signature of four miRNAs differentially expressed in plasma between clinical conditions that have potential to represent progression biomarkers for *C9orf72*-associated frontotemporal dementia and amyotrophic lateral sclerosis. This study suggests that dysregulation of miRNAs is dynamically altered throughout neurodegenerative diseases progression, and can be detectable even long before clinical onset.

Trial registration number NCT02590276.

INTRODUCTION

Frontotemporal dementia (FTD) designates neurodegenerative dementias characterised by progressive behavioural, executive and language impairments.¹ Amyotrophic lateral sclerosis (ALS) is a degenerative disease of motor neurons that leads to progressive muscle atrophy and motor deficit. FTD and ALS form a clinical continuum, as these two diseases may be associated in the same patients (FTD-ALS) or within families. They also share common pathophysiological mechanisms and genetic causes.² The most frequent genetic cause of familial FTD and ALS is a hexanucleotide (GGGGCC) repeat expansion in the chromosome 9 open reading frame 72 (*C9orf72*) gene.^{3,4} This autosomal dominant mutation may cause neurodegeneration through *C9orf72* loss of function, aggregation of mutant RNA in nuclear foci and of dipeptide repeats generated by repeat-associated non-AUG translation, ultimately leading to pathological inclusions of TAR-DNA binding protein 43 (TDP-43).⁵

There are no effective treatments available in *C9orf72* disease to date, but several promising trials including antisense therapies are being developed. Presymptomatic *C9orf72* carriers represent an optimal target population for the development of new therapeutic interventions for FTD and ALS.^{6,7} Therefore, it is of paramount importance to identify biomarkers of preclinical progression for FTD and ALS, which could be used to initiate and monitor potential disease-modifying treatments before any irreversible brain damage has occurred.

There is increasing evidence that microRNA (miRNA) expression in body fluids, such as plasma/serum⁸ or cerebrospinal fluid (CSF),⁹ correlates with the diagnosis and progression of many neurodegenerative diseases, including FTD¹⁰ and ALS.¹¹ MicroRNAs are a class of small non-coding RNAs that negatively regulate gene expression by promoting translational repression and messenger RNA degradation.¹² Since TDP-43 promotes miRNA biogenesis,¹³ the dysregulation of TDP-43 activity associated with FTD and ALS pathogenesis could impact miRNA expression levels.¹⁴ Notably,

miRNAs originating from neurons and glial cells are released through extracellular vesicles, especially exosomes, and can be measured in different body fluids, including CSF and plasma.¹⁵ Aberrant expression of miRNAs can be thus non-invasively detected in easily accessible body compartments, such as blood plasma, and potentially serve as biomarkers.¹⁶

Previous studies have explored selected plasma miRNAs as biomarkers for FTD/ALS¹⁷ or FTD^{18,19} using quantitative real-time PCR. Two of them have analysed the expression of a limited number of candidate miRNAs: nine miRNAs linked with apoptosis¹⁸ or 37 brain-enriched miRNAs.¹⁷ A wider miRNA profiling study¹⁹ analysed 752 miRNAs, as a first attempt to perform an unbiased assessment of circulating miRNAs in patients with FTD. In addition, a more recent study²⁰ assessed the expression levels of 2313 miRNAs in a merged cohort of patients with FTD with different genetic forms (*C9orf72*, *MAPT*, *GRN*, *TBK1*) or with sporadic forms, by next generation RNA sequencing (RNA-seq). However, results among different studies have been conflicting so far, probably due to the heterogeneity of cohorts with respect to the underlying pathology (genetic or sporadic). Besides, these studies only compared healthy controls and symptomatic patients, focussing on evaluating potential diagnostic biomarkers. To date, no studies have evaluated plasma miRNAs as progression biomarkers for FTD or ALS in presymptomatic individuals.

The present work aims at investigating expression levels of plasma miRNAs in a large homogeneous genetic cohort of *C9orf72* mutation carriers, both in the presymptomatic and in the clinical phases, to identify potential non-invasive biomarkers of preclinical and clinical progression in *C9orf72*-associated FTD and ALS. We hypothesise that performing large scale RNA-seq analyses in plasma samples, without a priori assumptions, will reveal significant differences in miRNA expression levels between healthy controls, presymptomatic and symptomatic mutation carriers.

MATERIAL AND METHODS

Participants

PREV-DEMALS (<https://clinicaltrials.gov/Identifier:NCT02590276>) is a national multicentric study focussed on *C9orf72* mutation carriers. Between 2015 and 2017, 111 individuals were investigated with the same protocol in four French university hospitals (Paris, Limoges, Lille and Rouen), as previously described.^{6,21} Written informed consents were obtained from all participants.

This cohort included 22 patients (15 FTD, 4 FTD/ALS and 3 ALS) carrying a *C9orf72* expansion and 89 asymptomatic first-degree relatives of *C9orf72* patients (who have 50% risk to carry the mutation), out of 64 families. A pathogenic expansion was detected in 46 of them, denoted as the 'presymptomatic group'. The control group was formed by the 43 asymptomatic individuals that did not carry an expansion.

At inclusion, each participant's cognitive and behavioural clinical status was assessed based on standardised interview with relatives, comprehensive neurological examination, an extensive neuropsychological battery assessing all cognitive domains (including, notably, mini-mental state examination, Frontal Assessment Battery, Mattis Dementia Rating Scale and Ekman faces test) and behavioural scales (including Frontal Behavioural Inventory and Apathy Evaluation Scale) (table 1). The cognitive and behavioural evaluations and their scores have been described in more detail elsewhere^{6,21} and in online supplemental appendix A1. Neuromuscular function was thoroughly

evaluated by means of quantitative motor testing according to Medical Research Council muscle scale, assessment of upper and lower motor neuron signs and administration of ALS-FRS (ALS-Functional Rating Scale), evaluating the degree of functional impairment. All participants underwent a systematic standardised interview to investigate the presence of cramps, fatigue, muscle pain, muscle weakness, muscle stiffness or fasciculations. Electromyography was proposed to the participants with even subtle motor signs or complaints.

One participant was excluded because mild cerebellar syndrome was detected at a neurological examination, after inclusion. Thus, the present study comprises 110 individuals (22 patients, 45 presymptomatic carriers and 43 healthy controls), all of which underwent plasma sampling at their inclusion. The demographic and clinical characteristics of the studied population are shown in table 1.

The participants have then been clinically followed after their inclusion during a 3-year period, from 2017 to 2020. Four out of the 45 *C9orf72* presymptomatic carriers have developed subtle frontal cognitive and/or behavioural changes and/or motor signs/symptoms during this period, without fitting diagnostic criteria for FTD or ALS, suggesting they were in the transitional 'prodromal' phase at the moment of or just after their inclusion visit. These cases are described in online supplemental appendix A2. All analyses in the presymptomatic group were performed with (n=45) and without (n=41) the four prodromal subjects. We also analysed these cases separately in an additional complementary approach.

Plasma collection and preparation

Blood samples were collected on EDTA using the same standardised collection and handling procedures for all participants across the centres. The mean disease duration at sampling was 6.2 ± 4.0 years in the patients' group. All were in fasted state. All samples were centralised at the ICM DNA and cell bank, and processed using the same protocol. Plasma was extracted at room temperature after centrifugation of blood samples at 2500 rpm for 10 min. Aliquots of 1 mL were stored in polypropylene tubes at -80°C .

MiRNA extraction and sequencing

MiRNA extraction was performed with a miRNeasy Serum/Plasma Kit (Qiagen) following the manufacturer's instructions. We used 200 μL of plasma quickly melted and directly added to 1 mL of QIAzol solution. MiRNAs were eluted in 14 μL of water; 5 μL were used for miRNA sequencing library preparation with QIAseq miRNA Library Kit (Qiagen) according to the manufacturer's protocol.

MiRNA sequencing was performed on Illumina NovaSeq 6000 in three independent batches, targeting a minimum of 10 million mapped reads per sample. Since batch effects may have a critical impact in high-throughput experiments, we randomly assigned each individual to one batch, equally distributing clinical status (control, presymptomatic and patient) and centres (Paris, Limoges, Lille and Rouen), to allow adjusting for batch effects during data analysis. Online supplemental table A1 describes the distribution of subjects across batches.

Raw reads to miRNA counts computation pipeline

Quality control of raw reads was performed with FastQC (Andrews S. 2010, <http://www.bioinformatics.babraham.ac.uk/projects/fastqc>). UMI-tools²² and Cutadapt²³ were used respectively to extract UMIs and suppress adapting sequences as well as

Table 1 Demographic and clinical characteristics of the studied population

	Control (n=43)	Presymptomatic (n=45)	Patient (n=22)	χ^2 P value		
Female gender	23 (53.5%)	28 (62.2%)	10 (45.4%)	0.408		
					Kruskal-Wallis P value	Comparison
Age at inclusion (years)	46.4±13.5	41.8±11.8	62.7±10.5	<0.001		Dunn's test P value
					Control vs presymptomatic	0.118
					Control vs patient	<0.001
					Presymptomatic vs patient	<0.001
ALS-FRS	39.5±1.3	39.5±1.9	33.4±7.7	<0.001	Control vs presymptomatic	0.827
					Control vs patient	<0.001
					Presymptomatic vs patient	<0.001
MMSE	29±1.2	28.5±1.4	17.8±8.4	<0.001	Control vs presymptomatic	0.183
					Control vs patient	<0.001
					Presymptomatic vs patient	<0.001
MDRS	142.1±1.8	141.2±3.0	97.3±36.7	<0.001	Control vs presymptomatic	0.431
					Control vs patient	<0.001
					Presymptomatic vs patient	<0.001
FAB	17±1.2	17.2±0.9	9.7±5.3	<0.001	Control vs presymptomatic	0.583
					Control vs patient	<0.001
					Presymptomatic vs patient	<0.001
Ekman faces test	30.1±2.6	30.1±2.3	18±9.1	0.001	Control vs presymptomatic	0.694
					Control vs patient	<0.001
					Presymptomatic vs patient	0.001
FBI	0.9±1.8	1.5±2.7	28.5±15.2	<0.001	Control vs presymptomatic	0.387
					Control vs patient	<0.001
					Presymptomatic vs patient	<0.001
AES	4.8±3.9	6.5±3.6	23.5±13.1	<0.001	Control vs presymptomatic	0.095
					Control vs patient	<0.001
					Presymptomatic vs patient	0.004

Values are expressed as mean±SD, or as number (%). Demographic characteristics were compared between groups using the χ^2 test for gender and Kruskal-Wallis with Dunn's test for numerical variables.

Statistically significant p values are in bold.

AES, Apathy Evaluation Scale; ALS-FRS, ALS Functional Rating Scale; FAB, Frontal Assessment Battery; FBI, Frontal Behavioral Inventory; MDRS, Mattis Dementia Rating Scale; MMSE, mini-mental state examination.

polyA tails. The resulting sequences were aligned with Bowtie²⁴ and sorted by genomic location with Samtools sort.²⁵ PCR bias was corrected with UMI-tools, its efficacy was assessed per chromosome with Samtools idxstats. After controlling for the overlap/ambiguity between miRNAs enrichment and Gencode annotation with FeatureCounts,²⁶ miRNAs were counted with miRDeep2.²⁷

Statistical analysis

Statistical analyses were performed using R V.3.6.1 (R Foundation for Statistical Computing, Vienna, Austria). The differential expression of miRNAs between clinical groups was assessed with the R package EdgeR.²⁸ The analysis began with a count matrix with 2576 rows (one per miRNA i) and 110 columns (one per individual j). Only miRNAs considered above noise level (minimum count of 50 reads for at least one sample and a minimum total count of 1000) were retained for statistical analyses, reducing the count matrix to 589 rows. We assumed that miRNA counts followed a negative binomial distribution with mean μ_{ij} and dispersion ϕ_i and used generalised linear models to fit a log-linear model

$$\log_2 \mu_{ij} = \mathbf{x}_j^T \beta_i$$

for each miRNA, where \mathbf{x}_j is the vector of covariates that describes sample j and β_i is the vector of coefficients to be fitted for miRNA i . To control for possible batch, centre, age and gender effects, we added these variables as covariates in the model, in addition of clinical status. Raw counts were normalised using a trimmed mean of M-values.²⁹ Once the models were fitted, quasi-likelihood F-test was employed to determine the subset of miRNAs differentially expressed between clinical conditions (miRNA signature). Statistical significance was set at level $\alpha = 0.05$ and p values were adjusted for multiple testing using the Benjamini-Hochberg method.

Machine learning for binary classification

After the differentially expressed miRNAs were identified, we implemented logistic regression classifiers with L2 regularisation in Python 3.8.0 using scikit-learn³⁰ V.0.22.1. We used the expression levels of the miRNA signature as features to train binary classification models for each pairwise comparison between clinical status: controls versus presymptomatic individuals, controls versus patients and presymptomatic individuals versus patients. A stratified nested cross-validation strategy (online supplemental figure A1) was chosen to find the optimal hyperparameter (L2 regularisation coefficient) and to assess model performance using

the area under the receiver operating characteristic curve (ROC AUC). We computed 90% CIs for the ROC AUC scores from 2000 bootstrap samples, by taking the 5th and 95th percentiles of the bootstrap distribution. Stratification with respect to clinical status was performed to preserve the proportion of healthy controls, presymptomatic subjects and patients in each fold.

Generalisation analysis

Since the differentially expressed miRNAs were computed with the entire data set, the test folds of the cross-validation were also used in the feature selection for our classification models, which could inflate prediction performance. To estimate this possible bias, we then incorporated feature selection in the nested 5-fold cross-validation process: differentially expressed miRNAs were computed using only the outer cross-validation loop training data (four out of five folds) at each iteration. The nested cross-validation was repeated 100 times with different fold splits to assess the generalisation performance of our classifiers.

Analysis of the transitional stage to clinical FTD/ALS disease

Since we hypothesised that the expression levels of differentially expressed miRNAs might provide information relevant to *C9orf72* disease progression, we designed an experiment to evaluate prediction performance of clinical conversion to FTD/ALS in presymptomatic carriers. A logistic regression classifier was fitted with the expression levels of differentially expressed miRNAs from controls and patients. We used a regular 5-fold cross-validation to determine the optimal hyperparameter (L2 regularisation coefficient). Subsequently, this model was tested with the expression levels from the four known presymptomatic carriers who were in their transitional stage to the clinical disease. Scores from 0 to 1 were provided for each subject, indicating proximity with the expression levels of controls (scores near 0) or patients (scores closer to 1).

Target prediction and pathway analysis

A target-gene based miRNA enrichment analysis was performed, to discover potential biological functions regulated by the differentially expressed miRNAs. We used the publicly available tool DIANA-miRPath V.3,³¹ which implements an in silico miRNA target prediction algorithm (DIANA-microT-CDS) as well as an experimentally validated miRNA:gene interaction dataset (DIANA-TarBase V.7.0). Both approaches were carried out to identify target genes and the associated Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways, using the set of differentially expressed miRNAs as input. The enrichment analysis method consisted of Fisher's exact test (hypergeometric distribution) with Benjamini-Hochberg adjusted p value threshold of 0.05, giving as output a union set of associated KEGG pathways.

RESULTS

Differentially expressed miRNAs computed with the entire data set

Table 2 displays all miRNAs identified as differentially expressed, for each pairwise comparison between clinical status, after correction for multiple comparisons. Four miRNAs were computed as differentially expressed between healthy controls and patients: miR-34a-5p and miR-345-5p were overexpressed, while miR-200c-3p and miR-10a-3p were underexpressed in symptomatic mutation carriers. Interestingly, miR-34a-5p was identified as significantly overexpressed also in presymptomatic mutation carriers compared with healthy controls, suggesting that miR-34a-5p expression is associated with *C9orf72* mutation

Table 2 Differentially expressed miRNAs identified by EdgeR, after correction for multiple comparisons, for each pairwise comparison between clinical status: Control (n=43), presymptomatic (n=45) and patient (n=22)

miRNA	Log-fold change	P value	Adjusted p value
Control vs presymptomatic			
miR-34a-5p	-1.433	5.251e-16	3.093e-13
Control vs patient			
miR-34a-5p	-1.239	1.650e-8	9.720e-6
miR-345-5p	-0.540	1.131e-5	3.330e-3
miR-200c-3p	0.333	3.109e-5	6.104e-3
miR-10a-3p	0.697	7.141e-5	1.051e-2
Presymptomatic vs patient			
miR-345-5p	-0.528	3.610e-5	2.126e-2

miRNA, microRNA.

status. Additionally, miR-345-5p was also significantly overexpressed in patients when compared with presymptomatic carriers. When removing the four prodromal subjects from the presymptomatic group, the same miRNAs were identified as differentially expressed, indicating that the differences between the presymptomatic and other groups were not mainly driven by the four prodromal subjects.

We considered these four miRNAs (miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p) as our miRNA signature for further analyses. The complete output from EdgeR is available in online supplemental table A2.

Figure 1 displays boxplots with the expression levels, for each clinical group, of the four miRNAs identified as differentially expressed. There is a clear difference in miR-34a-5p expression levels between controls and *C9orf72* expansion carriers (presymptomatic and symptomatic). Moreover, the other three identified miRNAs differentiate the mutation carriers at different stages of the pathology: miR-345-5p showed increased expression in patients, while miR-200c-3p and miR-10a-3p exhibited decreased expression. An expression heatmap of the miRNA signature is displayed in online supplemental figure A2.

MiRNA signature to classify between clinical groups

To assess whether the identified miRNA signature could distinguish between clinical groups, we implemented logistic regression models using as features the expression levels of the four differentially expressed miRNAs (miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p). The ROC AUC for the classification of healthy controls and presymptomatic mutation carriers was 0.90 (90% CI 0.83 to 0.95), for controls and patients was 0.90 (90% CI 0.82 to 0.97) and to distinguish presymptomatic carriers and patients was 0.80 (90% CI 0.67 to 0.90) (figure 2). The distributions of the bootstrapped ROC AUC scores are displayed in online supplemental figure A3.

Generalisation analysis

Since we used the entire data set to identify the miRNA signature, including test data, classification performance could be inflated. In order to assess the generality of our classification scores, we then incorporated feature selection in the nested cross-validation scheme (online supplemental figure A1), by using only the training data from the outer cross-validation loop to compute differentially expressed miRNAs. Figure 3 shows the distribution of miRNAs identified as differentially expressed after performing nested 5-fold cross-validation with 100 different

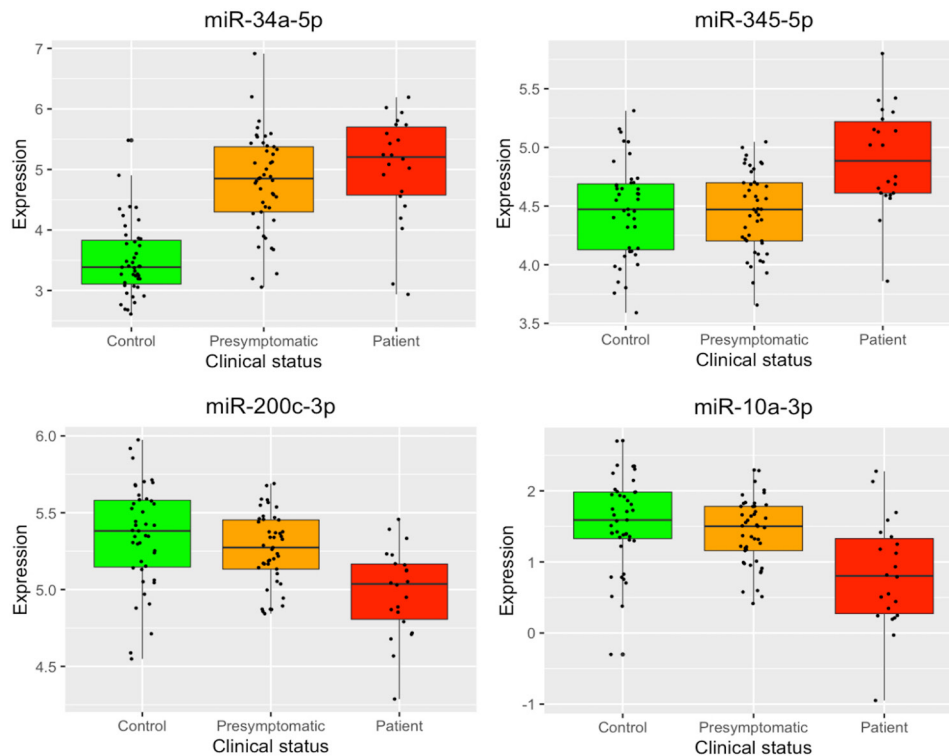


Figure 1 Boxplots depicting the normalised log₂ expression levels of the four microRNAs identified as differentially expressed. Box boundaries represent the first and third quartiles and the median is indicated by the line dividing the IQR. The upper whiskers extend to the values that are within 1.5×IQR over the third quartiles. The lower whiskers extend to the values that are within 1.5×IQR under the first quartiles.

fold splits. Notably, the most frequent miRNAs (highlighted in blue) correspond to the ones computed using the entire data set: miR-34a-5p (500 occurrences) when comparing healthy controls and presymptomatic mutation carriers; miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p (respectively 497, 335, 259 and 196 occurrences) for controls and patients; miR-345-5p (157 occurrences) when analysing presymptomatic subjects and patients.

Regarding prediction performance, the average ROC AUC when classifying controls versus presymptomatic subjects was 0.88 (90% CI 0.83 to 0.91), for controls versus patients was 0.89 (90% CI 0.83 to 0.94) and for presymptomatic individuals versus patients was 0.67 (90% CI 0.52 to 0.77). The distributions of the ROC AUC scores computed with 100 different fold splits are displayed in online supplemental figure A4.

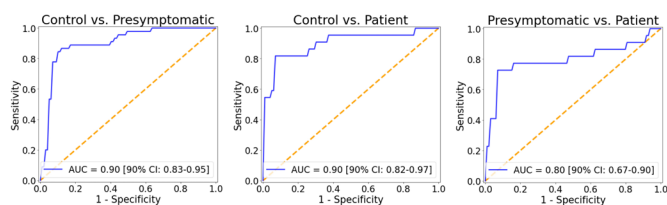


Figure 2 ROC (receiver operating characteristic) curves for each pairwise classification (control vs presymptomatic, control vs patient and presymptomatic vs patient) obtained with logistic regression using as features the expression levels of the microRNAs signature (miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p). Bootstrapped 90% CIs are reported in brackets. AUC, area under the ROC curve.

Analysis of the transitional stage to clinical FTD/ALS disease

We evaluated the performance to predict the transitional stage to FTD/ALS disease by training a logistic regression classifier with the expression levels from patients and controls and testing with the expression levels of presymptomatic individuals. The probability scores computed for the four subjects in their transitional stage were all above 0.50, indicating a stronger similarity with patients: 0.54, 0.75, 0.80 and 0.82. The distribution of probability scores for all presymptomatic subjects is displayed in online supplemental figure A5.

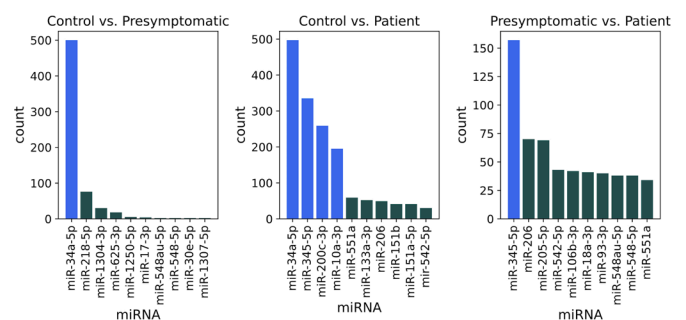


Figure 3 Number of times each miRNA was found differentially expressed, when performing a repeated 5-fold nested cross-validation for 100 times with different fold splits. In each step of the outer cross-validation loop, four of the five folds were used to identify differentially expressed miRNAs. Since one outer loop consists of five steps, and we performed 100 repetitions, 500 sets of miRNAs were computed for each pairwise comparison between groups, respectively: control vs presymptomatic, control vs patient and presymptomatic vs patient. MiRNAs from the signature computed with the entire data set are highlighted. miRNA, microRNA.

Table 3 Results from pathway analysis using the four differentially expressed microRNAs as input

Category	KEGG pathway	P value microT-CDS	P value TarBase
Cancer	Proteoglycans in cancer	7.941e-4	4.259e-8
	MicroRNAs in cancer	1.386e-3	3.356e-8
	Glioma	6.554e-2	1.423e-2
	Renal cell carcinoma	1.098e-2	9.254e-2
	Small cell lung cancer	3.220e-1	3.341e-2
Cell signalling/apoptosis	Hippo signalling pathway	4.556e-2	5.622e-4
	TGF-beta signalling pathway	5.008e-2	9.288e-4
	Thyroid hormone signalling pathway	2.132e-3	1.502e-2
	FoxO signalling pathway	2.368e-1	1.449e-2
	Neurotrophin signalling pathway	9.801e-3	3.113e-1
Intermediary metabolism	Lysine degradation	1.606e-2	7.882e-4
	Glycosphingolipid biosynthesis - lacto and neolacto series	3.885e-10	4.423e-2
Meiosis	Oocyte meiosis	2.487e-1	2.446e-3

Only significant pathways for at least one approach are shown. Statistically significant p values are in bold. KEGG, Kyoto Encyclopedia of Genes and Genomes.

Target prediction and pathway analysis

Using the four differentially expressed miRNAs (miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p) as input, we performed target prediction and pathway analysis with two methods available in DIANA-miRPath V.3. The in silico miRNA target prediction algorithm (microT-CDS) identified 31 influenced pathways (14 significant after Benjamini-Hochberg correction), while the experimentally supported approach (TarBase) resulted in 54 associated pathways (38 significant after Benjamini-Hochberg correction). Complete outputs concerning the list of the putative target genes and their related pathways are given in online supplemental tables A3 and A4. Table 3 reports the 13 pathways that were identified by both methods and have significant adjusted p values in at least one of them.

Online supplemental figure A6 shows miRNA versus KEGG pathways heatmaps, which depict the level of enrichment in significant KEGG pathways for the four differentially expressed miRNAs as computed by the two approaches.

DISCUSSION

The present study aimed to identify fluid biomarkers by analysing expression levels of plasma miRNAs without a priori knowledge in a large cohort of healthy controls, presymptomatic and symptomatic *C9orf72* carriers. We identified four miRNAs differentially expressed between clinical conditions: miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p. Significantly higher expression of miR-34a-5p was found in mutation carriers when compared with healthy controls, which suggests that miR-34a-5p expression is deregulated in cases with *C9orf72* mutation. Additionally, we observed miR-345-5p expression to be significantly increased in patients when compared with presymptomatic carriers, which supports the correlation of miR-345-5p expression with the progression of *C9orf72*-associated disease. Finally, our results also suggest that miR-200c-3p and miR-10a-3p underexpression might be associated with full-blown disease as decreased expression levels were significant only between patients and healthy controls.

We used the expression levels of the miRNA signature to train logistic regression classifiers, which were able to differentiate individuals from different clinical groups with good predictive performance (figure 2). Notably, presymptomatic and symptomatic *C9orf72* carriers were distinguished with ROC AUC of 0.80 (90% CI 0.67 to 0.90), which suggests the suitability of plasma

miRNAs for following preclinical progression and determining disease onset. We believe that this score was lower in our generalisation analysis (0.67, 90% CI 0.52 to 0.77) because the limited number of patients (22) led to a higher variability in the differentially expressed miRNAs in each step of the cross-validation loop (figure 3). Furthermore, we have obtained promising results regarding prediction performance of conversion from the presymptomatic to the clinical stage of FTD/ALS. The four presymptomatic subjects in transitional stage exhibited scores above 0.50, denoting a stronger similarity with the expression levels of patients. Although preliminary, these results suggest that the expression levels of our miRNA signature might be used as early predictors of the *C9orf72* disease conversion.

Previous studies have shown the potential of miRNAs in serum, plasma or CSF as diagnostic biomarkers for FTD and ALS,^{9 17-20} focussing on comparing healthy controls and patients. However, our findings differ from preceding results: only two miRNAs from our signature (miR-345-5p and miR-200c-3p) were identified as differentially expressed in one of these studies,²⁰ none in the others.¹⁷⁻¹⁹ Results are conflicting probably due to restricted choices for the analysed miRNAs^{17 18} and heterogeneous cohorts, either with sporadic forms^{18 19} or a mixture of sporadic and familial forms with different mutations.²⁰ To the best of our knowledge, the present work is the first to compare the expression levels of plasma miRNAs between presymptomatic and symptomatic carriers focussing on *C9orf72* mutation, in addition to providing a plasma miRNA signature that may contribute to the assessment of preclinical progression for *C9orf72*-associated FTD and ALS. Table 4 displays a comparison among studies evaluating miRNAs from blood samples (serum or plasma) of patients with FTD and/or ALS.

Overall, our work suggests that miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p are likely involved in neuronal degeneration and *C9orf72*-associated pathogenesis. Among the KEGG pathways identified in this study, some involved in neurodevelopment (Hippo signalling and FoxO signalling), inflammation (TGF-beta signalling), intracellular transduction (neurotrophin signalling) and apoptosis (TGF-beta and FoxO signalling) were relevant as previously shown to be involved in *C9orf72*-disease.³²⁻³⁴ Accordingly, these four miRNAs have been previously linked with a range of neurodevelopmental processes, neuropsychiatric and neurodegenerative conditions.³⁵⁻³⁸ For instance, miR-200c and miR-34a family members are implicated

Table 4 Comparison of studies investigating miRNAs from blood samples (serum or plasma) of patients with FTD and/or ALS

	Freischmidt <i>et al</i> 2014* ¹¹	Sheinerman <i>et al</i> 2017† ¹⁷	Piscopo <i>et al</i> 2018† ¹⁸	Grasso <i>et al</i> 2019† ¹⁹	Magen <i>et al</i> 2020† ²⁰	This study†
Disease	ALS	FTD, ALS	FTD	FTD	FTD, ALS	FTD, ALS
Cohort	Separate sporadic/genetic‡	Not mentioned	Sporadic	Sporadic	Mixed sporadic/genetic§	<i>C9orf72</i>
Patients, n=	9/13 genetic	50 FTD	54	10/48	52/117 FTD	22
Discovery/replication	14 sporadic	50 ALS			115 ALS	
Presymptomatic carriers, n=	18	–	–	–	–	45
Methods of analysis	Microarrays	37 selected miRNAs (qRT-PCR)	9 selected miRNAs (qRT-PCR)	752 selected miRNAs (qRT-PCR)	Large scale sequencing (RNA-seq)	Large scale sequencing (RNA-seq)
Major deregulated miRNAs	miR-4745-5p miR-3665 miR-1915-3p miR-4530 (validated from panel of 30 miRNAs)	miR-9/let-7e, miR-7/miR-451, miR335-5p/let-5e (FTD) miR-206/miR-338-3p, miR-9/miR-129-3p, miR-335-5p/miR-338-3p (ALS)	miR-127-3p	miR-663a miR-502-3p miR-206	Panels of 20, 147, 121 miRNAs for each cohort	miR-34a-5p miR-345-5p miR-200c-3p miR-10a-3p

*in serum.

†in plasma.

‡*SOD1, FUS, C9orf72, PFN1*.§*C9orf72, MAPT, GRN, TBK1*.

ALS, amyotrophic lateral sclerosis; FTD, frontotemporal dementia; miRNA, microRNA; qRT-PCR, quantitative real-time PCR; RNA-seq, RNA sequencing.

in synaptic function, neuronal maturation, differentiation and survival.^{39,40} Aberrant expression of miR-34a and miR-345 are also associated with neuronal apoptosis,⁴¹ whereas members of miR-10a family were found to be differentially expressed in the muscle tissue of patients with ALS.⁴²

How these four miRNAs are implicated in *C9orf72*-associated pathogenesis, and their relevance in brain pathology are important questions to go further. So far, only few studies addressing miRNA dysregulation in brain tissues of patients with FTD/ALS have been performed, and are summarised in online supplemental table A5. They specifically addressed *GRN*-associated,^{43,44} sporadic FTD,^{45,46} sporadic⁴⁷ or mixed genetic-sporadic ALS patients.⁴⁸ Notably, there was no miRNA dysregulation in common between the aforementioned studies, nor between any of those studies on the brain and ours on plasma. Those discrepancies may stem from the heterogeneity of the previous autoptic cohorts and the differences in the methods of miRNA expression analysis. Noteworthy, and differently from our investigation, none of the patient cohorts mentioned in online supplemental table A5 were exclusively made up of *C9orf72* carriers. Additionally, the observed differences between brain tissue and plasma miRNA profiles may be due to the tissue-specific expression of miRNA on the one hand, and to the time-dependent variations of detectable miRNAs all along the disease course on the other. Due to the disease process itself and other potential confounding factors, significant changes in miRNA expression are likely to occur between a relatively early phase of the disease, in which plasma miRNAs may be used as biomarkers, and the ultimate disease stage, at the moment of brain sampling. At this point, further miRNA profiling studies on *C9orf72* brain tissue are needed to better understand whether tissue miRNAs correlate with plasma expression profiles and their contribution to the disease pathogenesis.

Regardless, it is noteworthy that some studies pointed towards a direct relationship between these miRNAs and *C9orf72* pathogenesis. *C9orf72* stands as a putative target of miR-34a-5p, likely acting as a negative regulator of *C9orf72* mRNA expression.⁴⁹

Additionally, miR-200c-3p and miR-345-5p are down-regulated and up-regulated, respectively, in the extracellular vesicles secreted by induced astrocytes obtained from *C9orf72* patients.⁵⁰ Even if not completely explained so far, these important results parallel our study showing a comparable upregulation of miR-34a-5p and miR-345-5p and downregulation of miR-200c-3p in carriers, and provide converging evidence for a link between our set of miRNAs and *C9orf72*-pathogenesis, which will need further investigations.

Previous studies have provided the proof-of-concept that specific sets of miRNAs have the potential to serve as biomarkers of the preclinical/premanifest stages of other neurodegenerative diseases, such as ALS,¹¹ Huntington³⁹ and Prion diseases.⁵¹ Our study supports the usefulness of our four miRNAs as biomarkers of disease progression from the presymptomatic to the symptomatic phase of *C9orf72* disease. Nevertheless, some of them may be dysregulated in a broader range of neurodegenerative conditions. For instance, miR-345 and miR-200c-3p were also dysregulated during the presymptomatic stage of Prion⁵¹ and Huntington's diseases,³⁹ respectively. This would not prevent, however, their use in longitudinal monitoring of specific genetic neurodegenerative disorders, possibly in combination with other biomarkers. Together, all these studies and ours suggest that dysregulation of such miRNAs is dynamically altered throughout neurodegenerative diseases progression, and can be detectable even long before clinical onset.

The current study has limitations. First, the significant age difference between patients and the other clinical groups may have introduced a confounding factor, which we considered by including age as a covariate. Second, the absence of validation in other tissues or of a replication cohort means that further studies in independent cohorts are required to confirm our results, even though our generalisation analysis confirmed the identified miRNA signature. Finally, the limited number of patients does not allow any conclusions about the correlation of plasma miRNAs and different disease phenotypes. Future work will explore longitudinal analyses of plasma miRNAs to assess their use as biomarkers of FTD and ALS progression.

In summary, the current work revealed significant differences in miRNA expression levels in plasma when comparing healthy controls, presymptomatic and symptomatic *C9orf72* mutation carriers. Specifically, we highlighted the potential of miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p expression levels in plasma as biomarkers of preclinical progression for *C9orf72*-associated FTD and ALS. Our results encourage the use of plasma miRNAs, possibly in combination with other markers, to improve the design of clinical trials for these neurodegenerative disorders.

Author affiliations

- ¹Inria, Aramis project-team, F-75013, Paris, France
²Sorbonne Université, Paris Brain Institute – Institut du Cerveau – ICM, Inserm U1127, CNRS UMR 7225, AP-HP - Hôpital Pitié-Salpêtrière, Paris, France
³Centre de référence des démences rares ou précoces, IM2A, Département de Neurologie, AP-HP - Hôpital Pitié-Salpêtrière, Paris, France
⁴Département de Neurologie, AP-HP - Hôpital Pitié-Salpêtrière, Paris, France
⁵EPHE, PSL Research University, Paris, France
⁶CMRR Service de Neurologie, CHU de Limoges, Limoges, France
⁷Normandie Univ, UNIROUEN, Inserm U1245 and Rouen University Hospital, Department of Neurology and CNR-MAJ, Normandy Center for Genomic and Personalized Medicine, Rouen, France
⁸Univ Lille, CHU, Inserm U1172, DISTALZ, LICEND, Lille, France
⁹GenoSplice, Paris, France
¹⁰Paris Brain Institute – Institut du Cerveau – ICM, FrontLab, Paris, France
¹¹Univ Rennes, Inria, CNRS, IRISA, F-35000 Rennes, France

Twitter Emmanuelle Becker @EmmanuelleBeck4

Acknowledgements We thank Justine Guégan, from iCONICS (ICM bioinformatics facility) for microRNA raw reads to counts pipeline handling. We also thank Yannick Marie and Delphine Bouteiller, from iGenSeq (ICM sequencing facility), for library preparation and sequencing. We thank the DNA and cell bank of the ICM for the technical assistance, notably Philippe Martin-Hardy (DNA and cell bank, ICM). The study was conducted with the support of the Centre d'Investigation Clinique Neurosciences (CIC 1422), GH Pitié Salpêtrière, Paris, and the Centre pour l'Acquisition et le Traitement des Images platform.

Collaborators The PREV-DEMALS study group includes: Eve Benchetrit (Hôpital de la Salpêtrière, Paris), Anne Bertrand (Hôpital de la Salpêtrière, Paris), Anne Bissery (Hôpital de la Salpêtrière, Paris), Marie-Paule Boncoeur (CHU Dypuytren, Limoges), Stéphanie Bombois (CHU Roger Salengro, Lille), Agnès Camuzat (ICM, Paris), Mathieu Chastan (CHU Charles Nicolle, Rouen), Yaohua Chen (CHU Roger Salengro, Lille), Marie Chupin (ICM, Paris), Olivier Colliot (ICM, Paris), Philippe Courtatier (CHU Dypuytren, Limoges), Xavier Delbeuck (CHU Roger Salengro, Lille), Vincent Deramecourt (CHU Roger Salengro, Lille), Christine Delmaire (CHU Roger Salengro, Lille), Emmanuel Gerardin (CHU Charles Nicolle, Rouen), Claude Hossein-Foucher (CHU Roger Salengro, Lille), Bruno Dubois (Hôpital de la Salpêtrière, Paris), Marie-Odile Habert (Hôpital de la Salpêtrière, Paris), Didier Hannequin (CHU Charles Nicolle, Rouen), Géraldine Lautrette (CHU Dypuytren, Limoges), Thibaud Lebouvier (CHU Roger Salengro, Lille), Isabelle Le Ber (Hôpital de la Salpêtrière, Paris), Benjamin Le Toulec (ICM, Paris), Richard Levy (Hôpital de la Salpêtrière, Paris), Olivier Martinaud (CHU Charles Nicolle, Rouen), Kelly Martineau (ICM, Paris), Marie-Anne Mackowiak (CHU Roger Salengro, Lille), Jacques Monteil (CHU Dypuytren, Limoges), Florence Pasquier (CHU Roger Salengro, Lille), Gregory Petyt (CHU Roger Salengro, Lille), Pierre-François Pradat (Hôpital de la Salpêtrière, Paris), Assi-Hervé Oya (Hôpital de la Salpêtrière, Paris), Armelle Rametti-Lacroux (Hôpital de la Salpêtrière, Paris), Daisy Rinaldi (Hôpital de la Salpêtrière, Paris), Adeline Rollin-Sillaire (CHU Roger Salengro, Lille), François Salachas (Hôpital de la Salpêtrière, Paris), Sabrina Sayah (Hôpital de la Salpêtrière, Paris), David Wallon (CHU Charles Nicolle, Rouen).

Contributors VK had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concepts and study design: VK, VA, DS, ILB, OC and EB. Acquisition, analysis or interpretation of data: All authors. Manuscript drafting or manuscript revision for important intellectual content: All authors. Approval of final version of submitted manuscript: All authors. Literature research: VK, VA, DS and ILB. Statistical analysis: VK. Obtained funding: ILB and OC. Administrative, technical or material support: ILB, OC and EB. Study supervision: ILB, OC and EB.

Funding The research leading to these results has received funding from the programme 'Investissements d'avenir' ANR-10-IAIHU-06, from the French government under management of Agence Nationale de la Recherche as part of the 'Investissements d'avenir' programme, reference ANR-19-P3IA-0001 (PRAIRIE 3IA Institute), from Agence Nationale de la Recherche/DGOS (project ANR-PRTS PREV-DEMALS, grant number ANR-14-CE15-0016-07, promotion Assistance Publique-

Hopitaux de Paris), from the Inria Project Lab Program (project Neuromarkers), from Fondation Vaincre Alzheimer FR-17035 and from the Institut Français de Bioinformatique (ANR-11-INSB-0013).

Competing interests OC reports having received consulting fees from AskBio (2020), having received fees for writing a lay audience short paper from Expression Santé (2019), having received speaker fees for a lay audience presentation from Palais de la découverte (2017) and that his laboratory has received grants from Qynapse (2017-present). Members from his laboratory have co-supervised a PhD thesis with myBrainTechnologies (2016-present). OC's spouse is an employee of myBrainTechnologies (2015-present). OC has submitted a patent to the International Bureau of the World Intellectual Property Organization (PCT/IB2016/0526993, Schiratti J-B, Allassonniere S, Colliot O, Durrleman S, A method for determining the temporal progression of a biological phenomenon and associated methods and devices) (2016). ILB served as a member of advisory boards for Prevail Therapeutic and received research grants from ANR, DGOS, PHRC, Vaincre Alzheimer Association, ARSla Association, Fondation Plan Alzheimer outside of the present work. PG is co-founder and director of GenoSplice. NR is employee at GenoSplice.

Patient consent for publication Not required.

Ethics approval This study was approved by the Comité de Protection des Personnes CPP Ile-De-France VI (CPP 68-15 and ID RCB 2015-A00856-43).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request (isabelle.leber@upmc.fr).

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Virgilio Kmetzsch <http://orcid.org/0000-0003-3691-0180>

REFERENCES

- Rascovsky K, Hodges JR, Knopman D, *et al.* Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain* 2011;134:2456–77.
- Mackenzie IR, Rademakers R, Neumann M. Tdp-43 and FUS in amyotrophic lateral sclerosis and frontotemporal dementia. *Lancet Neurol* 2010;9:995–1007.
- DeJesus-Hernandez M, Mackenzie IR, Boeve BF, *et al.* Expanded GGGGCC hexanucleotide repeat in noncoding region of *C9orf72* causes chromosome 9p-linked FTD and ALS. *Neuron* 2011;72:245–56.
- Renton AE, Majounie E, Waite A, *et al.* A hexanucleotide repeat expansion in *C9orf72* is the cause of chromosome 9p21-linked ALS-FTD. *Neuron* 2011;72:257–68.
- Mackenzie IRA, Frick P, Neumann M. The neuropathology associated with repeat expansions in the *C9orf72* gene. *Acta Neuropathol* 2014;127:347–57.
- Bertrand A, Wen J, Rinaldi D, *et al.* Early Cognitive, Structural, and Microstructural Changes in Presymptomatic *C9orf72* Carriers Younger Than 40 Years. *JAMA Neurol* 2018;75:236–45.
- Eisen A, Kiernan M, Mitsumoto H, *et al.* Amyotrophic lateral sclerosis: a long preclinical period? *J Neurol Neurosurg Psychiatry* 2014;85:1232–8.
- Grasso M, Piscopo P, Confaloni A, *et al.* Circulating miRNAs as biomarkers for neurodegenerative disorders. *Molecules* 2014;19:6891–910.
- Schneider R, McKeever P, Kim T, *et al.* Downregulation of exosomal miR-204-5p and miR-632 as a biomarker for FTD: a GENFI study. *J Neurol Neurosurg Psychiatry* 2018;89:851–8.
- Denk J, Oberhauser F, Kornhuber J, *et al.* Specific serum and CSF microRNA profiles distinguish sporadic behavioural variant of frontotemporal dementia compared with Alzheimer patients and cognitively healthy controls. *PLoS One* 2018;13:e0197329.
- Freischmidt A, Müller K, Zondler L, *et al.* Serum microRNAs in patients with genetic amyotrophic lateral sclerosis and pre-manifest mutation carriers. *Brain* 2014;137:2938–50.
- Huntzinger E, Izaurralde E. Gene silencing by microRNAs: contributions of translational repression and mRNA decay. *Nat Rev Genet* 2011;12:99–110.
- Buratti E, Baralle FE. The multiple roles of TDP-43 in pre-mRNA processing and gene expression regulation. *RNA Biol* 2010;7:420–9.

- 14 Gascon E, Gao F-B. The emerging roles of microRNAs in the pathogenesis of frontotemporal dementia-amyotrophic lateral sclerosis (FTD-ALS) spectrum disorders. *J Neurogenet* 2014;28:30–40.
- 15 Li L, Wang J. Roles of extracellular microRNAs in central nervous system. *ExRNA* 2019;1:13.
- 16 Sohel MH. Extracellular/Circulating microRNAs: release mechanisms, functions and challenges. *Achiev Life Sci* 2016;10:175–86.
- 17 Sheinerman KS, Toledo JB, Tsivinsky VG, et al. Circulating brain-enriched microRNAs as novel biomarkers for detection and differentiation of neurodegenerative diseases. *Alzheimers Res Ther* 2017;9:89.
- 18 Piscopo P, Grasso M, Puopolo M, et al. Circulating miR-127-3p as a potential biomarker for differential diagnosis in frontotemporal dementia. *J Alzheimers Dis* 2018;65:455–64.
- 19 Grasso M, Piscopo P, Talarico G, et al. Plasma microRNA profiling distinguishes patients with frontotemporal dementia from healthy subjects. *Neurobiol Aging* 2019;84:240.e1–240.e12.
- 20 Magen I, Yacovzada N, Warren JD, et al. Classification and prediction of frontotemporal dementia based on plasma microRNAs. *medRxiv* 2020:2020.01.22.20018408.
- 21 Montembeault M, Sayah S, Rinaldi D, et al. Cognitive inhibition impairments in presymptomatic C9orf72 carriers. *J Neurol Neurosurg Psychiatry* 2020;91:366–72.
- 22 Smith T, Heger A, Sudbery I. UMI-tools: modeling sequencing errors in unique molecular identifiers to improve quantification accuracy. *Genome Res* 2017;27:491–9.
- 23 Martin M. Cutadapt removes adapter sequences from high-throughput sequencing reads. *EMBnet J* 2011;17:10–12.
- 24 Langmead B, Trapnell C, Pop M, et al. Ultrafast and memory-efficient alignment of short DNA sequences to the human genome. *Genome Biol* 2009;10:R25.
- 25 Li H, Handsaker B, Wysoker A, et al. The sequence Alignment/Map format and SAMtools. *Bioinformatics* 2009;25:2078–9.
- 26 Liao Y, Smyth GK, Shi W. featureCounts: an efficient General purpose program for assigning sequence reads to genomic features. *Bioinformatics* 2014;30:923–30.
- 27 Friedländer MR, Mackowiak SD, Li N, et al. miRDeep2 accurately identifies known and hundreds of novel microRNA genes in seven animal clades. *Nucleic Acids Res* 2012;40:37–52.
- 28 Robinson MD, McCarthy DJ, Smyth GK. edgeR: a Bioconductor package for differential expression analysis of digital gene expression data. *Bioinformatics* 2010;26:139–40.
- 29 Robinson MD, Oshlack A. A scaling normalization method for differential expression analysis of RNA-Seq data. *Genome Biol* 2010;11:R25.
- 30 Pedregosa F, Varoquaux G, Gramfort A, et al. Scikit-learn: machine learning in python. *J Mach Learn Res* 2011;12:2825–30.
- 31 Vlachos IS, Zagganas K, Paraskevopoulou MD, et al. DIANA-miRPath v3.0: deciphering microRNA function with experimental support. *Nucleic Acids Res* 2015;43:W460–6.
- 32 Atkinson RAK, Fernandez-Martos CM, Atkin JD, et al. C9orf72 expression and cellular localization over mouse development. *Acta Neuropathol Commun* 2015;3:59.
- 33 Farg MA, Konopka A, Soo KY, et al. The DNA damage response (DDR) is induced by the C9orf72 repeat expansion in amyotrophic lateral sclerosis. *Hum Mol Genet* 2017;26:2882–96.
- 34 Burberry A, Wells MF, Limone F, et al. C9orf72 suppresses systemic and neural inflammation induced by gut bacteria. *Nature* 2020;582:89–94.
- 35 Fu J, Peng L, Tao T, et al. Regulatory roles of the miR-200 family in neurodegenerative diseases. *Biomed Pharmacother* 2019;119:109409.
- 36 Chua CEL, Tang BL. miR-34A in neurophysiology and neuropathology. *J Mol Neurosci* 2019;67:235–46.
- 37 Cosín-Tomás M, Antonell A, Lladó A, et al. Plasma miR-34a-5p and miR-545-3p as Early Biomarkers of Alzheimer's Disease: Potential and Limitations. *Mol Neurobiol* 2017;54:5550–62.
- 38 van den Berg MMJ, Krauskopf J, Ramaekers JG, et al. Circulating microRNAs as potential biomarkers for psychiatric and neurodegenerative disorders. *Prog Neurobiol* 2020;185:101732.
- 39 Jin J, Cheng Y, Zhang Y, et al. Interrogation of brain miRNA and mRNA expression profiles reveals a molecular regulatory network that is perturbed by mutant huntingtin. *J Neurochem* 2012;123:477–90.
- 40 Jauhari A, Singh T, Singh P, et al. Regulation of miR-34 family in neuronal development. *Mol Neurobiol* 2018;55:936–45.
- 41 Modi PK, Jaiswal S, Sharma P. Regulation of neuronal cell cycle and apoptosis by microRNA 34a. *Mol Cell Biol* 2016;36:84–94.
- 42 Kovanda A, Leonardis L, Zidar J, et al. Differential expression of microRNAs and other small RNAs in muscle tissue of patients with ALS and healthy age-matched controls. *Sci Rep* 2018;8:5609.
- 43 Kocerha J, Kouri N, Baker M, et al. Altered microRNA expression in frontotemporal lobar degeneration with TDP-43 pathology caused by progranulin mutations. *BMC Genomics* 2011;12:527.
- 44 Chen-Plotkin AS, Unger TL, Gallagher MD, et al. Tmem106B, the risk gene for frontotemporal dementia, is regulated by the microRNA-132/212 cluster and affects progranulin pathways. *J Neurosci* 2012;32:11213–27.
- 45 Hébert SS, Wang W-X, Zhu Q, et al. A study of small RNAs from cerebral neocortex of pathology-verified Alzheimer's disease, dementia with Lewy bodies, hippocampal sclerosis, frontotemporal lobar dementia, and non-demented human controls. *J Alzheimers Dis* 2013;35:335–48.
- 46 Gascon E, Lynch K, Ruan H, et al. Alterations in microRNA-124 and AMPA receptors contribute to social behavioral deficits in frontotemporal dementia. *Nat Med* 2014;20:1444–51.
- 47 Jawaid A, Woldemichael BT, Kremer EA, et al. Memory decline and its reversal in aging and neurodegeneration involve miR-183/96/182 biogenesis. *Mol Neurobiol* 2019;56:3451–62.
- 48 Helfferich AM, Brockmann SJ, Reinders J, et al. Dysregulation of a novel miR-1825/TBCB/TUBA4A pathway in sporadic and familial ALS. *Cell Mol Life Sci* 2018;75:4301–19.
- 49 Lal A, Thomas MP, Altschuler G, et al. Capture of microRNA-bound mRNAs identifies the tumor suppressor miR-34a as a regulator of growth factor signaling. *PLoS Genet* 2011;7:e1002363.
- 50 Varianna A, Myszczyńska MA, Castelli LM, et al. Micro-Rnas secreted through astrocyte-derived extracellular vesicles cause neuronal network degeneration in C9orf72 ALS. *EBioMedicine* 2019;40:626–35.
- 51 Boese AS, Saba R, Campbell K, et al. MicroRNA abundance is altered in synaptoneuroosomes during prion disease. *Mol Cell Neurosci* 2016;71:13–24.

SUPPLEMENTARY MATERIAL

Appendix A1: Neuropsychological protocol.

Appendix A2: Description of the four cases at the transitional stage.

Table A1: Clinical status and center proportion in each batch.

Table A2: Complete output from EdgeR.

Table A3: List of the putative target genes.

Table A4: Complete output from DIANA-miRPath v.3.

Table A5: Comparison of studies investigating miRNAs from brain samples.

Figure A1: Stratified nested cross-validation.

Figure A2: Expression heatmap of miRNA signature.

Figure A3: Bootstrapped ROC AUC scores.

Figure A4: ROC AUC scores with 100 different fold splits.

Figure A5: Presymptomatic subjects probability scores.

Figure A6: Heatmap of the level of enrichment in KEGG pathways.

Appendix A1. Neuropsychological protocol

The PREV-DEMALS cognitive evaluation included standardized neuropsychological tests to investigate all cognitive domains, and in particular frontal lobe functions. The scores were provided previously (Bertrand et al., 2018).

Briefly, global cognitive efficiency was evaluated by means of Mini-Mental State Examination (MMSE) and Mattis Dementia Rating Scale (MDRS). Frontal executive functions were assessed with Frontal Assessment Battery (FAB), forward and backward digit spans, Trail Making Test part A and B (TMT-A and TMT-B), Wisconsin Card Sorting Test (WCST), and Symbol-Digit Modalities test. Hayling Sentence Completion Test was used to assess cognitive inhibition. Ekman faces test and Faux-pas test evaluated emotional assessment and social cognition.

Episodic verbal memory was assessed with the Free and Cued Selective Reminding Test (FCSRT), whereas visual memory with the Benson figure recall and identification test. Boston Naming Test (BNT), phonological and semantic fluencies, and Camel & Cactus test were used to evaluate language skills. Visuospatial abilities were assessed by means of Benson figure copy and the cube analysis task from the Visual Object and Space Perception (VOSP) battery. Limb-kinetic and ideo-motor apraxias were evaluated using a French validated scale.

Appendix A2. Description of the four cases at the transitional stage

Four *C9orf72* presymptomatic carriers have developed frontal cognitive and/or behavioral changes and/or subtle motor signs/symptoms during a 3-year follow-up period, without fitting diagnostic criteria for FTD or ALS, suggesting they were in the transitional ‘prodromal’ phase at the moment of or just after their baseline visit. They are described below.

The case 1 was a right-handed 42-year-old female with 13 years of schooling. Neurological examination, behavioral scores (FBI: 0; AES 9/42), and cognitive scores were normal (MDRS 138/144; FAB 18/18; WCST 20/20; forward/backward digit spans: 7/4), except for isolated moderate decrease of the faux-pas test score (21/30). Ekman test score was normal (31/35). At follow-up three years later (45 years), cognitive scores exhibited attentional deficit (forward/backward digit spans: 5/3), perseverations and social cognition deficit (faux-pas test 21/30). The Ekman score was 28/35. Neurological examination revealed upper and lower limbs brisk reflexes with propagation of reflexes.

The case 2 was a left-handed 47-year-old male with 15 years of education. When included in the study, neurological examination and behavior evaluation were normal. Cognitive scores (MMSE: 30; MDRS 134/144; WCST: 20/20) and behavioral scores (FBI: 4; AES score: 2) were normal except for mild impairment of social cognition (faux-pas test: 19/30). The frontal adapted version of CDR®+NACC-FTLD scored 0.5 at baseline. At clinical follow-up evaluation, three years later (50 years), he exhibited inappropriate familiarity and joviality, without any other behavioral changes. The AES score mildly increased (9/42) and the CDR®+NACC-FTLD reached a score of 1.0. Cognitive tests revealed attentional deficit (forward/backward digit spans: 5/3), slow processing of information and decline in several cognitive scores, among which MDRS (130/144) and faux-pas test (18/30). Motor evaluation revealed cramps and rare fasciculations.

The case 3 was a right-handed 69-year-old male with 11 years of schooling. At inclusion, neurological and behavioral evaluations were normal (FBI: 6/42; AES: 13). MDRS

(135/142) and WCST (18/20) were normal but executive dysfunction (FAB: 12/18) and social cognition deficit (faux-pas test: 18/30, Ekman 29/35) were present. Two years later, he presented loss of interests and apathy (AES 19, cut-off >13), irritability, familiarity and disinhibition (FBI: 12), and imitation behavior. Cognitive tests exhibited attentional (forward/backward digit spans: 3/3) and planning difficulties. The WCST was scored 9/20. Scores of MDRS, FAB, and faux-pas test were stable. Ekman score was 26/35. Motor examination was normal.

The case 4 was a right-handed female of high education level (17 years). She was included in the study at age 64. Neurological examination was normal at inclusion, as well as behavior. The FBI scored 0 and the AES scored 8. Cognitive scores were within normal ranges or just above the lower limits according to her age. MDRS scored 138/144, MMSE 26/30 (2 errors in attention subtest) FAB 17/18, WCST 18/20, and TMT was completely normal (0 errors). Reevaluation at age 67, three years after her inclusion in the study, evidenced decline in several cognitive scores, with the occurrence of executive dysfunction, deficit in mental flexibility and perseverations. WCST scored 9/20, MMSE 24/30 and FAB 15/18. She made 10 errors at the TMT. She presented global slowness, scoring 12 at the AES apathy scale. Her relative did not mention any other behavioral disorders (FBI score: 0). At motor evaluation, she exhibited decreased Achilles tendon reflexes, cramps and rare fasciculations never noticed before.

Table A1. Clinical status and center proportion in each batch

Table A1. Number of subjects analyzed in each RNA-seq batch, by clinical status (above) and by center (below).

Batch	Clinical status			Total
	Control	Presymptomatic	Patient	
Batch 1	25 (39.7%)	27 (42.9%)	11 (17.4%)	63 (100%)
Batch 2	9 (37.5%)	10 (41.7%)	5 (20.8%)	24 (100%)
Batch 3	9 (39.1%)	8 (34.8%)	6 (26.1%)	23 (100%)

Batch	Center				Total
	Paris	Rouen	Limoges	Lille	
Batch 1	51 (81.0%)	5 (7.9%)	5 (7.9%)	2 (3.2%)	63 (100%)
Batch 2	18 (75%)	2 (8.3%)	3 (12.5%)	1 (4.2%)	24 (100%)
Batch 3	15 (65.2%)	3 (13.0%)	4 (17.4%)	1 (4.4%)	23 (100%)

Table A2. Complete output from EdgeR

Table A2. Complete output from EdgeR, for each pairwise comparison between clinical groups (control vs. presymptomatic, control vs. patient, presymptomatic vs. patient). The columns show the 589 analyzed miRNAs (above noise level), the log-fold change when comparing the clinical groups, the average log-counts per million, the unadjusted p-values and finally the adjusted p-values after Benjamini-Hochberg.

miRNA	log-fold change	log-counts per million	p-value	adjusted p-value
		Control vs. Presymptomatic		
miR-34a-5p	-1.433	4.676	5.251e-16	3.093e-13
miR-218-5p	1.475	1.231	0.000	0.081
miR-1250-5p	-0.310	0.691	0.001	0.209
miR-625-3p	0.495	8.394	0.002	0.228
miR-548au-5p	-0.275	14.473	0.005	0.458
miR-548am-c-o-5p	-0.283	14.295	0.005	0.458
miR-30e-5p	-0.153	10.655	0.006	0.458
miR-1307-5p	-0.241	5.708	0.006	0.458
miR-200c-3p	0.150	5.273	0.007	0.458
miR-5010-3p	0.206	1.408	0.008	0.458
miR-17-3p	-0.238	3.215	0.010	0.511
miR-361-5p	0.124	8.171	0.014	0.605
miR-199a-5p	-0.260	8.817	0.016	0.605
miR-125b-5p	0.245	8.080	0.017	0.605
miR-23b-5p	0.327	1.691	0.018	0.605
miR-548h-5p	-0.669	6.935	0.019	0.605
miR-29b-3p	-0.423	9.739	0.022	0.605
miR-10a-5p	0.179	7.108	0.026	0.605
miR-23b-3p	0.140	9.599	0.028	0.605
miR-32-5p	-0.280	5.289	0.029	0.605
miR-10a-3p	0.269	1.500	0.030	0.605
let-7g-3p	-0.359	0.220	0.031	0.605
miR-509-3p	0.470	2.288	0.032	0.605
miR-942-5p	0.140	4.976	0.033	0.605
miR-197-3p	0.207	6.745	0.033	0.605
miR-142-3p	-0.218	13.185	0.033	0.605
miR-21-3p	-0.316	3.394	0.034	0.605
miR-301a-3p	-0.186	5.377	0.034	0.605
miR-4742-3p	0.235	1.378	0.035	0.605
miR-5584-5p	0.286	0.672	0.037	0.605
miR-625-5p	0.278	6.770	0.038	0.605
miR-375	0.567	2.730	0.038	0.605
miR-330-5p	-0.111	3.616	0.041	0.605
miR-100-5p	0.466	2.346	0.041	0.605
miR-19a-3p	-0.286	5.810	0.043	0.605
miR-101-3p	-0.227	11.459	0.047	0.605
miR-582-5p	-0.498	0.885	0.047	0.605
miR-27a-3p	-0.306	9.739	0.048	0.605
miR-548y	-1.266	-0.318	0.055	0.605
miR-548aq-3p	-0.265	9.450	0.056	0.605
miR-153-3p	-0.360	0.310	0.056	0.605
miR-377-5p	-0.350	-0.095	0.057	0.605
miR-191-5p	0.116	12.565	0.057	0.605
miR-548t-5p	-0.407	1.936	0.057	0.605
miR-29a-3p	-0.401	9.472	0.059	0.605
let-7c-5p	0.178	9.528	0.060	0.605
miR-548ay-5p	-0.214	13.403	0.060	0.605
miR-215-5p	0.276	2.194	0.060	0.605
miR-874-3p	-0.160	1.960	0.061	0.605
miR-548d-5p	-0.210	12.885	0.061	0.605
miR-29c-3p	-0.338	8.568	0.061	0.605
miR-136-5p	-0.395	2.770	0.061	0.605
miR-19b-3p	-0.323	10.256	0.063	0.605
miR-487a-3p	-0.442	0.530	0.063	0.605
miR-548ag	-0.300	6.333	0.063	0.605
miR-548p	-0.785	1.823	0.064	0.605
miR-326	-0.197	6.590	0.064	0.605
miR-369-3p	-0.445	4.919	0.065	0.605
miR-551b-3p	-0.258	1.815	0.065	0.605
miR-30d-3p	-0.213	1.671	0.065	0.605
miR-135a-5p	-0.439	1.965	0.066	0.605
miR-33a-5p	-0.261	1.653	0.068	0.605
miR-181d-5p	0.171	3.947	0.068	0.605
miR-154-5p	-0.410	3.881	0.070	0.605
let-7d-3p	0.116	6.419	0.073	0.605
miR-376b-3p	-0.410	3.330	0.074	0.605
miR-548u	-0.576	1.210	0.074	0.605
miR-142-5p	-0.235	10.854	0.074	0.605
miR-6873-3p	0.297	5.014	0.075	0.605
miR-18a-5p	-0.137	7.212	0.076	0.605
miR-133b	-0.493	-0.138	0.079	0.605
miR-1260b	0.191	3.783	0.080	0.605
let-7i-3p	-0.231	2.370	0.081	0.605
miR-548j-3p	-0.355	0.393	0.081	0.605
miR-138-5p	-0.316	0.000	0.082	0.605

miR-148b-5p	-0.113	2.775	0.083	0.605
miR-31-5p	-0.473	2.641	0.085	0.605
miR-424-3p	0.218	0.968	0.086	0.605
miR-6511a-3p	0.198	4.865	0.086	0.605
miR-3194-3p	-0.580	0.002	0.088	0.605
miR-339-5p	-0.139	11.621	0.092	0.605
miR-106b-5p	-0.271	4.658	0.092	0.605
miR-181b-3p	-0.397	0.083	0.093	0.605
miR-125a-3p	0.248	0.692	0.095	0.605
miR-1306-3p	0.210	2.215	0.096	0.605
miR-598-3p	-0.256	4.565	0.097	0.605
miR-130b-5p	0.167	5.414	0.097	0.605
miR-574-3p	0.151	5.403	0.098	0.605
miR-548ah-3p	-0.782	2.757	0.098	0.605
miR-1249	0.346	0.351	0.099	0.605
miR-873-5p	-0.418	1.352	0.099	0.605
miR-496	-0.337	1.970	0.100	0.605
miR-590-5p	-0.316	0.651	0.100	0.605
miR-106b-3p	0.155	6.995	0.101	0.605
miR-18b-5p	-0.205	2.410	0.101	0.605
miR-7110-3p	0.366	-0.067	0.102	0.605
let-7e-5p	0.212	9.484	0.102	0.605
miR-223-5p	0.119	7.682	0.103	0.605
miR-337-5p	-0.311	3.963	0.104	0.605
miR-889-3p	-0.322	3.340	0.104	0.605
miR-1268a	-1.055	3.542	0.104	0.605
miR-377-3p	-0.306	2.438	0.105	0.606
miR-22-3p	-0.084	8.495	0.106	0.607
miR-205-5p	0.390	2.270	0.111	0.629
miR-324-5p	-0.103	5.454	0.115	0.638
miR-3688-3p	-0.209	1.689	0.116	0.638
miR-548j-5p	0.139	9.735	0.118	0.638
miR-6513-3p	0.097	1.835	0.119	0.638
miR-5583-3p	0.225	0.528	0.119	0.638
miR-660-5p	-0.149	5.628	0.121	0.638
miR-219a-5p	-0.278	1.164	0.123	0.638
miR-222-3p	0.115	8.603	0.123	0.638
miR-2277-5p	0.130	0.413	0.127	0.638
miR-340-5p	-0.197	6.743	0.128	0.638
miR-616-3p	0.219	0.543	0.129	0.638
miR-339-3p	-0.109	5.037	0.129	0.638
miR-95-3p	-0.247	2.108	0.130	0.638
miR-1304-3p	0.717	3.254	0.133	0.638
miR-136-3p	-0.399	3.534	0.133	0.638
miR-144-3p	-0.283	5.293	0.135	0.638
miR-548al	-0.842	-0.392	0.140	0.638
miR-4286	-0.132	10.665	0.141	0.638
miR-21-5p	-0.171	12.294	0.141	0.638
miR-369-5p	-0.229	5.217	0.142	0.638
miR-378i	0.126	4.394	0.145	0.638
miR-651-5p	-0.210	1.314	0.145	0.638
miR-1285-5p	-0.472	8.438	0.147	0.638
miR-338-3p	-0.175	5.028	0.150	0.638
miR-548q	0.214	4.336	0.150	0.638
miR-3198	0.313	0.544	0.151	0.638
miR-130a-3p	-0.142	7.658	0.154	0.638
miR-624-5p	-0.271	0.116	0.156	0.638
miR-7641	0.282	5.298	0.157	0.638
miR-30b-5p	-0.312	7.651	0.159	0.638
miR-664a-3p	0.115	4.261	0.160	0.638
miR-362-5p	0.134	2.457	0.161	0.638
miR-30a-5p	-0.126	6.368	0.161	0.638
miR-99a-5p	0.168	4.162	0.162	0.638
miR-376a-5p	-0.331	0.104	0.162	0.638
miR-301a-5p	-0.207	1.602	0.162	0.638
miR-655-3p	-0.392	-0.112	0.163	0.638
miR-582-3p	-0.297	1.716	0.164	0.638
miR-301b	-0.159	1.088	0.164	0.638
miR-320c	0.260	8.553	0.164	0.638
miR-381-3p	-0.233	5.537	0.165	0.638
miR-548f-3p	-0.289	5.197	0.165	0.638
miR-320d	0.219	7.345	0.166	0.638
miR-3913-5p	-0.139	2.448	0.169	0.638
miR-15a-5p	-0.146	9.211	0.169	0.638
miR-193a-5p	0.390	3.243	0.169	0.638
miR-497-5p	-0.174	1.523	0.171	0.638
miR-548ap-5p	0.118	9.773	0.172	0.638
miR-221-3p	0.096	11.513	0.174	0.638
miR-9-3p	-0.171	3.953	0.175	0.638
miR-664b-5p	0.211	1.474	0.176	0.638
miR-122-5p	0.452	11.047	0.177	0.638
miR-556-3p	-0.202	1.254	0.178	0.638
miR-93-3p	0.112	4.195	0.178	0.638
miR-299-3p	-0.322	0.096	0.178	0.638
miR-3138	0.224	2.724	0.179	0.638
miR-487a-5p	-0.238	0.384	0.181	0.638
let-7b-5p	0.170	12.514	0.182	0.638
miR-374b-3p	-0.174	1.235	0.183	0.638
miR-320b	0.252	8.897	0.184	0.638
miR-3605-3p	0.210	1.394	0.184	0.638
miR-3928-3p	0.166	0.931	0.186	0.638
miR-23c	0.113	0.292	0.187	0.638
miR-133a-3p	-0.278	7.345	0.187	0.638
miR-6852-5p	0.222	2.746	0.188	0.638
miR-18a-3p	0.146	2.363	0.189	0.638
miR-9-5p	-0.168	5.867	0.190	0.638
miR-548e-5p	-0.258	1.838	0.190	0.638

miR-27b-5p	0.133	1.148	0.191	0.638
miR-25-5p	0.181	2.573	0.192	0.638
miR-664b-3p	0.132	2.162	0.192	0.638
miR-199b-5p	-0.278	4.252	0.193	0.638
miR-154-3p	-0.327	0.419	0.193	0.638
miR-125a-5p	0.199	9.141	0.193	0.638
let-7f-1-3p	-0.225	0.491	0.194	0.638
miR-376c-5p	-0.379	1.518	0.196	0.640
miR-378g	0.251	0.027	0.198	0.640
let-7a-5p	0.131	17.835	0.198	0.640
miR-145-5p	0.172	6.318	0.199	0.640
miR-1273d	-1.451	4.498	0.201	0.643
miR-29b-1-5p	0.154	0.138	0.204	0.647
miR-146b-5p	-0.142	9.310	0.205	0.647
miR-103a-2-5p	-0.266	-0.340	0.209	0.647
miR-376b-5p	-0.370	1.487	0.210	0.647
miR-140-5p	-0.106	6.331	0.210	0.647
miR-411-5p	-0.225	5.491	0.211	0.647
miR-3620-5p	0.702	3.024	0.212	0.647
let-7f-2-3p	-0.256	0.250	0.213	0.647
miR-10b-5p	0.226	4.540	0.214	0.647
miR-941	0.156	9.475	0.214	0.647
miR-374a-3p	-0.192	2.987	0.217	0.647
miR-323b-3p	-0.201	4.932	0.219	0.647
miR-542-3p	-0.221	2.341	0.219	0.647
miR-3161	0.757	-0.951	0.221	0.647
miR-664a-5p	0.142	5.295	0.222	0.647
miR-885-5p	0.370	0.498	0.227	0.647
miR-92a-3p	0.174	13.677	0.227	0.647
miR-6859-5p	0.193	3.735	0.228	0.647
miR-1270	0.226	3.003	0.228	0.647
miR-378a-3p	0.098	9.082	0.229	0.647
miR-539-3p	-0.309	1.473	0.229	0.647
miR-376c-3p	-0.268	5.292	0.229	0.647
miR-1268b	-0.555	0.512	0.230	0.647
miR-766-5p	0.111	2.287	0.230	0.647
miR-3613-5p	0.223	9.506	0.230	0.647
miR-92b-5p	0.321	-0.009	0.232	0.647
miR-132-3p	0.091	3.504	0.233	0.647
miR-505-5p	0.165	3.558	0.234	0.647
miR-760	0.262	1.310	0.234	0.647
miR-4507	1.115	1.601	0.235	0.647
miR-3173-5p	0.234	1.011	0.245	0.665
miR-548aa	-0.271	10.786	0.245	0.665
miR-548t-3p	-0.271	10.786	0.245	0.665
miR-4772-3p	-0.289	1.699	0.247	0.665
miR-382-5p	-0.212	8.383	0.247	0.665
miR-5095	-1.849	8.523	0.251	0.670
miR-545-3p	-0.166	1.909	0.251	0.670
miR-361-3p	-0.075	6.970	0.253	0.672
miR-576-5p	0.107	6.414	0.255	0.675
miR-186-3p	-0.112	0.571	0.257	0.676
miR-155-5p	0.079	8.603	0.262	0.677
miR-590-3p	-0.212	6.770	0.262	0.677
miR-382-3p	-0.210	3.232	0.262	0.677
miR-744-5p	0.149	7.986	0.263	0.677
miR-5187-5p	0.170	2.108	0.263	0.677
miR-376a-3p	-0.239	6.560	0.265	0.677
miR-20a-5p	-0.097	9.087	0.266	0.677
miR-32-3p	-0.151	0.143	0.273	0.690
miR-545-5p	-0.199	1.482	0.274	0.690
miR-495-5p	-0.198	-0.270	0.279	0.690
miR-92b-3p	0.184	3.086	0.280	0.690
miR-409-5p	-0.166	3.705	0.280	0.690
miR-27a-5p	0.170	2.220	0.280	0.690
miR-671-3p	0.158	3.284	0.282	0.690
miR-2355-5p	-0.175	0.457	0.283	0.690
miR-619-5p	0.846	11.202	0.284	0.690
miR-641	-0.081	1.385	0.284	0.690
miR-98-3p	-0.192	0.779	0.285	0.690
miR-23a-5p	0.186	1.003	0.286	0.690
miR-221-5p	0.070	5.310	0.288	0.690
miR-589-5p	0.082	3.684	0.288	0.690
miR-6842-3p	0.103	1.371	0.288	0.690
miR-628-5p	-0.092	4.677	0.296	0.707
let-7d-5p	0.090	10.427	0.299	0.708
miR-30e-3p	-0.111	7.059	0.299	0.708
miR-454-5p	0.059	3.780	0.302	0.711
miR-548e-3p	-0.132	2.682	0.303	0.711
miR-99b-3p	0.151	2.773	0.308	0.719
miR-29a-5p	-0.115	0.831	0.312	0.719
miR-627-5p	-0.075	0.873	0.313	0.719
miR-544a	-0.367	0.669	0.315	0.719
miR-186-5p	-0.086	8.853	0.317	0.719
miR-365a-3p	0.189	4.151	0.318	0.719
miR-365b-3p	0.189	4.151	0.318	0.719
miR-548a-3p	-0.142	5.676	0.318	0.719
miR-618	0.314	-0.303	0.320	0.719
miR-1185-2-3p	-0.203	0.123	0.320	0.719
miR-548h-3p	-0.274	8.937	0.321	0.719
miR-548z	-0.274	8.937	0.321	0.719
let-7g-5p	-0.053	10.980	0.326	0.725
miR-6734-5p	0.166	0.555	0.326	0.725
miR-23a-3p	0.061	11.962	0.328	0.726
miR-103a-3p	0.051	15.095	0.330	0.726
miR-550a-3-5p	0.116	2.398	0.332	0.726
miR-548ak	-0.536	2.923	0.334	0.726

miR-758-3p	-0.186	1.734	0.335	0.726
miR-181a-5p	0.102	10.817	0.335	0.726
miR-4477b	-0.222	0.399	0.335	0.726
miR-5193	0.104	1.173	0.338	0.730
miR-134-5p	-0.187	7.091	0.340	0.732
miR-374a-5p	-0.135	7.594	0.342	0.732
miR-1277-3p	-0.146	1.948	0.345	0.734
miR-501-3p	0.147	2.746	0.345	0.734
miR-548an	-0.264	1.688	0.347	0.734
miR-28-3p	0.059	10.686	0.352	0.737
miR-1301-3p	0.130	5.720	0.353	0.737
miR-548d-3p	-0.277	1.169	0.354	0.737
miR-2115-3p	0.243	0.295	0.355	0.737
miR-1	-0.241	8.318	0.356	0.737
miR-423-3p	0.124	8.841	0.356	0.737
miR-450b-5p	-0.153	2.048	0.357	0.737
miR-1306-5p	0.240	2.765	0.361	0.743
miR-629-5p	0.097	6.404	0.363	0.743
miR-379-5p	-0.153	7.187	0.364	0.743
miR-7706	0.159	-0.037	0.366	0.743
miR-20a-3p	-0.083	1.922	0.366	0.743
miR-320a	0.145	11.779	0.371	0.743
miR-126-5p	-0.103	11.057	0.372	0.743
miR-148b-3p	-0.077	9.436	0.374	0.743
miR-548k	-0.082	1.443	0.377	0.743
miR-493-3p	-0.149	5.508	0.378	0.743
miR-548av-5p	-0.082	1.444	0.378	0.743
miR-4677-3p	-0.107	0.746	0.380	0.743
miR-99b-5p	0.118	7.865	0.380	0.743
miR-3615	0.175	5.538	0.381	0.743
miR-27b-3p	-0.088	10.051	0.381	0.743
miR-424-5p	-0.141	3.748	0.382	0.743
miR-199a-3p	-0.086	15.594	0.383	0.743
miR-199b-3p	-0.086	15.594	0.383	0.743
let-7a-3p	-0.155	4.497	0.384	0.743
miR-335-3p	0.107	5.333	0.385	0.743
miR-548a-5p	-0.212	1.849	0.390	0.746
miR-628-3p	0.072	5.661	0.391	0.746
miR-141-3p	-0.104	3.127	0.392	0.746
miR-429	-0.092	0.270	0.393	0.746
miR-30a-3p	-0.061	3.079	0.394	0.746
miR-192-5p	-0.088	7.507	0.394	0.746
miR-3143	-0.097	-0.186	0.395	0.746
miR-1273c	0.106	1.024	0.397	0.746
miR-296-5p	-0.139	1.358	0.398	0.746
miR-1277-5p	-0.124	12.138	0.402	0.749
miR-16-2-3p	-0.115	3.631	0.402	0.749
miR-1303	0.278	4.458	0.403	0.749
miR-4446-3p	0.120	3.069	0.408	0.756
miR-127-5p	-0.147	1.654	0.411	0.758
miR-210-3p	-0.070	2.393	0.414	0.758
miR-574-5p	0.407	14.568	0.415	0.758
miR-450a-5p	-0.176	0.853	0.415	0.758
miR-3200-3p	-0.171	0.193	0.417	0.758
miR-548f-5p	-0.382	0.762	0.419	0.758
miR-1307-3p	0.142	7.329	0.420	0.758
miR-548az-5p	-0.231	5.839	0.423	0.758
miR-3120-3p	-0.073	2.583	0.424	0.758
miR-500a-3p	0.065	4.766	0.425	0.758
miR-1294	0.127	1.946	0.426	0.758
miR-1226-3p	0.119	1.073	0.426	0.758
miR-1185-1-3p	-0.150	3.358	0.427	0.758
miR-6513-5p	0.074	0.012	0.428	0.758
miR-487b-3p	-0.132	5.402	0.428	0.758
miR-340-3p	-0.055	3.655	0.434	0.763
miR-7849-3p	0.090	0.247	0.434	0.763
miR-191-3p	0.057	3.805	0.439	0.763
miR-4659a-3p	0.100	0.124	0.442	0.763
miR-5585-3p	-0.861	6.719	0.443	0.763
miR-548ar-5p	-0.300	7.739	0.444	0.763
miR-106a-5p	-0.098	1.761	0.445	0.763
miR-548I	0.089	1.877	0.446	0.763
miR-3617-5p	0.124	0.442	0.448	0.763
miR-206	0.336	1.104	0.449	0.763
miR-26b-5p	-0.061	12.787	0.452	0.763
miR-4433b-3p	-0.174	2.351	0.452	0.763
miR-744-3p	-0.155	-0.457	0.455	0.763
miR-548ab	-0.320	4.211	0.455	0.763
miR-652-5p	-0.103	1.446	0.455	0.763
let-7b-3p	0.078	1.579	0.456	0.763
miR-548x-3p	-0.740	2.828	0.457	0.763
miR-539-5p	-0.189	0.162	0.458	0.763
miR-185-5p	-0.041	9.811	0.459	0.763
miR-183-5p	0.142	5.546	0.461	0.763
miR-548g-3p	-0.546	1.192	0.462	0.763
miR-409-3p	-0.123	8.698	0.462	0.763
miR-335-5p	-0.090	7.461	0.462	0.763
miR-1229-3p	0.115	0.765	0.466	0.763
miR-1255b-5p	0.121	7.593	0.466	0.763
miR-30b-3p	0.068	0.223	0.469	0.763
miR-1908-5p	0.183	2.300	0.470	0.763
miR-502-3p	0.065	3.800	0.470	0.763
miR-548aj-5p	-0.267	7.504	0.472	0.763
miR-548g-5p	-0.267	7.504	0.472	0.763
miR-548x-5p	-0.267	7.504	0.472	0.763
miR-1185-5p	-0.156	2.420	0.477	0.768
miR-6772-3p	0.116	0.690	0.478	0.768

miR-6500-3p	-0.300	-0.223	0.479	0.768
miR-15b-3p	-0.092	5.648	0.480	0.768
miR-328-3p	0.114	5.945	0.481	0.768
miR-1972	-0.999	5.510	0.486	0.770
miR-425-5p	0.050	10.913	0.486	0.770
miR-148a-5p	0.075	0.933	0.486	0.770
miR-331-3p	-0.064	4.398	0.490	0.771
miR-16-5p	-0.049	17.408	0.491	0.771
miR-181a-3p	-0.090	4.944	0.491	0.771
miR-654-3p	-0.114	7.125	0.495	0.775
miR-548n	-0.071	4.212	0.498	0.777
miR-548ap-3p	-0.159	10.374	0.501	0.777
miR-378a-5p	0.083	2.841	0.501	0.777
miR-379-3p	-0.124	1.468	0.503	0.777
miR-548av-3p	-0.207	3.903	0.504	0.777
miR-550a-5p	0.087	1.899	0.506	0.777
miR-378c	-0.064	5.108	0.508	0.777
miR-6803-3p	0.151	-0.112	0.509	0.777
miR-665	-0.139	0.677	0.510	0.777
miR-196a-5p	-0.149	2.899	0.511	0.777
let-7i-5p	0.041	13.259	0.511	0.777
miR-483-5p	0.252	1.834	0.512	0.777
miR-4659b-3p	-0.063	0.948	0.521	0.787
miR-378d	-0.241	0.023	0.524	0.787
miR-584-3p	-0.084	0.426	0.524	0.787
miR-145-3p	0.089	1.763	0.525	0.787
miR-182-5p	0.085	7.556	0.525	0.787
miR-671-5p	0.084	4.210	0.526	0.787
miR-548ax	-0.065	5.062	0.530	0.791
miR-1233-3p	-0.379	-0.544	0.533	0.792
miR-130b-3p	-0.041	5.063	0.534	0.792
miR-431-3p	-0.111	0.193	0.535	0.792
miR-25-3p	0.046	10.901	0.536	0.792
miR-548ae	-0.626	3.953	0.538	0.792
miR-6511b-3p	0.076	2.078	0.539	0.792
miR-584-5p	0.065	9.252	0.541	0.793
miR-20b-5p	-0.057	5.620	0.547	0.799
miR-548as-5p	-0.162	3.448	0.551	0.801
miR-224-5p	0.123	7.850	0.551	0.801
miR-1290	0.167	4.532	0.554	0.804
miR-642a-3p	0.118	0.484	0.556	0.804
miR-1179	0.056	1.832	0.558	0.804
miR-30d-5p	0.029	11.785	0.559	0.804
miR-28-5p	-0.035	6.656	0.560	0.804
miR-324-3p	-0.039	4.372	0.561	0.804
miR-139-3p	0.118	4.524	0.563	0.806
miR-150-3p	0.107	1.296	0.567	0.807
miR-181c-3p	-0.055	3.538	0.567	0.807
miR-423-5p	0.126	10.597	0.572	0.811
miR-452-5p	-0.106	2.671	0.574	0.811
miR-22-5p	-0.057	3.999	0.574	0.811
miR-4433b-5p	0.100	7.929	0.575	0.811
miR-485-3p	-0.133	5.831	0.585	0.821
miR-2110	0.100	3.338	0.589	0.821
miR-425-3p	-0.033	6.606	0.591	0.821
miR-126-3p	-0.032	14.192	0.591	0.821
miR-190a-5p	-0.068	5.571	0.592	0.821
miR-6741-3p	0.106	0.231	0.592	0.821
miR-431-5p	-0.086	7.576	0.593	0.821
miR-769-3p	0.075	0.674	0.594	0.821
miR-30c-1-3p	0.036	2.582	0.597	0.824
miR-548w	-0.140	5.896	0.601	0.827
miR-3158-3p	-0.118	1.499	0.609	0.836
miR-542-5p	0.072	1.306	0.612	0.836
miR-503-5p	0.056	3.907	0.614	0.836
miR-2355-3p	-0.038	3.959	0.615	0.836
miR-195-5p	-0.053	3.376	0.616	0.836
miR-495-3p	-0.093	3.399	0.616	0.836
miR-337-3p	-0.111	2.407	0.620	0.839
miR-29b-2-5p	0.031	1.605	0.621	0.839
miR-329-3p	-0.076	5.645	0.625	0.843
miR-17-5p	-0.053	8.427	0.629	0.844
miR-363-3p	-0.055	6.300	0.631	0.844
miR-4448	0.078	4.223	0.632	0.844
miR-5189-3p	0.140	0.435	0.632	0.844
miR-451a	-0.077	11.183	0.635	0.846
miR-342-5p	0.053	3.944	0.640	0.848
miR-139-5p	-0.070	6.068	0.640	0.848
miR-548at-5p	-0.088	4.401	0.641	0.848
miR-374b-5p	-0.064	6.920	0.647	0.854
miR-4301	-0.207	2.532	0.650	0.856
miR-30c-5p	-0.049	11.296	0.652	0.857
miR-4732-3p	0.134	3.928	0.654	0.858
miR-493-5p	-0.075	5.498	0.657	0.858
miR-548o-3p	0.153	2.775	0.658	0.858
miR-1273g-3p	-0.575	11.153	0.661	0.858
miR-190b	0.026	3.267	0.661	0.858
miR-421	0.021	5.199	0.663	0.858
miR-96-5p	-0.093	3.856	0.663	0.858
miR-194-5p	-0.055	7.337	0.666	0.860
miR-485-5p	-0.101	3.492	0.674	0.860
miR-1302	-0.295	2.800	0.674	0.860
miR-98-5p	0.029	8.594	0.675	0.860
miR-5009-5p	-0.076	0.291	0.676	0.860
miR-532-5p	-0.038	5.499	0.676	0.860
miR-26b-3p	-0.026	3.623	0.677	0.860
miR-3064-5p	0.036	0.924	0.678	0.860

miR-5010-5p	0.102	0.210	0.678	0.860
miR-203a	0.087	-0.173	0.682	0.860
miR-6511b-5p	0.183	1.158	0.683	0.860
miR-1304-5p	-0.282	0.167	0.683	0.860
miR-766-3p	-0.039	5.380	0.684	0.860
miR-494-3p	-0.073	5.857	0.686	0.861
miR-3180	-0.174	0.868	0.692	0.865
miR-3180-3p	-0.174	0.868	0.692	0.865
miR-4732-5p	0.115	3.999	0.701	0.875
miR-3187-3p	0.060	0.369	0.705	0.875
miR-4435	0.064	1.570	0.705	0.875
miR-1273h-5p	0.056	11.451	0.709	0.875
miR-483-3p	0.132	1.205	0.709	0.875
miR-1285-3p	-0.041	8.508	0.710	0.875
miR-144-5p	-0.078	7.018	0.710	0.875
miR-1255a	0.075	4.833	0.714	0.878
miR-4785	-0.038	0.526	0.716	0.878
miR-589-3p	0.028	1.137	0.718	0.878
miR-181b-5p	0.035	8.044	0.719	0.878
miR-196b-5p	0.023	5.658	0.720	0.878
miR-299-5p	-0.058	2.468	0.724	0.882
miR-223-3p	0.025	14.649	0.727	0.882
miR-486-3p	0.068	5.430	0.729	0.884
miR-204-5p	-0.062	1.457	0.732	0.884
miR-181a-2-3p	-0.025	5.645	0.733	0.884
miR-93-5p	0.017	11.309	0.735	0.885
miR-1273h-3p	0.044	7.277	0.740	0.889
miR-1299	-0.190	4.630	0.741	0.889
miR-548am-3p	-0.232	2.613	0.742	0.889
miR-143-5p	0.055	1.979	0.747	0.893
let-7f-5p	0.022	16.225	0.751	0.895
miR-514a-3p	-0.097	0.606	0.755	0.897
miR-491-5p	0.027	3.945	0.756	0.897
miR-504-5p	0.042	0.213	0.757	0.897
miR-1287-5p	0.025	3.050	0.758	0.897
miR-185-3p	0.034	4.607	0.762	0.898
miR-1292-5p	-0.057	0.211	0.764	0.898
miR-1468-5p	-0.027	0.552	0.767	0.898
miR-1180-3p	0.077	2.024	0.767	0.898
miR-152-3p	-0.025	7.210	0.768	0.898
miR-150-5p	-0.056	10.272	0.769	0.898
miR-652-3p	-0.020	7.109	0.773	0.898
miR-330-3p	-0.017	3.864	0.773	0.898
miR-432-5p	0.057	7.959	0.774	0.898
miR-4645-3p	0.028	0.811	0.775	0.898
miR-15b-5p	-0.030	9.487	0.781	0.904
miR-26a-5p	-0.017	15.391	0.785	0.905
miR-6770-3p	0.059	0.142	0.787	0.905
miR-486-5p	0.061	14.249	0.787	0.905
miR-6516-5p	0.030	1.586	0.788	0.905
miR-342-3p	0.030	10.283	0.790	0.905
miR-454-3p	0.017	8.563	0.793	0.906
miR-1233-5p	-0.164	-0.221	0.794	0.906
miR-146a-5p	-0.019	12.934	0.795	0.906
miR-484	0.039	7.854	0.800	0.909
miR-877-3p	-0.065	2.150	0.801	0.909
miR-3179	0.070	-0.272	0.809	0.915
miR-487b-5p	-0.043	0.849	0.809	0.915
miR-370-3p	-0.053	5.773	0.812	0.916
miR-1246	0.063	5.861	0.815	0.916
miR-3133	0.114	-0.564	0.815	0.916
miR-148a-3p	-0.022	10.002	0.817	0.916
miR-26a-2-3p	0.037	-0.153	0.818	0.916
miR-433-3p	-0.043	1.880	0.824	0.920
miR-3679-5p	0.030	2.384	0.827	0.922
miR-500b-5p	-0.036	2.709	0.829	0.922
miR-505-3p	0.011	4.359	0.833	0.922
miR-7-5p	-0.021	10.227	0.834	0.922
miR-24-3p	0.011	12.655	0.834	0.922
miR-3960	-0.107	3.467	0.834	0.922
miR-127-3p	0.032	7.007	0.838	0.925
miR-181c-5p	0.025	3.046	0.842	0.927
miR-128-3p	-0.012	10.346	0.846	0.927
miR-550a-3p	0.032	3.973	0.849	0.927
miR-151a-3p	0.017	11.573	0.849	0.927
miR-378f	0.021	1.820	0.850	0.927
miR-3065-5p	0.022	2.573	0.850	0.927
miR-146b-3p	-0.016	3.582	0.851	0.927
miR-151b	0.017	11.596	0.853	0.927
miR-200a-3p	0.016	2.514	0.855	0.927
miR-151a-3p	-0.009	12.424	0.863	0.927
miR-548i	-0.068	3.203	0.866	0.927
miR-4454	0.028	9.159	0.866	0.927
miR-19b-1-5p	-0.015	0.495	0.868	0.927
miR-4685-3p	0.034	0.669	0.868	0.927
miR-769-5p	-0.008	4.654	0.868	0.927
miR-6511a-5p	0.076	1.038	0.868	0.927
miR-548ai	0.104	0.527	0.870	0.927
miR-570-5p	0.104	0.527	0.870	0.927
miR-708-5p	-0.071	2.615	0.870	0.927
miR-329-5p	-0.031	2.442	0.874	0.929
miR-146a-3p	0.109	2.291	0.877	0.929
miR-548aq-5p	0.103	2.543	0.877	0.929
miR-4326	0.042	1.874	0.881	0.931
miR-345-5p	-0.012	4.607	0.884	0.931
miR-4662a-5p	-0.019	1.907	0.884	0.931
miR-532-3p	-0.018	2.783	0.887	0.931

miR-143-3p	0.024	9.208	0.887	0.931
miR-6859-3p	-0.050	0.719	0.890	0.932
miR-3065-3p	-0.018	0.404	0.892	0.932
miR-1271-3p	-0.013	1.919	0.893	0.932
miR-5096	-0.072	11.722	0.901	0.939
miR-412-5p	-0.039	2.206	0.910	0.947
miR-1271-3p	-0.063	-0.768	0.914	0.948
miR-548b-5p	-0.016	7.793	0.915	0.948
miR-132-5p	0.010	0.644	0.917	0.948
miR-543	-0.015	3.379	0.919	0.948
miR-3074-5p	0.018	1.854	0.920	0.948
miR-576-3p	0.008	5.501	0.922	0.948
miR-3140-3p	0.011	0.699	0.923	0.948
miR-3180-5p	0.037	-0.295	0.924	0.948
miR-323a-3p	-0.014	4.078	0.927	0.949
miR-1289	0.028	-0.148	0.932	0.953
miR-7976	-0.008	1.801	0.940	0.959
miR-877-5p	-0.005	2.378	0.941	0.959
miR-107	-0.004	10.028	0.947	0.963
miR-7851-3p	-0.013	3.495	0.953	0.968
miR-29c-5p	-0.004	4.579	0.955	0.968
miR-7-1-3p	-0.006	2.452	0.959	0.971
miR-140-3p	-0.002	9.249	0.971	0.981
miR-500a-5p	-0.005	3.026	0.975	0.981
miR-200b-3p	-0.003	2.188	0.976	0.981
miR-26a-1-3p	0.002	2.985	0.978	0.981
miR-1296-5p	-0.002	2.226	0.978	0.981
miR-551a	-0.003	-0.321	0.988	0.989
miR-548c-3p	0.000	2.905	1.000	1.000
miRNA	log-fold change	log-counts per million	p-value	adjusted p-value
Control vs. Patient				
miR-34a-5p	-1.239	4.676	1.650E-08	9.720E-06
miR-345-5p	-0.540	4.607	1.131E-05	0.003
miR-200c-3p	0.333	5.273	3.109E-05	0.006
miR-10a-3p	0.697	1.500	7.141E-05	0.011
miR-151a-5p	0.411	11.573	0.001	0.096
miR-151b	0.406	11.596	0.001	0.096
miR-551a	-1.102	-0.321	0.001	0.096
miR-133a-3p	-0.949	7.345	0.002	0.119
miR-206	-1.883	1.104	0.002	0.119
miR-133b	-1.200	-0.138	0.002	0.123
miR-542-5p	-0.636	1.306	0.003	0.161
miR-296-5p	-0.637	1.358	0.006	0.262
miR-660-5p	-0.378	5.628	0.006	0.262
miR-18a-3p	-0.440	2.363	0.007	0.262
miR-223-3p	-0.276	14.649	0.007	0.262
miR-205-5p	-1.031	2.270	0.008	0.262
miR-361-3p	-0.251	6.970	0.008	0.262
let-7b-3p	-0.407	1.579	0.008	0.262
miR-30a-5p	-0.334	6.368	0.009	0.262
miR-93-3p	-0.315	4.195	0.009	0.262
let-7f-5p	0.246	16.225	0.011	0.296
miR-532-3p	-0.480	2.783	0.011	0.296
miR-144-3p	-0.677	5.293	0.012	0.296
miR-425-3p	-0.215	6.606	0.012	0.300
miR-550a-3p	-0.641	3.973	0.013	0.300
miR-10a-5p	0.282	7.108	0.013	0.300
miR-17-5p	0.363	8.427	0.014	0.314
miR-451a	-0.569	11.183	0.016	0.326
miR-7976	-0.396	1.801	0.016	0.326
miR-196b-5p	0.212	5.658	0.017	0.326
miR-135a-5p	-0.682	1.965	0.017	0.326
miR-106b-3p	-0.322	6.995	0.018	0.340
miR-148a-5p	-0.354	0.933	0.021	0.375
miR-25-3p	-0.248	10.901	0.022	0.377
miR-1289	-1.046	-0.148	0.023	0.385
miR-324-3p	-0.214	4.372	0.024	0.387
miR-5583-3p	0.460	0.528	0.024	0.387
miR-30b-3p	0.295	0.223	0.026	0.391
miR-23b-3p	0.194	9.599	0.028	0.391
miR-326	-0.326	6.590	0.028	0.391
miR-3158-3p	-0.743	1.499	0.028	0.391
miR-146a-5p	0.214	12.934	0.029	0.391
miR-532-5p	-0.283	5.499	0.029	0.391
miR-1303	-1.127	4.458	0.029	0.391
miR-378a-5p	-0.396	2.841	0.030	0.391
miR-16-5p	-0.218	17.408	0.032	0.403
miR-155-5p	0.215	8.603	0.032	0.403
miR-3615	-0.647	5.538	0.033	0.403
miR-26b-5p	0.235	12.787	0.034	0.403
miR-140-3p	-0.168	9.249	0.036	0.418
miR-331-3p	0.268	4.398	0.036	0.418
miR-484	-0.463	7.854	0.037	0.418
miR-4785	-0.304	0.526	0.038	0.418
miR-374a-3p	0.435	2.987	0.040	0.432
miR-224-5p	-0.584	7.850	0.040	0.432
miR-502-3p	-0.265	3.800	0.042	0.440
miR-26b-3p	-0.179	3.623	0.043	0.440
miR-769-5p	-0.130	4.654	0.044	0.443
miR-412-5p	1.005	2.206	0.045	0.443
miR-4286	-0.248	10.665	0.045	0.443
miR-6513-5p	0.252	0.012	0.047	0.443
miR-339-5p	-0.233	11.621	0.047	0.443
miR-30e-5p	-0.151	10.655	0.048	0.443
miR-28-5p	0.161	6.656	0.049	0.443

miR-183-5p	-0.553	5.546	0.049	0.443
miR-664a-3p	0.222	4.261	0.051	0.443
miR-339-3p	-0.196	5.037	0.051	0.443
miR-618	-0.905	-0.303	0.051	0.443
miR-363-3p	-0.320	6.300	0.052	0.443
miR-5584-5p	0.373	0.672	0.053	0.443
miR-130a-3p	0.257	7.658	0.054	0.444
miR-192-5p	-0.286	7.507	0.055	0.444
miR-6513-3p	0.167	1.835	0.055	0.444
miR-203a	-0.524	-0.173	0.056	0.445
miR-642a-3p	-0.565	0.484	0.057	0.448
miR-139-5p	0.384	6.068	0.058	0.452
miR-148b-3p	0.223	9.436	0.060	0.455
miR-340-3p	0.180	3.655	0.060	0.455
miR-96-5p	-0.563	3.856	0.062	0.455
miR-10b-5p	-0.515	4.540	0.062	0.455
miR-514a-3p	0.836	0.606	0.065	0.456
miR-374a-5p	0.353	7.594	0.066	0.456
miR-550a-3-5p	-0.320	2.398	0.068	0.456
miR-196a-5p	-0.585	2.899	0.068	0.456
miR-1233-5p	-1.587	-0.221	0.069	0.456
miR-26a-5p	0.158	15.391	0.069	0.456
miR-1180-3p	-0.699	2.024	0.070	0.456
miR-627-5p	-0.189	0.873	0.070	0.456
miR-486-5p	-0.615	14.249	0.071	0.456
miR-98-5p	0.169	8.594	0.071	0.456
miR-3679-5p	-0.350	2.384	0.071	0.456
miR-4685-3p	-0.526	0.669	0.072	0.456
miR-629-5p	-0.272	6.404	0.073	0.456
miR-365a-3p	-0.506	4.151	0.075	0.456
miR-365b-3p	-0.506	4.151	0.075	0.456
miR-370-3p	-0.548	5.773	0.075	0.456
miR-22-3p	-0.129	8.495	0.075	0.456
miR-154-3p	0.617	0.419	0.081	0.478
miR-4732-3p	-0.787	3.928	0.081	0.478
miR-3120-3p	0.215	2.583	0.081	0.478
miR-26a-1-3p	0.163	2.985	0.084	0.485
miR-664b-3p	0.243	2.162	0.084	0.485
miR-186-3p	-0.234	0.571	0.086	0.492
miR-146b-3p	-0.205	3.582	0.087	0.492
miR-500b-5p	-0.405	2.709	0.089	0.498
miR-941	-0.319	9.475	0.090	0.498
miR-500a-5p	-0.362	3.026	0.093	0.506
miR-29b-2-5p	0.145	1.605	0.093	0.506
miR-590-3p	0.419	6.770	0.096	0.506
miR-7706	-0.429	-0.037	0.096	0.506
miR-150-5p	-0.472	10.272	0.097	0.506
miR-454-3p	0.150	8.563	0.097	0.506
miR-1277-5p	0.339	12.138	0.098	0.506
miR-665	-0.484	0.677	0.098	0.506
miR-548u	0.763	1.210	0.101	0.508
miR-93-5p	-0.115	11.309	0.101	0.508
miR-628-5p	0.195	4.677	0.102	0.508
miR-550a-5p	-0.314	1.899	0.103	0.508
miR-548j-5p	0.202	9.735	0.103	0.508
miR-548ap-5p	0.197	9.773	0.103	0.508
miR-204-5p	0.418	1.457	0.105	0.513
miR-1296-5p	-0.158	2.226	0.107	0.516
miR-4677-3p	0.267	0.746	0.109	0.518
miR-652-5p	0.301	1.446	0.109	0.518
miR-199b-5p	-0.489	4.252	0.111	0.523
miR-103a-3p	0.115	15.095	0.113	0.524
miR-425-5p	-0.160	10.913	0.114	0.524
miR-486-3p	-0.452	5.430	0.115	0.524
miR-500a-3p	-0.183	4.766	0.117	0.524
miR-4645-3p	0.212	0.811	0.117	0.524
miR-539-5p	0.517	0.162	0.119	0.524
miR-589-5p	-0.171	3.684	0.119	0.524
miR-769-3p	-0.317	0.674	0.119	0.524
miR-495-3p	0.390	3.399	0.119	0.524
miR-1277-3p	0.327	1.948	0.121	0.524
miR-548am-c-o-5p	0.214	14.295	0.122	0.524
miR-92a-3p	-0.321	13.677	0.122	0.524
miR-194-5p	-0.285	7.337	0.124	0.530
miR-21-3p	-0.308	3.394	0.126	0.534
miR-548au-5p	0.205	14.473	0.127	0.535
miR-338-3p	-0.257	5.028	0.128	0.535
miR-766-5p	0.195	2.287	0.131	0.538
miR-335-5p	0.248	7.461	0.134	0.538
miR-152-3p	0.169	7.210	0.134	0.538
miR-199a-3p	0.198	15.594	0.136	0.538
miR-199b-3p	0.198	15.594	0.136	0.538
miR-616-3p	-0.313	0.543	0.136	0.538
miR-26a-2-3p	0.331	-0.153	0.136	0.538
miR-874-3p	-0.175	1.960	0.136	0.538
miR-539-3p	0.506	1.473	0.137	0.538
miR-150-3p	-0.405	1.296	0.141	0.546
miR-32-3p	0.273	0.143	0.141	0.546
miR-181b-5p	-0.199	8.044	0.142	0.548
miR-424-5p	-0.337	3.748	0.143	0.549
miR-491-5p	-0.180	3.945	0.147	0.554
miR-1292-5p	-0.399	0.211	0.147	0.554
miR-27a-5p	0.329	2.220	0.148	0.554
miR-590-5p	0.371	0.651	0.149	0.554
miR-92b-3p	-0.346	3.086	0.151	0.556
miR-3200-3p	-0.439	0.193	0.153	0.556
miR-501-3p	-0.323	2.746	0.154	0.556

miR-1273d	-1.478	4.498	0.155	0.556
miR-16-2-3p	-0.272	3.631	0.156	0.556
miR-340-5p	0.244	6.743	0.158	0.556
miR-382-3p	0.367	3.232	0.159	0.556
let-7f-1-3p	-0.336	0.491	0.159	0.556
miR-185-3p	-0.222	4.607	0.159	0.556
let-7i-3p	-0.254	2.370	0.160	0.556
miR-431-3p	-0.343	0.193	0.161	0.556
miR-375	-0.564	2.730	0.161	0.556
miR-3180-5p	-0.853	-0.295	0.161	0.556
miR-545-5p	0.338	1.482	0.165	0.564
miR-1273h-3p	-0.261	7.277	0.166	0.564
miR-548ab	0.855	4.211	0.168	0.566
miR-30c-1-3p	0.129	2.582	0.169	0.566
miR-92b-5p	-0.536	-0.009	0.169	0.566
miR-1255a	0.392	4.833	0.171	0.570
miR-423-5p	-0.444	10.597	0.175	0.574
miR-576-5p	-0.183	6.414	0.175	0.574
miR-126-3p	0.109	14.192	0.176	0.574
miR-1307-5p	-0.161	5.708	0.177	0.576
miR-3180	-0.899	0.868	0.180	0.578
miR-3180-3p	-0.899	0.868	0.180	0.578
miR-423-3p	-0.252	8.841	0.181	0.578
miR-766-3p	-0.179	5.380	0.183	0.582
miR-378d	-0.691	0.023	0.184	0.582
miR-7-5p	0.181	10.227	0.190	0.598
miR-138-5p	-0.323	0.000	0.191	0.600
miR-548am-3p	1.170	2.613	0.194	0.604
miR-106a-5p	0.226	1.761	0.196	0.606
miR-548ay-5p	-0.201	13.403	0.197	0.607
miR-378i	-0.158	4.394	0.200	0.614
miR-582-3p	-0.385	1.716	0.201	0.614
miR-30d-5p	-0.090	11.785	0.203	0.614
miR-25-5p	-0.254	2.573	0.205	0.614
miR-3928-3p	-0.227	0.931	0.206	0.614
miR-221-5p	0.114	5.310	0.209	0.614
let-7b-5p	-0.226	12.514	0.213	0.614
miR-5193	0.191	1.173	0.214	0.614
miR-3688-3p	-0.227	1.689	0.214	0.614
miR-223-5p	-0.127	7.682	0.214	0.614
miR-2115-3p	-0.478	0.295	0.215	0.614
miR-4732-5p	-0.560	3.999	0.216	0.614
miR-1908-5p	-0.442	2.300	0.217	0.614
miR-7641	-0.356	5.298	0.218	0.614
miR-582-5p	-0.430	0.885	0.219	0.614
miR-641	0.128	1.385	0.219	0.614
miR-5009-5p	-0.330	0.291	0.220	0.614
miR-190b	-0.101	3.267	0.221	0.614
miR-3617-5p	0.260	0.442	0.221	0.614
miR-9-3p	0.209	3.953	0.222	0.614
miR-6511a-3p	0.196	4.865	0.222	0.614
miR-4446-3p	0.245	3.069	0.222	0.614
miR-1233-3p	1.024	-0.544	0.223	0.614
miR-29a-3p	-0.360	9.472	0.227	0.619
miR-1250-5p	-0.155	0.691	0.228	0.619
let-7e-5p	0.217	9.484	0.229	0.619
miR-548d-5p	-0.185	12.885	0.229	0.619
miR-487a-3p	0.382	0.530	0.237	0.638
miR-193a-5p	-0.485	3.243	0.243	0.648
miR-548d-3p	0.454	1.169	0.243	0.648
miR-130b-5p	0.165	5.414	0.246	0.648
miR-497-5p	-0.196	1.523	0.248	0.648
miR-1972	2.620	5.510	0.249	0.648
miR-6873-3p	-0.289	5.014	0.249	0.648
miR-4448	-0.265	4.223	0.249	0.648
miR-624-5p	-0.302	0.116	0.250	0.648
miR-374b-3p	0.198	1.235	0.254	0.655
miR-20b-5p	-0.151	5.620	0.254	0.655
miR-495-5p	-0.277	-0.270	0.260	0.665
miR-301b	0.174	1.088	0.261	0.665
miR-24-3p	-0.078	12.655	0.264	0.665
miR-671-5p	-0.210	4.210	0.264	0.665
miR-548c-3p	-0.556	2.905	0.266	0.665
miR-429	-0.167	0.270	0.267	0.665
miR-2110	-0.296	3.338	0.267	0.665
miR-7849-3p	0.175	0.247	0.268	0.665
miR-19b-3p	-0.263	10.256	0.270	0.668
miR-330-3p	0.090	3.864	0.272	0.670
miR-376a-5p	-0.350	0.104	0.274	0.672
let-7g-3p	-0.248	0.220	0.278	0.676
miR-3613-5p	-0.275	9.506	0.280	0.676
miR-545-3p	0.217	1.909	0.281	0.676
let-7g-5p	0.080	10.980	0.283	0.676
miR-15a-5p	-0.157	9.211	0.283	0.676
miR-181d-5p	0.136	3.947	0.285	0.676
miR-1307-3p	-0.265	7.329	0.286	0.676
miR-126-5p	0.166	11.057	0.286	0.676
miR-574-3p	0.133	5.403	0.288	0.676
miR-221-3p	0.102	11.513	0.288	0.676
miR-362-5p	-0.142	2.457	0.288	0.676
miR-130b-3p	0.095	5.063	0.290	0.678
miR-1271-5p	-0.140	1.919	0.291	0.679
miR-548e-5p	-0.272	1.838	0.297	0.688
miR-3065-3p	-0.179	0.404	0.300	0.691
miR-29a-5p	0.160	0.831	0.300	0.691
miR-95-3p	-0.236	2.108	0.303	0.695
miR-30e-3p	0.149	7.059	0.305	0.695

miR-31-5p	-0.387	2.641	0.305	0.695
miR-483-5p	-0.617	1.834	0.315	0.712
miR-144-5p	-0.293	7.018	0.316	0.712
miR-5010-5p	-0.365	0.210	0.318	0.714
miR-320a	-0.232	11.779	0.320	0.717
miR-1285-3p	-0.156	8.508	0.322	0.718
miR-5096	-0.816	11.722	0.324	0.718
miR-378a-3p	-0.114	9.082	0.324	0.718
miR-1246	-0.379	5.861	0.326	0.718
miR-320b	-0.272	8.897	0.327	0.718
miR-5585-3p	-1.718	6.719	0.329	0.720
miR-548a-5p	0.308	1.849	0.334	0.728
miR-6516-5p	0.140	1.586	0.335	0.728
miR-1468-5p	0.124	0.552	0.340	0.733
miR-320c	-0.261	8.553	0.340	0.733
miR-3143	-0.152	-0.186	0.344	0.740
miR-378c	-0.129	5.108	0.346	0.740
miR-18b-5p	-0.162	2.410	0.348	0.741
miR-191-5p	0.079	12.565	0.351	0.741
miR-100-5p	-0.311	2.346	0.351	0.741
miR-186-5p	-0.110	8.853	0.351	0.741
miR-432-5p	-0.256	7.959	0.352	0.741
miR-125b-5p	0.136	8.080	0.356	0.742
miR-6852-5p	-0.223	2.746	0.357	0.742
miR-143-5p	0.225	1.979	0.357	0.742
let-7f-2-3p	-0.257	0.250	0.358	0.742
miR-504-5p	0.175	0.213	0.361	0.743
miR-1185-2-3p	0.249	0.123	0.361	0.743
miR-1271-3p	0.667	-0.768	0.367	0.749
miR-671-3p	-0.187	3.284	0.368	0.749
miR-1255b-5p	-0.217	7.593	0.368	0.749
miR-125a-3p	-0.189	0.692	0.369	0.749
miR-1294	-0.198	1.946	0.378	0.760
miR-376a-3p	0.259	6.560	0.378	0.760
miR-548f-5p	-0.617	0.762	0.378	0.760
miR-320d	-0.202	7.345	0.381	0.761
miR-548y	-0.913	-0.318	0.382	0.761
miR-548e-3p	0.154	2.682	0.383	0.761
miR-760	-0.272	1.310	0.384	0.761
miR-450b-5p	-0.205	2.048	0.385	0.762
let-7a-3p	-0.213	4.497	0.387	0.762
miR-376b-3p	0.260	3.330	0.392	0.770
miR-431-5p	-0.187	7.576	0.394	0.771
miR-136-5p	-0.235	2.770	0.397	0.771
miR-151a-3p	0.064	12.424	0.398	0.771
miR-29b-3p	-0.212	9.739	0.398	0.771
miR-182-5p	-0.158	7.556	0.401	0.774
miR-15b-3p	-0.148	5.648	0.407	0.780
miR-548ax	0.114	5.062	0.408	0.780
miR-20a-3p	0.103	1.922	0.408	0.780
miR-548as-5p	0.295	3.448	0.411	0.784
miR-1290	-0.334	4.532	0.418	0.795
miR-452-5p	-0.198	2.671	0.420	0.795
miR-1299	-0.665	4.630	0.421	0.795
miR-374b-5p	0.150	6.920	0.430	0.810
miR-4507	1.007	1.601	0.434	0.810
miR-30c-5p	0.117	11.296	0.436	0.810
miR-376c-3p	0.233	5.292	0.439	0.810
miR-454-5p	-0.061	3.780	0.440	0.810
miR-199a-5p	-0.111	8.817	0.442	0.810
miR-1304-5p	0.685	0.167	0.444	0.810
miR-6772-3p	0.171	0.690	0.445	0.810
miR-4772-3p	-0.276	1.699	0.445	0.810
miR-483-3p	-0.400	1.205	0.448	0.810
miR-20a-5p	0.089	9.087	0.448	0.810
miR-369-3p	0.240	4.919	0.449	0.810
miR-411-5p	0.183	5.491	0.449	0.810
miR-23a-5p	-0.189	1.003	0.449	0.810
miR-873-5p	-0.269	1.352	0.450	0.810
miR-4301	-0.455	2.532	0.451	0.810
let-7c-5p	0.099	9.528	0.455	0.815
miR-29c-3p	-0.183	8.568	0.461	0.816
miR-329-3p	-0.157	5.645	0.463	0.816
miR-27a-3p	-0.152	9.739	0.466	0.816
miR-1229-3p	0.163	0.765	0.466	0.816
let-7d-3p	-0.066	6.419	0.467	0.816
miR-3138	-0.170	2.724	0.471	0.816
miR-181a-5p	-0.106	10.817	0.473	0.816
miR-17-3p	-0.089	3.215	0.473	0.816
miR-548g-3p	0.711	1.192	0.473	0.816
miR-153-3p	0.182	0.310	0.474	0.816
miR-1306-5p	-0.256	2.765	0.479	0.816
miR-450a-5p	-0.216	0.853	0.480	0.816
miR-1273g-3p	-1.238	11.153	0.481	0.816
miR-548aa	-0.229	10.786	0.481	0.816
miR-548t-3p	-0.229	10.786	0.481	0.816
miR-548f-3p	0.207	5.197	0.481	0.816
miR-503-5p	-0.112	3.907	0.481	0.816
miR-548ap-3p	-0.231	10.374	0.482	0.816
miR-142-5p	-0.126	10.854	0.482	0.816
miR-1260b	0.105	3.783	0.485	0.816
miR-181a-2-3p	0.073	5.645	0.486	0.816
miR-1268a	-0.657	3.542	0.487	0.816
miR-4326	-0.270	1.874	0.489	0.816
miR-154-5p	-0.214	3.881	0.490	0.816
miR-143-3p	0.167	9.208	0.490	0.816
miR-9-5p	0.117	5.867	0.493	0.816

miR-342-3p	-0.109	10.283	0.493	0.816
miR-210-3p	-0.083	2.393	0.495	0.816
miR-548a-3p	0.130	5.676	0.496	0.816
miR-3194-3p	-0.309	0.002	0.498	0.817
miR-2355-5p	-0.150	0.457	0.501	0.819
miR-381-3p	-0.152	5.537	0.502	0.819
miR-548h-3p	-0.265	8.937	0.505	0.819
miR-548z	-0.265	8.937	0.505	0.819
miR-1268b	0.419	0.512	0.512	0.827
miR-487a-5p	0.159	0.384	0.513	0.827
miR-22-5p	0.089	3.999	0.514	0.827
miR-191-3p	-0.065	3.805	0.522	0.837
miR-218-5p	-0.374	1.231	0.523	0.837
miR-889-3p	0.169	3.340	0.525	0.837
miR-1301-3p	-0.122	5.720	0.528	0.837
miR-619-5p	0.709	11.202	0.529	0.837
miR-377-5p	-0.152	-0.095	0.531	0.837
miR-140-5p	-0.072	6.331	0.531	0.837
miR-3161	0.517	-0.951	0.532	0.837
miR-09b-3p	0.130	2.773	0.533	0.837
miR-548o-3p	-0.280	2.775	0.537	0.840
miR-548x-3p	0.760	2.828	0.537	0.840
miR-299-3p	0.190	0.096	0.539	0.840
miR-625-3p	0.114	6.770	0.541	0.840
miR-6500-3p	0.374	-0.223	0.543	0.840
miR-134-5p	0.162	7.091	0.543	0.840
miR-29e-5p	-0.053	4.579	0.549	0.845
miR-3187-3p	-0.138	0.369	0.550	0.845
miR-485-5p	-0.194	3.492	0.551	0.845
miR-6859-5p	-0.135	3.735	0.554	0.847
miR-215-5p	0.120	2.194	0.557	0.848
miR-18a-5p	0.060	7.212	0.559	0.848
miR-548aq-3p	0.109	9.450	0.560	0.848
miR-548q	0.122	4.336	0.561	0.848
miR-185-5p	0.044	9.811	0.562	0.848
miR-4477b	0.180	0.399	0.564	0.848
miR-1302	0.605	2.800	0.567	0.848
miR-99a-5p	-0.097	4.162	0.568	0.848
miR-3605-3p	-0.128	1.394	0.572	0.848
miR-5095	1.128	8.523	0.573	0.848
miR-328-3p	-0.123	5.945	0.575	0.848
miR-7851-3p	-0.174	3.495	0.577	0.848
miR-329-5p	-0.149	2.442	0.581	0.848
miR-6741-3p	0.153	0.231	0.582	0.848
miR-125a-5p	0.119	9.141	0.583	0.848
miR-548b-5p	0.111	7.793	0.584	0.848
miR-99b-5p	0.103	7.865	0.585	0.848
miR-324-5p	-0.048	5.454	0.588	0.848
miR-3198	-0.168	0.544	0.589	0.848
miR-424-3p	-0.097	0.968	0.589	0.848
miR-197-3p	-0.073	6.745	0.590	0.848
miR-299-5p	0.123	2.468	0.590	0.848
miR-598-3p	-0.113	4.565	0.590	0.848
miR-1285-5p	0.259	8.438	0.591	0.848
miR-548j-3p	0.149	0.393	0.592	0.848
miR-494-3p	0.130	5.857	0.595	0.848
miR-548k	0.068	1.443	0.595	0.848
miR-3179	0.206	-0.272	0.596	0.848
miR-1270	-0.143	3.003	0.597	0.848
miR-379-3p	0.129	1.468	0.597	0.848
miR-548t-5p	-0.150	1.936	0.602	0.848
miR-379-5p	0.116	7.187	0.602	0.848
miR-195-5p	0.073	3.376	0.603	0.848
miR-3620-5p	0.390	3.024	0.604	0.848
miR-33a-5p	0.097	1.653	0.605	0.848
miR-142-3p	0.070	13.185	0.608	0.849
miR-21-5p	0.080	12.294	0.608	0.849
miR-3064-5p	0.060	0.924	0.610	0.850
miR-146a-3p	0.565	2.291	0.613	0.850
miR-4435	-0.119	1.570	0.614	0.850
miR-548n	0.073	4.212	0.615	0.850
miR-548av-5p	0.064	1.444	0.617	0.851
miR-181b-3p	-0.159	0.083	0.620	0.853
miR-487b-5p	-0.121	0.849	0.621	0.853
miR-330-5p	-0.036	3.616	0.628	0.860
miR-32-5p	0.084	5.289	0.631	0.860
miR-2355-3p	-0.050	3.959	0.632	0.860
miR-107	-0.041	10.028	0.633	0.860
miR-7-1-3p	0.078	2.452	0.634	0.860
miR-744-3p	-0.132	-0.457	0.638	0.863
miR-190a-5p	0.077	5.571	0.642	0.864
miR-3173-5p	-0.137	1.011	0.644	0.864
miR-342-5p	0.074	3.944	0.647	0.864
miR-6803-3p	-0.148	-0.112	0.647	0.864
miR-1	-0.163	8.318	0.647	0.864
miR-3960	-0.367	3.467	0.648	0.864
miR-628-3p	0.053	5.661	0.649	0.864
miR-146b-5p	0.070	9.310	0.650	0.864
miR-106b-5p	0.097	4.658	0.652	0.865
miR-6842-3p	-0.061	1.371	0.658	0.867
miR-98-3p	-0.108	0.779	0.659	0.867
miR-625-3p	-0.098	8.394	0.660	0.867
miR-132-3p	-0.048	3.504	0.660	0.867
miR-103a-2-5p	0.126	-0.340	0.661	0.867
miR-4742-3p	0.068	1.378	0.662	0.867
miR-4433b-3p	-0.137	2.351	0.664	0.867
miR-885-5p	-0.203	0.498	0.670	0.874

miR-551b-3p	0.079	1.815	0.674	0.875
miR-548i	-0.250	3.203	0.675	0.875
miR-3133	-0.280	-0.564	0.688	0.880
miR-548aj-5p	-0.202	7.504	0.689	0.880
miR-548g-5p	-0.202	7.504	0.689	0.880
miR-548x-5p	-0.202	7.504	0.689	0.880
miR-543	0.081	3.379	0.689	0.880
miR-181c-3p	-0.053	3.538	0.689	0.880
miR-148b-5p	-0.035	2.775	0.690	0.880
miR-1179	-0.051	1.832	0.693	0.880
miR-4662a-5p	0.072	1.907	0.693	0.880
miR-181a-3p	0.070	4.944	0.693	0.880
let-7i-5p	0.033	13.259	0.701	0.886
miR-122-5p	-0.203	11.047	0.703	0.886
miR-548ar-5p	-0.201	7.739	0.706	0.886
miR-101-3p	-0.058	11.459	0.706	0.886
miR-145-5p	-0.073	6.318	0.709	0.886
miR-487b-3p	-0.084	5.402	0.710	0.886
miR-377-3p	0.093	2.438	0.712	0.886
miR-23b-5p	-0.071	1.691	0.713	0.886
miR-548ah-3p	0.227	2.757	0.715	0.886
miR-19b-1-5p	0.046	0.495	0.716	0.886
miR-548p	0.203	1.823	0.717	0.886
miR-548ai	0.297	0.527	0.718	0.886
miR-570-5p	0.297	0.527	0.718	0.886
miR-141-3p	-0.060	3.127	0.720	0.888
miR-222-3p	-0.036	8.603	0.726	0.893
miR-548aq-5p	0.291	2.543	0.731	0.897
let-7a-5p	0.049	17.835	0.733	0.898
miR-1185-1-3p	0.082	3.358	0.740	0.900
miR-323a-3p	-0.069	4.078	0.740	0.900
miR-301a-3p	0.039	5.377	0.740	0.900
miR-200a-3p	0.039	2.514	0.746	0.904
miR-409-3p	0.074	8.698	0.747	0.904
miR-27b-5p	0.044	1.148	0.748	0.904
miR-181c-5p	0.056	3.046	0.749	0.904
miR-496	0.086	1.970	0.756	0.910
miR-6511b-3p	0.053	2.078	0.757	0.910
miR-1185-5p	0.090	2.420	0.762	0.911
miR-421	0.021	5.199	0.764	0.911
let-7d-5p	0.036	10.427	0.764	0.911
miR-1304-3p	-0.211	3.254	0.767	0.911
miR-1287-5p	0.033	3.050	0.770	0.911
miR-337-5p	-0.074	3.963	0.772	0.911
miR-200b-3p	-0.036	2.188	0.772	0.911
miR-29b-1-5p	-0.050	0.138	0.773	0.911
miR-505-5p	0.056	3.558	0.774	0.911
miR-548ag	-0.063	6.333	0.775	0.911
miR-544a	-0.137	0.669	0.776	0.911
miR-382-5p	0.070	8.383	0.778	0.911
miR-548h-5p	0.110	6.935	0.780	0.911
miR-3140-3p	-0.044	0.699	0.780	0.911
miR-556-3p	0.056	1.254	0.781	0.911
miR-4454	0.065	9.159	0.783	0.912
miR-574-5p	-0.198	14.568	0.786	0.913
miR-4659a-3p	0.047	0.124	0.795	0.921
miR-4433b-5p	0.064	7.929	0.797	0.923
miR-942-5p	-0.022	4.976	0.807	0.932
miR-509-3p	-0.079	2.288	0.808	0.932
miR-378f	-0.037	1.820	0.811	0.933
miR-376b-5p	0.094	1.487	0.812	0.933
miR-376c-5p	0.091	1.518	0.816	0.933
miR-19a-3p	0.044	5.810	0.817	0.933
miR-128-3p	0.019	10.346	0.818	0.933
miR-651-5p	0.044	1.314	0.819	0.933
miR-576-3p	0.024	5.501	0.821	0.933
miR-139-3p	-0.064	4.524	0.822	0.933
miR-127-3p	-0.047	7.007	0.824	0.934
miR-589-3p	0.024	1.137	0.827	0.935
miR-3913-5p	0.029	2.448	0.834	0.940
miR-542-3p	-0.052	2.341	0.835	0.940
miR-7110-3p	0.063	-0.067	0.839	0.941
miR-1226-3p	0.043	1.073	0.840	0.941
miR-664a-5p	-0.033	5.295	0.840	0.941
miR-1306-3p	0.035	2.215	0.842	0.941
miR-323b-3p	-0.044	4.932	0.846	0.941
miR-877-5p	0.019	2.378	0.846	0.941
miR-548an	0.077	1.688	0.847	0.941
miR-335-3p	-0.030	5.333	0.858	0.951
miR-23c	0.021	0.292	0.859	0.951
miR-127-5p	0.040	1.654	0.867	0.958
miR-548ak	0.119	2.923	0.881	0.967
miR-708-5p	0.090	2.615	0.882	0.967
miR-132-5p	0.019	0.644	0.883	0.967
miR-136-3p	0.052	3.534	0.886	0.967
miR-758-3p	0.036	1.734	0.887	0.967
miR-664b-5p	-0.031	1.474	0.888	0.967
miR-485-3p	0.047	5.831	0.889	0.967
miR-584-5p	-0.020	9.252	0.889	0.967
miR-30b-5p	0.040	7.651	0.892	0.967
miR-505-3p	-0.010	4.359	0.893	0.967
miR-548av-3p	-0.055	3.903	0.893	0.967
miR-654-3p	0.029	7.125	0.900	0.968
miR-4659b-3p	0.017	0.948	0.901	0.968
miR-23a-3p	0.010	11.962	0.904	0.968
miR-145-3p	0.024	1.763	0.905	0.968
miR-548ae	0.165	3.953	0.905	0.968

miR-493-5p	0.027	5.498	0.905	0.968
miR-378g	0.033	0.027	0.905	0.968
miR-5187-5p	0.024	2.108	0.910	0.969
miR-5189-3p	0.046	0.435	0.911	0.969
miR-6859-3p	-0.055	0.719	0.912	0.969
miR-584-3p	-0.019	0.426	0.913	0.969
miR-877-3p	0.039	2.150	0.916	0.970
miR-1249	0.032	0.351	0.919	0.970
miR-493-3p	-0.023	5.508	0.919	0.970
miR-15b-5p	0.013	9.487	0.928	0.978
miR-369-5p	0.018	5.217	0.932	0.980
miR-548al	0.066	-0.392	0.936	0.983
miR-301a-5p	-0.015	1.602	0.940	0.983
miR-5010-3p	-0.008	1.408	0.942	0.983
miR-6734-5p	-0.016	0.555	0.946	0.983
miR-2277-5p	0.035	0.413	0.947	0.983
miR-655-3p	0.025	-0.112	0.948	0.983
miR-3074-5p	-0.017	1.854	0.949	0.983
miR-361-5p	-0.004	8.171	0.950	0.983
miR-548az-5p	0.025	5.839	0.951	0.983
miR-28-3p	0.005	10.686	0.954	0.983
miR-744-5p	-0.010	7.986	0.956	0.983
miR-219a-5p	0.013	1.164	0.957	0.983
miR-3065-5p	-0.008	2.573	0.958	0.983
miR-548l	-0.008	1.877	0.959	0.983
miR-548at-5p	0.013	4.401	0.959	0.983
miR-30d-3p	0.005	1.671	0.974	0.994
miR-337-3p	0.009	2.407	0.975	0.994
miR-30a-3p	-0.003	3.079	0.976	0.994
miR-6511a-5p	-0.016	1.038	0.980	0.994
miR-1273h-5p	-0.004	11.451	0.983	0.994
miR-433-3p	-0.005	1.880	0.984	0.994
miR-652-3p	-0.002	7.109	0.985	0.994
miR-1273c	0.003	1.024	0.986	0.994
miR-148a-3p	-0.002	10.002	0.986	0.994
miR-6511b-5p	0.010	1.158	0.987	0.994
miR-409-5p	0.002	3.705	0.990	0.996
miR-6770-3p	-0.003	0.142	0.992	0.996
miR-548w	0.003	5.896	0.994	0.996
miR-27b-3p	0.000	10.051	0.998	0.998
miRNA	log-fold change	log-counts per million	p-value	adjusted p-value
Presymptomatic vs. Patient				
miR-345-5p	-0.528	4.607	3.610E-05	0.021
miR-205-5p	-1.421	2.270	0.000	0.065
miR-206	-2.218	1.104	0.000	0.065
miR-18a-3p	-0.586	2.363	0.001	0.083
miR-93-3p	-0.426	4.195	0.001	0.083
miR-106b-3p	-0.477	6.995	0.001	0.083
miR-548am-c-o-5p	0.497	14.295	0.001	0.083
miR-548au-5p	0.480	14.473	0.001	0.083
miR-551a	-1.098	-0.321	0.002	0.097
miR-218-5p	-1.849	1.231	0.002	0.097
miR-542-5p	-0.709	1.306	0.002	0.097
let-7b-3p	-0.484	1.579	0.003	0.137
miR-151a-5p	0.394	11.573	0.004	0.150
miR-151b	0.389	11.596	0.004	0.150
miR-223-3p	-0.300	14.649	0.005	0.190
miR-374a-3p	0.627	2.987	0.005	0.190
miR-130a-3p	0.399	7.658	0.005	0.190
miR-375	-1.131	2.730	0.006	0.195
miR-1303	-1.405	4.458	0.007	0.224
miR-148a-5p	-0.428	0.933	0.009	0.224
miR-548u	1.339	1.210	0.009	0.224
miR-10b-5p	-0.741	4.540	0.009	0.224
miR-17-5p	0.416	8.427	0.009	0.224
miR-618	-1.220	-0.303	0.010	0.224
miR-25-3p	-0.293	10.901	0.010	0.224
miR-3615	-0.822	5.538	0.010	0.224
miR-625-3p	-0.593	8.394	0.010	0.224
miR-154-3p	0.944	0.419	0.011	0.224
miR-26b-5p	0.296	12.787	0.012	0.226
miR-378a-5p	-0.478	2.841	0.012	0.226
miR-550a-3p	-0.674	3.973	0.012	0.226
miR-590-5p	0.686	0.651	0.013	0.232
miR-941	-0.475	9.475	0.015	0.232
miR-616-3p	-0.532	0.543	0.015	0.232
miR-331-3p	0.332	4.398	0.015	0.232
miR-10a-3p	0.428	1.500	0.016	0.232
miR-365a-3p	-0.696	4.151	0.016	0.232
miR-365b-3p	-0.696	4.151	0.016	0.232
miR-502-3p	-0.330	3.800	0.016	0.232
miR-340-5p	0.441	6.743	0.016	0.232
miR-487a-3p	0.824	0.530	0.017	0.232
miR-374a-5p	0.488	7.594	0.017	0.232
miR-224-5p	-0.706	7.850	0.017	0.232
miR-148b-3p	0.301	9.436	0.018	0.232
miR-550a-3-5p	-0.436	2.398	0.018	0.232
miR-532-3p	-0.462	2.783	0.019	0.237
miR-590-3p	0.630	6.770	0.019	0.237
miR-340-3p	0.235	3.655	0.021	0.240
miR-183-5p	-0.695	5.546	0.022	0.240
miR-629-5p	-0.370	6.404	0.023	0.240

miR-539-3p	0.815	1.473	0.023	0.240
miR-7976	-0.387	1.801	0.023	0.240
miR-1289	-1.074	-0.148	0.023	0.240
miR-642a-3p	-0.683	0.484	0.024	0.240
miR-628-5p	0.286	4.677	0.024	0.240
miR-100-5p	-0.778	2.346	0.025	0.240
miR-200c-3p	0.183	5.273	0.025	0.240
miR-6873-3p	-0.586	5.014	0.025	0.240
miR-92a-3p	-0.495	13.677	0.025	0.240
miR-223-5p	-0.246	7.682	0.025	0.240
miR-203a	-0.610	-0.173	0.026	0.240
miR-146a-5p	0.232	12.934	0.026	0.240
miR-28-5p	0.196	6.656	0.026	0.240
let-7f-5p	0.224	16.225	0.028	0.259
miR-7706	-0.588	-0.037	0.030	0.264
miR-3120-3p	0.288	2.583	0.030	0.264
miR-378i	-0.285	4.394	0.030	0.264
miR-589-5p	-0.253	3.684	0.031	0.264
miR-484	-0.502	7.854	0.031	0.264
miR-382-3p	0.578	3.232	0.032	0.269
miR-1277-3p	0.473	1.948	0.032	0.269
miR-32-3p	0.424	0.143	0.033	0.270
miR-1277-5p	0.463	12.138	0.033	0.270
miR-376b-3p	0.671	3.330	0.034	0.270
miR-133a-3p	-0.671	7.345	0.034	0.270
miR-4677-3p	0.374	0.746	0.036	0.271
miR-9-3p	0.380	3.953	0.037	0.271
miR-545-5p	0.537	1.482	0.037	0.271
miR-139-5p	0.454	6.068	0.038	0.271
miR-92b-5p	-0.857	-0.009	0.039	0.271
miR-369-3p	0.685	4.919	0.039	0.271
miR-92b-3p	-0.530	3.086	0.040	0.271
miR-3928-3p	-0.393	0.931	0.040	0.271
let-7b-5p	-0.395	12.514	0.040	0.271
miR-296-5p	-0.499	1.358	0.040	0.271
miR-514a-3p	0.933	0.606	0.040	0.271
miR-25-5p	-0.435	2.573	0.041	0.271
miR-576-5p	-0.290	6.414	0.042	0.271
miR-7641	-0.638	5.298	0.042	0.271
miR-301b	0.333	1.088	0.043	0.271
miR-196b-5p	0.190	5.658	0.043	0.271
miR-500a-3p	-0.248	4.766	0.043	0.271
miR-451a	-0.491	11.183	0.044	0.271
miR-153-3p	0.543	0.310	0.044	0.271
miR-652-5p	0.405	1.446	0.044	0.271
miR-425-3p	-0.182	6.606	0.045	0.271
miR-193a-5p	-0.874	3.243	0.045	0.271
miR-412-5p	1.044	2.206	0.045	0.271
miR-374b-3p	0.372	1.235	0.046	0.271
miR-539-5p	0.706	0.162	0.046	0.271
miR-199a-3p	0.283	15.594	0.047	0.271
miR-199b-3p	0.283	15.594	0.047	0.271
miR-550a-5p	-0.401	1.899	0.048	0.274
miR-142-3p	0.288	13.185	0.048	0.274
miR-140-3p	-0.166	9.249	0.050	0.278
miR-425-5p	-0.210	10.913	0.050	0.278
miR-32-5p	0.365	5.289	0.051	0.278
miR-501-3p	-0.470	2.746	0.051	0.278
miR-125a-3p	-0.437	0.692	0.052	0.279
miR-362-5p	-0.275	2.457	0.053	0.283
miR-4732-3p	-0.921	3.928	0.053	0.283
miR-197-3p	-0.280	6.745	0.054	0.284
miR-23b-5p	-0.398	1.691	0.054	0.284
miR-335-5p	0.338	7.461	0.055	0.284
miR-1180-3p	-0.775	2.024	0.056	0.287
miR-26a-5p	0.175	15.391	0.057	0.291
miR-641	0.209	1.385	0.058	0.291
miR-423-3p	-0.376	8.841	0.059	0.293
miR-548aq-3p	0.374	9.450	0.059	0.293
miR-5010-3p	-0.214	1.408	0.060	0.293
miR-486-5p	-0.676	14.249	0.060	0.293
let-7d-3p	-0.182	6.419	0.061	0.293
miR-495-3p	0.483	3.399	0.064	0.307
miR-3679-5p	-0.380	2.384	0.069	0.318
miR-769-3p	-0.392	0.674	0.070	0.318
miR-3613-5p	-0.498	9.506	0.070	0.318
miR-320c	-0.521	8.553	0.070	0.318
miR-301a-3p	0.225	5.377	0.070	0.318
miR-4685-3p	-0.560	0.669	0.072	0.318
miR-532-5p	-0.246	5.499	0.072	0.318
miR-2115-3p	-0.721	0.295	0.072	0.318
miR-320b	-0.524	8.897	0.073	0.318
miR-769-5p	-0.123	4.654	0.073	0.318
miR-150-3p	-0.511	1.296	0.073	0.318
miR-548h-5p	0.779	6.935	0.074	0.318
miR-545-3p	0.383	1.909	0.074	0.318
miR-18a-5p	0.197	7.212	0.075	0.318
miR-33a-5p	0.358	1.653	0.075	0.318
miR-548ab	1.175	4.211	0.076	0.318
miR-361-3p	-0.176	6.970	0.076	0.318
miR-324-3p	-0.176	4.372	0.077	0.319

miR-889-3p	0.491	3.340	0.077	0.319
miR-93-5p	-0.132	11.309	0.078	0.319
miR-133b	-0.707	-0.138	0.078	0.319
miR-3158-3p	-0.626	1.499	0.079	0.321
miR-204-5p	0.480	1.457	0.082	0.327
miR-6852-5p	-0.445	2.746	0.083	0.327
miR-106a-5p	0.324	1.761	0.084	0.327
miR-486-3p	-0.521	5.430	0.084	0.327
miR-4785	-0.266	0.526	0.084	0.327
miR-320d	-0.422	7.345	0.084	0.327
miR-548d-3p	0.731	1.169	0.084	0.327
miR-361-5p	-0.128	8.171	0.085	0.328
miR-378a-3p	-0.212	9.082	0.086	0.328
miR-548j-3p	0.504	0.393	0.087	0.332
miR-29a-5p	0.275	0.831	0.091	0.345
miR-551b-3p	0.337	1.815	0.092	0.345
let-7g-5p	0.133	10.980	0.093	0.347
miR-30e-3p	0.260	7.059	0.094	0.348
miR-942-5p	-0.162	4.976	0.097	0.356
miR-423-5p	-0.571	10.597	0.098	0.357
miR-126-3p	0.141	14.192	0.100	0.357
miR-26b-3p	-0.152	3.623	0.100	0.357
miR-370-3p	-0.494	5.773	0.101	0.357
miR-30b-3p	0.226	0.223	0.101	0.357
miR-181b-5p	-0.234	8.044	0.101	0.357
miR-1908-5p	-0.625	2.300	0.102	0.357
miR-411-5p	0.408	5.491	0.102	0.357
miR-376a-3p	0.498	6.560	0.104	0.357
miR-424-3p	-0.315	0.968	0.104	0.357
miR-660-5p	-0.229	5.628	0.104	0.357
miR-19a-3p	0.330	5.810	0.105	0.357
miR-126-5p	0.269	11.057	0.105	0.357
miR-509-3p	-0.548	2.288	0.106	0.357
miR-26a-1-3p	0.161	2.985	0.107	0.357
miR-760	-0.534	1.310	0.108	0.357
miR-152-3p	0.194	7.210	0.109	0.357
miR-1233-3p	1.403	-0.544	0.109	0.357
miR-1185-2-3p	0.452	0.123	0.109	0.357
miR-30a-5p	-0.208	6.368	0.110	0.357
miR-376c-3p	0.501	5.292	0.110	0.357
miR-30d-5p	-0.119	11.785	0.111	0.357
miR-106b-5p	0.368	4.658	0.112	0.357
miR-16-5p	-0.169	17.408	0.112	0.357
miR-491-5p	-0.207	3.945	0.112	0.357
miR-487a-5p	0.397	0.384	0.113	0.359
miR-548f-3p	0.497	5.197	0.115	0.361
miR-9-5p	0.285	5.867	0.115	0.361
miR-299-3p	0.512	0.096	0.116	0.361
miR-500a-5p	-0.358	3.026	0.117	0.361
miR-548p	0.989	1.823	0.118	0.361
miR-671-3p	-0.345	3.284	0.118	0.361
miR-3138	-0.395	2.724	0.119	0.363
miR-1307-3p	-0.407	7.329	0.120	0.366
miR-363-3p	-0.265	6.300	0.122	0.367
miR-377-3p	0.400	2.438	0.122	0.367
miR-185-3p	-0.256	4.607	0.123	0.368
miR-320a	-0.378	11.779	0.125	0.368
miR-146b-3p	-0.190	3.582	0.125	0.368
miR-1233-5p	-1.423	-0.221	0.125	0.368
miR-548e-3p	0.286	2.682	0.125	0.368
miR-1273h-3p	-0.305	7.277	0.127	0.370
miR-99a-5p	-0.266	4.162	0.132	0.380
miR-1296-5p	-0.156	2.226	0.132	0.380
miR-21-5p	0.252	12.294	0.132	0.380
miR-548a-5p	0.521	1.849	0.135	0.385
miR-671-5p	-0.294	4.210	0.139	0.395
miR-548am-3p	1.402	2.613	0.140	0.396
miR-20a-5p	0.186	9.087	0.141	0.397
miR-500b-5p	-0.369	2.709	0.142	0.398
miR-3180-5p	-0.890	-0.295	0.144	0.401
miR-190b	-0.127	3.267	0.145	0.401
miR-496	0.423	1.970	0.145	0.401
miR-96-5p	-0.469	3.856	0.146	0.401
miR-3198	-0.481	0.544	0.151	0.414
miR-548ah-3p	1.009	2.757	0.152	0.414
miR-454-5p	-0.120	3.780	0.154	0.415
miR-150-5p	-0.416	10.272	0.155	0.415
miR-23a-5p	-0.375	1.003	0.155	0.415
miR-98-5p	0.141	8.594	0.156	0.415
miR-130b-3p	0.136	5.063	0.156	0.415
miR-20a-3p	0.186	1.922	0.159	0.418
miR-4732-5p	-0.674	3.999	0.159	0.418
miR-3605-3p	-0.338	1.394	0.159	0.418
miR-2110	-0.396	3.338	0.161	0.420
miR-144-3p	-0.394	5.293	0.162	0.420
miR-4448	-0.343	4.223	0.162	0.420
miR-454-3p	0.132	8.563	0.168	0.432
miR-222-3p	-0.152	8.603	0.169	0.432
miR-6859-5p	-0.327	3.735	0.170	0.432
miR-1268b	0.974	0.512	0.170	0.432
miR-7-5p	0.203	10.227	0.170	0.432

miR-1294	-0.324	1.946	0.171	0.433
miR-1285-5p	0.731	8.438	0.174	0.438
miR-483-5p	-0.869	1.834	0.176	0.440
miR-181a-5p	-0.208	10.817	0.179	0.447
miR-6513-5p	0.178	0.012	0.181	0.449
miR-30d-3p	0.218	1.671	0.181	0.449
miR-1255b-5p	-0.338	7.593	0.187	0.459
miR-548a-3p	0.272	5.676	0.187	0.459
miR-5095	2.977	8.523	0.189	0.463
miR-146b-5p	0.212	9.310	0.194	0.471
miR-4645-3p	0.185	0.811	0.195	0.471
miR-1972	3.618	5.510	0.196	0.471
miR-155-5p	0.135	8.603	0.196	0.471
miR-1270	-0.368	3.003	0.198	0.472
miR-103a-2-5p	0.391	-0.340	0.198	0.472
miR-1306-5p	-0.496	2.765	0.199	0.472
miR-196a-5p	-0.436	2.899	0.199	0.472
miR-192-5p	-0.197	7.507	0.200	0.472
miR-134-5p	0.349	7.091	0.203	0.477
miR-26a-2-3p	0.293	-0.153	0.208	0.486
miR-29b-2-5p	0.114	1.605	0.211	0.492
miR-651-5p	0.255	1.314	0.214	0.497
miR-1301-3p	-0.252	5.720	0.220	0.507
miR-330-3p	0.107	3.864	0.220	0.507
miR-5010-5p	-0.466	0.210	0.224	0.510
miR-132-3p	-0.139	3.504	0.224	0.510
miR-4477b	0.403	0.399	0.224	0.510
miR-136-3p	0.450	3.534	0.225	0.510
miR-548ax	0.179	5.062	0.226	0.510
miR-194-5p	-0.230	7.337	0.229	0.510
miR-122-5p	-0.655	11.047	0.231	0.510
miR-145-5p	-0.245	6.318	0.231	0.510
miR-24-3p	-0.088	12.655	0.232	0.510
miR-556-3p	0.258	1.254	0.232	0.510
miR-182-5p	-0.243	7.556	0.232	0.510
miR-1292-5p	-0.342	0.211	0.233	0.510
miR-665	-0.345	0.677	0.233	0.510
miR-3173-5p	-0.371	1.011	0.238	0.519
miR-548as-5p	0.457	3.448	0.241	0.522
miR-379-5p	0.269	7.187	0.241	0.522
miR-1304-3p	-0.927	3.254	0.248	0.533
miR-3913-5p	0.168	2.448	0.248	0.533
miR-885-5p	-0.573	0.498	0.249	0.533
miR-369-5p	0.247	5.217	0.254	0.540
miR-376c-5p	0.470	1.518	0.256	0.540
miR-432-5p	-0.313	7.959	0.257	0.540
miR-6842-3p	-0.164	1.371	0.258	0.540
miR-1290	-0.501	4.532	0.258	0.540
miR-17-3p	0.149	3.215	0.258	0.540
miR-219a-5p	0.291	1.164	0.259	0.541
miR-1250-5p	0.155	0.691	0.261	0.542
miR-191-3p	-0.122	3.805	0.261	0.542
miR-382-5p	0.282	8.383	0.263	0.544
miR-29b-1-5p	-0.204	0.138	0.264	0.544
miR-376b-5p	0.464	1.487	0.266	0.545
miR-5583-3p	0.235	0.528	0.267	0.545
miR-30b-5p	0.352	7.651	0.268	0.545
miR-548k	0.150	1.443	0.268	0.545
miR-1468-5p	0.150	0.552	0.274	0.555
miR-548av-5p	0.146	1.444	0.282	0.568
miR-548g-3p	1.256	1.192	0.286	0.574
miR-1246	-0.442	5.861	0.287	0.574
miR-374b-5p	0.214	6.920	0.288	0.574
miR-1255a	0.317	4.833	0.288	0.574
miR-6500-3p	0.674	-0.223	0.290	0.574
miR-548x-3p	1.500	2.828	0.292	0.574
miR-185-5p	0.085	9.811	0.292	0.574
miR-548al	0.909	-0.392	0.295	0.577
miR-655-3p	0.417	-0.112	0.295	0.577
miR-30c-5p	0.166	11.296	0.298	0.581
miR-627-5p	-0.113	0.873	0.300	0.581
miR-101-3p	0.168	11.459	0.302	0.581
miR-664b-5p	-0.242	1.474	0.304	0.581
miR-3180	-0.726	0.868	0.304	0.581
miR-3180-3p	-0.726	0.868	0.304	0.581
miR-548c-3p	-0.556	2.905	0.304	0.581
miR-4742-3p	-0.167	1.378	0.309	0.589
miR-328-3p	-0.238	5.945	0.311	0.592
miR-664a-5p	-0.176	5.295	0.313	0.592
miR-379-3p	0.253	1.468	0.315	0.595
miR-548ag	0.236	6.333	0.320	0.601
miR-22-5p	0.146	3.999	0.320	0.601
miR-503-5p	-0.168	3.907	0.327	0.609
miR-766-3p	-0.140	5.380	0.327	0.609
miR-1249	-0.314	0.351	0.329	0.611
miR-199a-5p	0.149	8.817	0.330	0.611
miR-330-5p	0.075	3.616	0.337	0.622
miR-1304-5p	0.967	0.167	0.338	0.622
miR-548n	0.144	4.212	0.343	0.628
miR-1306-3p	-0.175	2.215	0.343	0.628
miR-431-3p	-0.232	0.193	0.346	0.631

miR-30c-1-3p	0.093	2.582	0.350	0.637
miR-483-3p	-0.532	1.205	0.352	0.637
miR-1271-3p	0.730	-0.768	0.353	0.637
miR-337-5p	0.237	3.963	0.359	0.644
miR-7110-3p	-0.303	-0.067	0.360	0.644
miR-301a-5p	0.192	1.602	0.361	0.644
miR-1271-5p	-0.127	1.919	0.362	0.644
miR-151a-3p	0.074	12.424	0.362	0.644
miR-1185-1-3p	0.232	3.358	0.364	0.646
miR-664a-3p	0.108	4.261	0.367	0.649
miR-5009-5p	-0.255	0.291	0.370	0.651
miR-4286	-0.116	10.665	0.370	0.651
miR-181a-2-3p	0.098	5.645	0.372	0.651
miR-34a-5p	0.194	4.676	0.373	0.651
miR-548o-3p	-0.433	2.775	0.374	0.651
miR-5096	-0.744	11.722	0.375	0.651
miR-10a-5p	0.103	7.108	0.376	0.651
miR-6803-3p	-0.300	-0.112	0.379	0.655
miR-3065-3p	-0.161	0.404	0.384	0.661
miR-195-5p	0.126	3.376	0.387	0.665
miR-186-3p	-0.123	0.571	0.395	0.674
miR-181a-3p	0.160	4.944	0.395	0.674
miR-409-3p	0.197	8.698	0.400	0.675
miR-3200-3p	-0.268	0.193	0.400	0.675
miR-625-5p	-0.164	6.770	0.402	0.675
miR-326	-0.129	6.590	0.403	0.675
miR-342-3p	-0.139	10.283	0.404	0.675
miR-548an	0.340	1.688	0.404	0.675
miR-758-3p	0.222	1.734	0.405	0.675
miR-548t-5p	0.257	1.936	0.406	0.675
miR-103a-3p	0.064	15.095	0.406	0.675
miR-148b-5p	0.077	2.775	0.407	0.675
miR-378d	-0.451	0.023	0.410	0.678
miR-1302	0.901	2.800	0.411	0.679
miR-339-3p	-0.086	5.037	0.414	0.679
miR-190a-5p	0.144	5.571	0.415	0.679
miR-135a-5p	-0.243	1.965	0.417	0.679
miR-29b-3p	0.211	9.739	0.417	0.679
miR-3187-3p	-0.198	0.369	0.418	0.679
miR-744-5p	-0.159	7.986	0.420	0.681
miR-1185-5p	0.246	2.420	0.425	0.684
miR-424-5p	-0.195	3.748	0.425	0.684
miR-494-3p	0.203	5.857	0.425	0.684
miR-377-5p	0.198	-0.095	0.427	0.685
miR-409-5p	0.168	3.705	0.431	0.691
miR-1179	-0.107	1.832	0.433	0.692
miR-16-2-3p	-0.157	3.631	0.436	0.694
miR-299-5p	0.181	2.468	0.437	0.694
miR-6513-3p	0.070	1.835	0.441	0.696
miR-335-3p	-0.137	5.333	0.443	0.696
miR-215-5p	-0.157	2.194	0.444	0.696
miR-127-5p	0.187	1.654	0.445	0.696
miR-2277-5p	-0.095	0.413	0.445	0.696
miR-339-5p	-0.093	11.621	0.446	0.696
miR-664b-3p	0.111	2.162	0.453	0.705
miR-574-5p	-0.605	14.568	0.454	0.705
miR-548ak	0.655	2.923	0.456	0.705
miR-378g	-0.219	0.027	0.456	0.705
miR-4326	-0.312	1.874	0.459	0.708
miR-23c	-0.091	0.292	0.469	0.722
miR-125b-5p	-0.109	8.080	0.472	0.723
miR-181b-3p	0.238	0.083	0.473	0.723
miR-4435	-0.183	1.570	0.475	0.725
miR-6734-5p	-0.182	0.555	0.479	0.729
miR-6516-5p	0.110	1.586	0.481	0.731
miR-144-5p	-0.214	7.018	0.489	0.740
miR-27a-3p	0.154	9.739	0.491	0.740
miR-323b-3p	0.158	4.932	0.491	0.740
miR-1285-3p	-0.115	8.508	0.494	0.743
miR-199b-5p	-0.212	4.252	0.500	0.748
miR-27a-5p	0.160	2.220	0.500	0.748
miR-20b-5p	-0.094	5.620	0.504	0.752
miR-143-5p	0.171	1.979	0.506	0.752
miR-504-5p	0.133	0.213	0.508	0.754
miR-5187-5p	-0.146	2.108	0.514	0.761
miR-598-3p	0.143	4.565	0.518	0.764
miR-1307-5p	0.080	5.708	0.523	0.770
miR-542-3p	0.169	2.341	0.531	0.780
miR-548ap-5p	0.079	9.773	0.536	0.785
miR-3617-5p	0.136	0.442	0.538	0.785
miR-766-5p	0.084	2.287	0.539	0.785
miR-154-5p	0.196	3.881	0.539	0.785
miR-27b-3p	0.088	10.051	0.543	0.788
miR-654-3p	0.143	7.125	0.547	0.790
miR-139-3p	-0.182	4.524	0.548	0.790
miR-27b-5p	-0.088	1.148	0.550	0.790
miR-29c-3p	0.155	8.568	0.550	0.790
miR-548b-5p	0.127	7.793	0.552	0.790
miR-548az-5p	0.256	5.839	0.553	0.790
miR-23b-3p	0.054	9.599	0.557	0.792
miR-324-5p	0.055	5.454	0.559	0.792

miR-22-3p	-0.045	8.495	0.559	0.792
miR-3194-3p	0.272	0.002	0.560	0.792
miR-4446-3p	0.125	3.069	0.563	0.795
miR-142-5p	0.109	10.854	0.567	0.797
miR-136-5p	0.160	2.770	0.568	0.797
let-7c-5p	-0.079	9.528	0.568	0.797
miR-143-3p	0.144	9.208	0.571	0.797
miR-28-3p	-0.054	10.686	0.571	0.797
miR-4659b-3p	0.080	0.948	0.573	0.798
miR-30a-3p	0.058	3.079	0.575	0.798
miR-548l	-0.098	1.877	0.575	0.798
miR-1299	-0.475	4.630	0.577	0.798
miR-584-5p	-0.085	9.252	0.579	0.798
miR-23a-3p	-0.051	11.962	0.581	0.798
miR-493-3p	0.126	5.508	0.581	0.798
let-7a-5p	-0.082	17.835	0.585	0.802
miR-1273c	-0.103	1.024	0.588	0.802
miR-1260b	-0.086	3.783	0.589	0.802
miR-5193	0.087	1.173	0.589	0.802
miR-29c-5p	-0.049	4.579	0.594	0.806
miR-3133	-0.394	-0.564	0.596	0.806
miR-505-5p	-0.109	3.558	0.597	0.806
miR-485-3p	0.180	5.831	0.601	0.810
miR-7849-3p	0.085	0.247	0.609	0.819
miR-5585-3p	-0.858	6.719	0.618	0.830
miR-7851-3p	-0.161	3.495	0.627	0.835
miR-548ae	0.791	3.953	0.627	0.835
miR-7-1-3p	0.084	2.452	0.627	0.835
miR-548j-5p	0.063	9.735	0.628	0.835
miR-4662a-5p	0.091	1.907	0.632	0.837
miR-429	-0.075	0.270	0.632	0.837
let-7g-3p	0.112	0.220	0.638	0.842
miR-338-3p	-0.082	5.028	0.641	0.844
miR-19b-1-5p	0.061	0.495	0.645	0.846
miR-221-5p	0.044	5.310	0.645	0.846
miR-544a	0.230	0.669	0.646	0.846
miR-543	0.096	3.379	0.648	0.846
miR-431-5p	-0.101	7.576	0.650	0.847
miR-378c	-0.065	5.108	0.655	0.852
miR-493-5p	0.103	5.498	0.660	0.855
miR-5584-5p	0.087	0.672	0.662	0.855
let-7f-1-3p	-0.111	0.491	0.663	0.855
miR-329-5p	-0.118	2.442	0.663	0.855
miR-146a-3p	0.456	2.291	0.669	0.860
let-7d-5p	-0.054	10.427	0.672	0.862
miR-548q	-0.092	4.336	0.677	0.867
miR-191-5p	-0.037	12.565	0.681	0.870
miR-107	-0.037	10.028	0.682	0.870
miR-4301	-0.249	2.532	0.685	0.872
miR-873-5p	0.149	1.352	0.692	0.878
miR-1268a	0.398	3.542	0.698	0.884
miR-337-3p	0.121	2.407	0.706	0.892
miR-329-3p	-0.081	5.645	0.711	0.896
miR-1273g-3p	-0.663	11.153	0.712	0.896
miR-548w	0.143	5.896	0.716	0.897
miR-3620-5p	-0.312	3.024	0.717	0.897
miR-127-3p	-0.079	7.007	0.717	0.897
miR-548at-5p	0.101	4.401	0.719	0.897
miR-452-5p	-0.092	2.671	0.721	0.897
miR-381-3p	0.081	5.537	0.725	0.898
miR-378f	-0.058	1.820	0.726	0.898
miR-128-3p	0.031	10.346	0.727	0.898
miR-125a-5p	-0.079	9.141	0.727	0.898
miR-1226-3p	-0.076	1.073	0.735	0.903
miR-584-3p	0.064	0.426	0.735	0.903
miR-548av-3p	0.152	3.903	0.736	0.903
miR-3179	0.136	-0.272	0.739	0.904
miR-548y	0.353	-0.318	0.742	0.904
miR-548f-5p	-0.235	0.762	0.742	0.904
miR-98-3p	0.084	0.779	0.744	0.904
miR-3143	-0.055	-0.186	0.745	0.904
miR-3140-3p	-0.055	0.699	0.746	0.904
miR-3960	-0.260	3.467	0.752	0.907
miR-487b-5p	-0.078	0.849	0.754	0.907
miR-495-5p	-0.079	-0.270	0.755	0.907
miR-145-3p	-0.065	1.763	0.755	0.907
miR-15b-3p	-0.056	5.648	0.765	0.918
miR-548i	-0.182	3.203	0.776	0.927
miR-485-5p	-0.093	3.492	0.776	0.927
miR-4659a-3p	-0.054	0.124	0.780	0.929
miR-140-5p	0.034	6.331	0.782	0.929
miR-15b-5p	0.043	9.487	0.783	0.929
miR-582-3p	-0.088	1.716	0.784	0.929
miR-3161	-0.240	-0.951	0.786	0.929
miR-1273h-5p	-0.060	11.451	0.788	0.929
miR-505-3p	-0.022	4.359	0.789	0.929
miR-181d-5p	-0.035	3.947	0.792	0.930
miR-877-3p	0.105	2.150	0.793	0.930
miR-323a-3p	-0.055	4.078	0.794	0.930
miR-6511b-5p	-0.173	1.158	0.798	0.932
miR-200b-3p	-0.033	2.188	0.799	0.932

miR-141-3p	0.044	3.127	0.802	0.933
miR-708-5p	0.161	2.615	0.807	0.937
miR-19b-3p	0.060	10.256	0.809	0.938
miR-18b-5p	0.043	2.410	0.812	0.940
miR-6772-3p	0.055	0.690	0.816	0.941
miR-877-5p	0.024	2.378	0.817	0.941
let-7a-3p	-0.058	4.497	0.823	0.946
miR-31-5p	0.085	2.641	0.826	0.947
miR-548aq-5p	0.187	2.543	0.827	0.947
miR-5189-3p	-0.093	0.435	0.831	0.947
miR-548ai	0.194	0.527	0.832	0.947
miR-570-5p	0.194	0.527	0.832	0.947
miR-450b-5p	-0.053	2.048	0.834	0.947
miR-487b-3p	0.048	5.402	0.835	0.947
miR-548ap-3p	-0.072	10.374	0.837	0.947
miR-1	0.078	8.318	0.838	0.947
miR-1229-3p	0.048	0.765	0.840	0.948
miR-6770-3p	-0.062	0.142	0.844	0.950
miR-3064-5p	0.024	0.924	0.846	0.951
miR-186-5p	-0.024	8.853	0.848	0.951
miR-582-5p	0.068	0.885	0.853	0.954
miR-3065-5p	-0.030	2.573	0.854	0.954
miR-200a-3p	0.023	2.514	0.855	0.954
miR-652-3p	0.018	7.109	0.857	0.954
miR-181c-5p	0.031	3.046	0.866	0.962
miR-548ar-5p	0.098	7.739	0.868	0.962
miR-6741-3p	0.046	0.231	0.875	0.962
miR-628-3p	-0.019	5.661	0.877	0.962
miR-548d-5p	0.025	12.885	0.878	0.962
miR-4454	0.037	9.159	0.881	0.962
miR-576-3p	0.017	5.501	0.882	0.962
miR-433-3p	0.038	1.880	0.885	0.962
miR-148a-3p	0.020	10.002	0.889	0.962
miR-574-3p	-0.018	5.403	0.890	0.962
miR-29a-3p	0.041	9.472	0.894	0.962
miR-4433b-5p	-0.036	7.929	0.895	0.962
miR-6511a-5p	-0.091	1.038	0.895	0.962
miR-3074-5p	-0.035	1.854	0.897	0.962
miR-6511b-3p	-0.023	2.078	0.898	0.962
miR-497-5p	-0.022	1.523	0.900	0.962
miR-548aa	0.043	10.786	0.900	0.962
miR-548t-3p	0.043	10.786	0.900	0.962
let-7i-3p	-0.024	2.370	0.901	0.962
miR-450a-5p	-0.040	0.853	0.901	0.962
miR-619-5p	-0.136	11.202	0.902	0.962
miR-874-3p	-0.015	1.960	0.903	0.962
miR-342-5p	0.021	3.944	0.903	0.962
miR-548aj-5p	0.066	7.504	0.907	0.962
miR-548g-5p	0.066	7.504	0.907	0.962
miR-548x-5p	0.066	7.504	0.907	0.962
miR-624-5p	-0.031	0.116	0.908	0.962
miR-2355-3p	-0.012	3.959	0.913	0.965
miR-4433b-3p	0.037	2.351	0.914	0.965
miR-2355-5p	0.025	0.457	0.916	0.965
miR-210-3p	-0.013	2.393	0.918	0.965
miR-99b-3p	-0.021	2.773	0.922	0.968
miR-3688-3p	-0.018	1.689	0.926	0.971
let-7i-5p	-0.008	13.259	0.930	0.973
miR-4507	-0.108	1.601	0.938	0.978
miR-744-3p	0.023	-0.457	0.938	0.978
miR-548ay-5p	0.012	13.403	0.942	0.979
miR-99b-5p	-0.014	7.865	0.943	0.979
miR-15a-5p	-0.011	9.211	0.944	0.979
miR-132-5p	0.009	0.644	0.945	0.979
miR-1287-5p	0.008	3.050	0.950	0.980
miR-221-3p	0.006	11.513	0.950	0.980
miR-376a-5p	-0.019	0.104	0.955	0.983
miR-548e-5p	-0.015	1.838	0.958	0.985
miR-95-3p	0.011	2.108	0.963	0.988
miR-21-3p	0.009	3.394	0.967	0.991
miR-589-3p	-0.004	1.137	0.971	0.992
miR-4772-3p	0.013	1.699	0.971	0.992
miR-30e-5p	0.003	10.655	0.974	0.993
miR-138-5p	-0.007	0.000	0.980	0.993
let-7e-5p	0.005	9.484	0.980	0.993
miR-548h-3p	0.009	8.937	0.983	0.993
miR-548z	0.009	8.937	0.983	0.993
miR-1273d	-0.027	4.498	0.983	0.993
miR-181c-3p	0.002	3.538	0.987	0.994
miR-130b-5p	-0.002	5.414	0.987	0.994
miR-421	-0.001	5.199	0.991	0.995
miR-6859-3p	-0.005	0.719	0.992	0.995
miR-6511a-3p	-0.001	4.865	0.993	0.995
let-7f-2-3p	-0.001	0.250	0.998	0.998

Table A3. List of the putative target genes

Table A3. List of the putative target genes for each miRNA from our signature (miR-34a-5p, miR-345-5p, miR-200c-3p, miR-10a-3p), as indicated by DIANA-miRPath v.3 using TarBase (experimentally supported approach).

miR-34a-5p								
ARHGAP1	TMEM33	HUWE1	HNRNPU	KIAA1897(hsa)	MMP9	SLC36A1	KIAA0899(hsa)	PCYOX1
BMI1	POLI	MAP4	TAB2	MOCS2	MRPS2	RDRC(hsa)	SLC30A3	SCML2
TMSB10	LRSAM1	ETFDH	ANO9	RAD2(hsa)	PTGER2	A2RP(hsa)	LRRC46	RAD17
KDRF(hsa)	ZNF76	FRS2	FXN	ZFPL1	LZTFL1	PRSS1	SGPP1	IL6
RGP1	SLC37A3	BIN1	TCF19	MED16	ABCD1	STAR	HDAC8	CMPK(hsa)
TGDS	REEP6	TRIM7	SAPL(hsa)	GDA	POLR1B	KIF11	FAM111A	PPF1A1
NA	MTERFD2	LMNTD2	APOO	NCEH1	AF131216.5	ELMOD1	ATP1A1	RNF141
CDC46(hsa)	VPS37D	KLHL17	PPP1R18	TPM4	BCL7B	CITED2	KIAA0004(hsa)	OK/SW-cl.29(hsa)
ALR(hsa)	H2AFM(hsa)	AP5Z1	COQ9	BRCA1	DIAPH1	NLGN2	H4/K(hsa)	TRIB1
GOLPH3L	D3S48E(hsa)	SPTB2(hsa)	C17orf99	AGBL5	CHST6	KDELRL1	SNF8	CTSH
VPS4A	ETV6	CAPZA2	PNPLA8	THEM4	MLST8	NUDT22	ST20	hCG_2005629(hsa)
NOTUM	ADCY7	DPYSL4	H4FI(hsa)	GOLGA7	PTP4A2	NPIP4	NUCKS(hsa)	H1F4(hsa)
ZDHHC18	BCAT2	GOLGA8B	GLI4	GPC3	FGD3	P1725(hsa)	CNOT6L	MAPK1
RTN4	MMGT1	KLF12	UBE2I	LAD1	COG5	SURF4	TACSTD2	ADTB2(hsa)
SEMA3G	LIMD2	UTS2	MAGED1	LYPD8	PPP1R14C	N4BP4(hsa)	AS3MT	CLTB
C17orf85	FGFR3	MRPS12	SLC16A4	FAF2	CHERP	PSMD9	SNX5	IMP3
ARPC5	H2AFC(hsa)	RAD54B	VEPH1	GGA3	TK1	MPI	EHD1	AMER1
ERLIN1	STX5	DMBT1	GXYLT1	LPCAT4	ZDHHC4	WIPF3	KNSL1(hsa)	FNDC3A
EPB41L4A	H2AFX	STXBP5	C6orf141	MCM2	RNASEK	ANX4(hsa)	FLOT2	SDCBP
NEK3	LTN1	KIF2A	WIZ	452K12.5-012(hsa)	ORMDL2	SKA1	SLC2A12	SLAIN2
COPS7A	FAM86C1	TPCN2	SNX15	EHPB1	MECP2	RAD1	CLSTN1	PLOD1
PPP1CA	ARF5	H2AFG(hsa)	EZH2	SMG6	MAPRE3	PPP6R2	SSBP3	PAX9
E2F7	C19orf66	TIAF1	CDK6	SYNC	ZFP36L1	WBSCR20(hsa)	USP3	ANO7
TRIB3	LPHN2	LOXL2	HRG	POU6F1	ARV1	KIAA1914(hsa)	CHKA	KANK3
DHRS4-AS1	PTPRN2	SPDEF	SORBS1	NUP214	H3FB(hsa)	PUS7	RSBN1	LRRC41
H3FI(hsa)	SLC25A15	GTF3C1	USP30	ANK3	CORIN	ST7	KCNK6	SUCLG1
TMSA(hsa)	REPS1	BTBD19	RHEB	CROT	PDGFRL	SHARPIN	PICH(hsa)	RNF168
SLC44A2	C16orf58	GDF15	TFAP2A	PSD3	ARID1A	HNGS1(hsa)	ITPR3	TLN1
SLC2A14	KCNE3	CLAPM1(hsa)	ACAA2	LARP1	UBA1	PYGO2	KIAA0731(hsa)	PRO1777(hsa)
FBXO5	SCAF4	PLEKHH3	DCAF10	C15orf65	PANK2	PLXNB1	MPP2	C1QL1
SYNGR4	IP6K1	TBC1D17	SPTAN1	FH	STRAP	SLC12A9	SERF1A	RAD51AP1
PFN1	CRKL	LTBP2	VPS37B	HRIHFB2091(hsa)	FAM49B	EEF1G	TRIM21	HIST1H2AC
SCLT1	HIST1H1C	H2BFQ(hsa)	SLC25A29	RSRC1	CCDC82	IGF2BP3	FAM198A	KNSTRN
KIAA0765(hsa)	PTPN23	DRAM1	ZDHHC19	PRDX4	PRDX1	G3(hsa)	VWA1	DYRK1B
KRT32	ATXN2L	CDC48	SP1507(hsa)	MLLT1	TMEM86B	NFRKB	ZNF573	ERCC6L
RNF114	AK4	MCM4	FOXN2	STK17B	SLC7A8	ELAVL1	H4FG(hsa)	RRAGC
C12orf73	NAT8L	AC013268.5.1	FYN	HNRNPUL2	FAM126A	FAM178B	PXT1	UACA
RBM14	C6orf136	HIST2H3D	TMEM104	NCAM2	CCDC116	PHKA1	EMILIN2	TRIT1
NSL1	HP1BP3	RBM23	NQO1	ITFG2	F8	ZBTB21	ZER1	C22orf29
SLC25A44	HN1	SLC26A1	UREB1(hsa)	ZNF697	AP2A2	SNCG	ALDH9A1	TMPRSS4
NA	GPRC5C	KNS1(hsa)	KIAA1307(hsa)	LYPD6	BEND4	CCDC88A	EFTUD1	L3MBTL3
HSPA13	WHSC1L1	SETD3	HACE1	RNASEH1	SMARCA1	CDC20	CTTNBP2NL	NFATC1
FCHO1	ANKRD13D	NTN1	PDIA6	DMWD	DOK7	EMP2	H4FC(hsa)	RNASEH2B
KLHL28	ARHGAP33	DNAJC10	PUS10	TRIM59	MYPOP	AP2A1	APOL2	DKFZp686N2176(hsa)
NDUFC1	UVSSA	ORMDL3	IGF2BP1	GNPI(hsa)	KXD1	CCDC50	hCG_17321(hsa)	FGF7

OAZ3	CNOT4	AREG	MDH2	H4/N(hsa)	MYL9	RP5-824I19__A.1-002(hsa)	hCG_33495(hsa)	RFC3
FAM155B	STK4	C7orf50	BCAS4	PGM2L1	CENPO	ARSG	UBR7	PRO0992(hsa)
RNF11	ARTN	GOT1	RSRP1	CCAR1	CTBS	DKFZp686L08115(hsa)	TPP1	TMPPE
BRAF	VTA1	LACS2(hsa)	USP54	WDHD1	MTPN	PPP1R12C	ACSM3	SPT5(hsa)
FHL2	DNASE1L1	FAM69A	SLC35A4	CENPK	STX17	PM227(hsa)	ZHX2	FHIT
HGSNAT	RP11-835E18.2	STK11	SNAPC2	MAL2	SOCS5	CALD1	ZO2(hsa)	RPL27A
POU2F1	MAP2K2	PAPOLG	S100A11	DDX24	TFRC	ADNP	RLF	AIP
SFT2D1	c-met(hsa)	PPP3R1	WDR62	CSRP1	CABLES1	LCLAT1	FUT10	RANBP9
UBASH3B	SLC25A46	RDX	TGFB1	EBF3	PFDN1	NF1	SEC22C	DHCR7
FASN	RASA2	IFT122	SERINC1	GSN	VIM	PI2(hsa)	IGSF3	SYNGR1
CDH26	PPP2R3A	HIST1H4C	LIPT1	DMD	DSN1	JPH1	XPO4	DIAPH2
CDC6	ZNF775	HERC6	ZNF789	CRTC2	BMP2K	TMEM219	ZNRF2	HIST1H2AB
HIST1H1A	MAP7D3	TOB1	DNAJC9	CSEIL	ABHD4	NAA11	WBSCR20A(hsa)	SERPINE1
ACTB	RBM45	ZFP36	NDFIP1	CNIH1	RNF34	IGBP1	SLC29A4	HMMR
1144G6.4-006(hsa)	POLDIP2	INPP5F	MARK3	KANSL1	CNRIP1	ERCC4	ZNF311	ZNF33A
BLZF1	UFC1	ADAT2	RPIA	KIAA0010(hsa)	CXCL11	SERPINB1	ZNF585A	NKIRAS2
DCLRE1A	REXO1	SYNJ2BP	CASP2	RNF145	MAPKAPK3	FZD1	QDPR	VPS35
EAF1	PIGX	CRYA1(hsa)	GDIL(hsa)	POP7	TMED10	KDSR	KIAA0922	SCARB2
ACAS2L(hsa)	FEN1	XB130(hsa)	BLOC1S3	USP2	STIL	STK25	DHX9	FAM73B
TTC7B	SNP70(hsa)	KRT15	CREB3	KBTBD4	FOXA1	MYT1	CPLX1	GAS1
SNAP23	COA1	WAC	SHMT2	TSKU	CBLC	FAM45A	ANKRD28	KIF4(hsa)
DUSP4	MORC2	MIEN1	GBF1	CERS2	WDR73	CDM(hsa)	PCYOX1L	AGTRAP
PHLPP2	FYCO1	IQGAP1	COX16	ANP32A	DLL1	MED28	TCEA2	PLAU
MTO1	CDC8(hsa)	UBTD1	ZNF189	MAP3K14	HIST1H3C	UBAP2	DERL1	ASB9
PRLR	BID	NRBP2	ZC3H3	SYNGR2	SNCA	EMR2	LMNA	SMYD5
MPHOSPH8	CLIC4	GAN	CORO1C	SLC9A1	HRIHFB2157(hsa)	ZNF398	NDC1	CIRBP
FOXJ2	BTRC	PSME1	RDH5	SP4	KPNA1	TMEM106C	SLC7A2	A2D(hsa)
BSCL2	NPRL3	TRIP11	MAP3K11	CDH1	RCN(hsa)	PQLC3	CANT1	CDK16
C15orf13(hsa)	C1orf74	ARHGAP32	MCM7	PARP6	CORO1B	YAF2	AUH	MTFR2
DDAH2	PRR3	ASXL1	HIP1R	RAB11FIP2	SLC25A39	RNASEH2C	CCDC74A	LPCAT3
LIG1	CYR61	WNK1	FBL	LHPP	PIM1	DTNA	TULP4	CYBRD1
HLN(hsa)	CHD1	MNT	TCP1	CENPA	TPA1(hsa)	SLCO4A1	FN1	MGAT4A
ZSCAN5A	FAM195B	RUFY3	AP1M1	PITPNM3	IL17RB	ABCC3	ACSL1	CYB5R3
SEC16A	HIST1H2AE	PEX16	FKBP1A	TGFB1I1	SRPR	PTK6	ARHGEF9	SCN1B
MSAP(hsa)	SIRT6	NRTN	CHD4	C9orf72	ZNF692	HIBADH	AMACR	CCNG2
PPP1R37	LYRM5	GSE1	CXCL2	CHKB	KIAA1462	GTF2IRD2	IFFO1	HELLS
RAB3GAP1	ACER3	FTSJ1	DENND1A	RNF106(hsa)	CALML4	YY1	SEPT2	SNX17
H3FJ(hsa)	TMEM39A	GPATCH2	SMARCD1	ZC4H2	PRRT1	KIAA1228(hsa)	UBN2	ABTB2
ACKR3	HIST2H4(hsa)	PMF1	ARHGDI1	LIME1	ARNTL2	DAMA-236L13.16-003(hsa)	H4F2(hsa)	GTSE1
ZEB2	RCAN1	CDC5L	C11orf57	FECH	ZC3H12C	HSD11B2	IPO8	BTG1
MLK4	ATE1	VPS29	MBD1	PITPNM2	COL1A1	C10orf88	GATAD2B	C11orf80
UNRIP(hsa)	FAIM3	PBX1	SIRPA	SMC4	DNM1	CDC21(hsa)	SGTA	PIDD1
AFAP1L2	CCNL2	C16orf46	TYRO3	SLC30A8	PRKACA	KIAA1491(hsa)	ANXA11	SPIRE2
KIAA0164(hsa)	NTE(hsa)	EXD2	ZNF707	SFXN1	ZNF496	ARID5B	SPTA2(hsa)	ITSN1
STAG3L3	CCNA2	CRTC1	PPIA	MYH14	VCP	B4GALT3	SNAI3	USP22
NETO2	HIST3H3	NBR1	MTMR12	RAP1GAP	DNAJC15	TESK1	EPS15L1	A2LG(hsa)
TROAP	CLEC2D	RPL37	ZNF304	UBL7	MEI	DUSP7	RRP12	SIX2
TCF3	FBP11(hsa)	OPA3	FOXRED2	PIKFYVE	CACNB1	VSNL1	RAB22A	ZSCAN9
XXbac-BPG296P20.4-014(hsa)	SEL1L3	SEMA4F	ERP44	PPP1R12A	HCN3	H3FD(hsa)	RAD54L2	RNF26
H4FN(hsa)	RMI1	ARID1B	MSN	C5orf55	hCG_2023614(hsa)	PIGB	PKN2	hCG_1685949(hsa)
CASP8AP2	RSP1(hsa)	KIAA0432(hsa)	ASF1B	AFAR(hsa)	SUPT5H	KLHDC8B	AKTIP	UGT8
FAM195A	FAM111B	IRGQ	PACS2	DPPA4	LGALS3	PLD2	SEMA4D	VAT1
HIST1H3B	HNRNPD	SRCAP	SNIP1	TH1(hsa)	SYT1	JAG1	GRAP2	GCFC2
SNRPD3	SPC25	H4/A(hsa)	ITGB5	CMIP	NYMEL3(hsa)	DUSP3	GSTT2B	HSPC225(hsa)
DPP3	NT5C2	CANPL1(hsa)	PIP5K1B	NAV1	C10orf69(hsa)	KIAA1846(hsa)	TNC	MPP3
HIPK2	CHST11	SLC17A5	MORF4L2	FOXL2	PARD3B	C11orf54	C2orf27A	H3.3B(hsa)
TMEM63B	PITPNC1	TRPS1	MAPK13	RER(hsa)	IRF3	KPNA3	CRIP1	TLDC1
CNOT6	SH3BP5	RAF1	TRAM2	MB	DUT	JADE2	C21orf59	TSPYL2

TMED8	NXPH4	GPSM1	DNF15S2(hsa)	C3orf33	C6orf106	C3orf58	RNF182	FKBP1B
SMAP2	LZIC	ADO	ZNF107	RIF1	CDC42EP4	MDM4	AP3S2	HSPB11
HSD17B6	STXBP6	WNK2	ACTA2	SF3B3	FNBP3(hsa)	LARS	EIF4G3	NUCB1
LACS(hsa)	UCK2	FNBP1L	EPC1	CDKN1C	MOGS	SLC2A4RG	TMEM30A	CAPN5
DHRS7B	CDC47(hsa)	CDCA4	RHPN1	TYMS	LYSMD2	RTCA	ASTN2	PATL1
MPC1	APLNR	PRKRIR	PAX8	TMED1	XRCC3	KIAA0661(hsa)	BAG6	ZCCHC17
CRTC3	EROL1	C19orf60	RAB17	ICA1	ZMYM2	SEMA4B	CDKN1A	MRNP41(hsa)
MEN1	DCTN5	FRK	RAP6(hsa)	ANAPC4	APLP2	OGFRL1	NAGPA	TMUB1
SCYL3	PLC1(hsa)	REM2	H2AFD(hsa)	KCTD21	C19orf48	MYO7B	SGPP2	LRRC40
RNF44	MSJ1(hsa)	MRPL2	CASKIN2	AGO1	DNAJA3	SSR3	BCLAF1	FACL4(hsa)
CTDSP1	SFMBT2	MST1R	MTMR10	HCST	FAM20B	DKFZp434G1035(hsa)	SWT1	FAM129A
MOV10	TCF4	FES	PP6R3(hsa)	NECAP1	CD86	CSNK1G1	MAP2K1	ENTPD4
DSCR4	NUP153	ATP7A	CDABP0131(hsa)	TRERF1	NDUFV3	ADI1	PCIF1	TRIM32
DHHD	MIER2	GYLTL1B	PDS5B	SLN	WASF2	GOT2	STMN1	DNMBP
GPR63	TLR1	GIN3	DBF4B	FBXL6	PIG4(hsa)	SWS1(hsa)	UHMK1	VP572
SOX4	MAP3K3	EXOSC10	CAPG	HOTAIR	CARF(hsa)	FNIP1	DCAF15	MTCL1
HID1	ZNFX1	MMS19L(hsa)	UMK(hsa)	GGA2	GDE1	SLC39A6	RHOF	LMF1
H3FC(hsa)	SRL300(hsa)	KDELRL3	FGFBP1	RP11-664D7.4	TBC1D31	SYNJ2	TYW5	ALG3
CDIP1	AP1G2	PLIC2(hsa)	RSPH3	NAV2	NFKBIA	BTF3L4	RALB	RTN4IP1
FBXL3	TSPAN18	TCIRG1	ALKBH5	CLAPB1(hsa)	FBXO10	FUT11	POFUT1	TAF3
AFAR3(hsa)	FUT3	ZNF764	ZNF337	DLG4	MYO5A	SMIM13	NAPEPLD	TMEM79
FBXO11	SOCS2	NBN	TMEM256-PLSCR3	PKP4	NENF	PROSC	WTAP	WDR83OS
PYCR1	XTP3TPA(hsa)	LIMCH1	EPAS1	CYB5M(hsa)	MYCBP	PRKCB	PIG30(hsa)	ZNRF3
PKIA	MICAL1	TIAM2	LACS1(hsa)	GBX1	PEREC1(hsa)	KLC1	IRAK2	CRISPLD2
PRO2286(hsa)	FACL1(hsa)	RANBP10	NAP1L5	BBIP1	BEGAIN	CDC73	SYNE2	TAX1BP3
PHKA2	GTF2H1	CIT	LBR	SMG9	AK3	MRPL24	SLC25A19	TRIM13
CHST12	INHBB	FBXO4	CKAP5	RFXAP	RNF19A	RBPMS	ATP8B2	TMUB2
ESYT1	NME4	B3GALT4	ADAM19	H3FA(hsa)	CENPB	PPA2	C3orf38	ZNF623
OAS3	GNAS	C7orf43	hCG_41078(hsa)	H2BFR(hsa)	FAHD1	UNQ2441/PRO5003/PRO9924(hsa)	ZNF354A	RP11-51112.1-003(hsa)
DTL	PCLO	TRIM62	TBC1D30	HIST2H2A A4	H3F2(hsa)	SPRY1	C13orf10(hsa)	H3FT(hsa)
SDCCAG16(hsa)	IP6K2	ZNF664	NREP	CLIP1	NME7	TNRC18	CLSPN	KIAA1279
FARP1	C1QTNF6	ARFGAP3	KCNE2	NOTCH1	EIF4G1	HPRT(hsa)	JRK	MYBL2
DDAH(hsa)	KIAA0784(hsa)	GMNN	SLC35A2	GPR143	MIA3	CDC23	CHTF8	RUFY1
GMIP	CORO6	MAPK8IP1	HIST1H2BD	SELM	H3FK(hsa)	TRPC4AP	TNFRSF12A	TMEM143
TNK1	GOSR1	ATPAF1	SH3BGRL3	RP4-697E16.3-004(hsa)	RBBP5	MARK1	C20orf27	KIAA0224(hsa)
NFIX	CIB2	ATG4D	TFPI	RSU1	NIPA2	MTERFD3	DOCK9	ROR2
KEL	MKL1	FBR3	KIAA1612(hsa)	CAPN12	236L13.16-004(hsa)	CXorf3(hsa)	AAK1	ARHGEF26
RNF183	WARS	PIGM	ERGIC2	FMNL2	CEMIP	SERF2	TNRC6A	AKNA
CDKN2C	SIX3	ECH1	IKZF1	GANAB	H4/E(hsa)	ECD	BCAN	SCAMP4
CRLF1	LAMA5	VWCE	C4orf46	PLCG1	MED31	PEAR1	TRAPPC1	GMEB1
SLC48A1	OBFC1	SLC25A51	DST	FAM89B	CITED1	ARHGAP29	TP53INP2	TNPO3
PHF19	BRPF3	BCL11A	HIST1H2BA	POLR2A	DENND6A	YBX1	FBXO18	PDK2
SCAMP2	ZNF10	NT5(hsa)	SSX3	TMEFF1	KIT	FYB	ULBP2	ANKRD10
ARG2	THAP9	ZNF501	ABHD2	BTG2	LY6E	STK16	SLC2A1	KCNQ1
MYBL1	LEKR1	CGI-82(hsa)	EFNA5	POLR2M	FCER1G	REPS2	HMCES	ZBTB25
CWF19L1	TMOD2	TSGA10	KIAA0101	DNAL1	HIRA	PSMC3IP	ARF6	DKFZp586K2.222(hsa)
RHEBL1	RGS4	CIDEC	HES1	PDLIM1	RBL1	NMT1	NA	SLC4A11
TRIM11	PPME1	NT5E	PLAGL1	ZNF395	HIST1H2BG	ILF2	KHDC1	DADB-70P7.10-002(hsa)
TXNL1	SLC25A3	ERLIN2	BMP8B	C1RL	ACSF2	NSMCE4A	AKR7A2	DNAJC2
ATG7	TAF9B	ZSCAN22	VASN	ENO1	XYLT2	GGT1	C1orf109	HSPC075(hsa)
H3FM(hsa)	CRK	ZNF507	CENPL	NCOR2	SCNM1	MELK	SAMD5	C14orf159
A2LP(hsa)	SRP54	ANAPC8(hsa)	KBTBD6	SLC16A14	JMJD1C	LAMC1	IRX3	NEIL3
SIN3B	RED(hsa)	ZNF706	PPM1M	TSC2	VEGFC	FOXF1	MBNL1	ATF7
C18orf21	OTX2	LIN9	FAM204A	ARL15	PLIN3	RAI14	PRC1	PCBP4
TBCD	GUCY1A3	BCL2	ZNF746	DGKZ	HNRNPM	RAB40C	WDR4	H2BFH(hsa)
DTYMK	ALDH9(hsa)	CAT	OSGEPL1	B4GALT1	RBM26	SFR1	C14orf182	GPR161
ARL6IP5	SSH1	CPSF6	PDS5A	H3.3A(hsa)	ZBED3	RPS6KA3	AZIN2	HBP(hsa)
HMG20B	GATA3	DAGLB	ALDH6A1	HPS1	KCTD7	FAM124A	TMEM201	STK40

TUBGCP3	TRIM37	PDXK	TSH2B(hsa)	PABPC1L	KE04(hsa)	FBXW4	NANP	MBD5
FKBP3	CFL1	CD151	ZNF575	PAQR7	ABHD14A	NFE2L1	NFIA	KPNB1
PSD4	COL12A1	UBA52	ADIPOR2	AK6	PDE12	NEDD4	KLRD1	RBAF600(hsa)
SPARC	IQGAP3	LRP11	PAST(hsa)	JUN	TTK	NDUF2	NP95(hsa)	MYRF
PHF7	FKSG27(hsa)	ARSB	FAM60A	MCM3AP	AAMP	CNPPD1	SRSF11	BRWD1
UGCG	ARF3	SLC1A1	CAPRIN1	KIAA1521(hsa)	ERCC1	FOXJ3	HIST2H2A	CBX5
LPPR2	CC2D1A	NRSN2	MTRF1L	ZDHHC2	SAMD14	ZNF414	ABHD12	KLF4
SAR1A	POLR3F	HIST2H4	SLC3A2	RPS12	DIS3L2	SFI1	COBLL1	STARD4
GUCD1	TS(hsa)	SPT5H(hsa)	IER5	FAM3A	SUOX	MKI67	ATP2B4	TTPAL
STAT3	EMILIN3	PTPRM	ARAF	GPR19	NCAPG	TSPAN14	OGFOD1	NLRP11
TAGLN	RNF123	M7V1(hsa)	LYPLAL1	CRTAP	UBE2Q1	POC5	NOL10	RAD9A
HYPJ(hsa)	NDUFAF6	MAP2K3	EMS1(hsa)	PPP1R15B	C1orf213	AMHR2	ANKHD1-EIF4EBP3	PODXL
TRIM68	ZNF114	HSD17B10	DDX10	RBMS2	TRIM33	TAF1A	MAMLD1	HMGCL
PDE4B	ARMC8	PHB	MTFR1L	PDLIM2	CREBZF	IGF1	TEAD2	DMKN
MAN2A2	ARRDC4	CD40	SPIN4	WDR33	TGOLN2	RRP1B	GNMG4	MXRA7
E2EPF(hsa)	ELANH2(hsa)	SLC45A3	KIAA1109	HIST2H2A	IL1RN	LMAN1	PDZK1IP1	TBL1XR1
HPCAL1	SIRT1	MYH9	ZBTB20	IL9R	SLC39A9	KAT2B	BHLHB9	FANCB
NUFIP1	HOXB8	HBP1	CCDC64	CDK3	CTMT4	PAXBP1	TNFAIP1	HIST1H3J
PDGFRA	SLC35G1	FAM20A	MYSM1	AMZ2	CPT2	KLC2	DISP1	SMOX
TPRK	MED14	TPBG	DCTN2	C19orf54	GTF3A	LRRCC8E	ZWILCH	NAA60
TSPAN1	THBS1	RFX1	ABI2	TMEM173	WDR45B	APEX2	ATG9A	DYNC1I2
EFCAB14	STOM	CD3D	NFX1	DSCR3	MAPT	ACD	RPMS13(hsa)	ATP6V0A2
HS1BP3	TBC1D23	IMMT	SHISA4	BABAM1	MUC1	PRKAR1A	HSD17B12	ATRN
ARGLU1	RUNX1	BIRC5	DPM2	FAM209B	DAG1	PEF1	LINC00337	FABP3
DIP2A	LACS4(hsa)	TUBB	KRTAP2-3	NCAPD2	RNGTT	VMA21	EIF2S2	HIST2H3A
PRKCQ	IPO9	SLC31A1	IFNAR2	FAM208B	ASNA1	KIAA0109(hsa)	ALG13	DAN26(hsa)
SSX1	EIF4A3	KIAA0430	SP2	TOP2A	SF3A2	MYADM	PRKCH	H4FM(hsa)
FERMT2	ZNF521	BCAM	CREM	CCND1	HIST1H4H	PROSER1	HHLA3	ASXL2
ENPP3	EIF3H	SNX9	CRAT	IMPAD1	SMKR1	SAP30L	DADB-333F21.4-002(hsa)	GPS1
TOX4	HIST3H2A	MACF1	GPR183	MAN2B1	INTS9	PIG28(hsa)	MON1B	SECISBP2L
RNF144A	KLRC3	PTPN21	C12orf10	GPC1	ZNF263	CSNK1E	EIF4EBP2	LYPLA1
POMZP3	USP6NL	CCNF	KIF12	JAK2	ARL6IP6	SLC39A13	LSM12	ESAM
CSNK2A2	MTMR6	TAF9	PREB	GRPEL2	PAFAH1B3	RP11-452K12.5-010(hsa)	INA	KLHL18
NBL1	PTRF	H4/G(hsa)	NCL	ILF3	MSANTD2	DES11	MLXIP	TGFBR2
CACNA1A	SPATA33	SNTB2	POC1A	ZNF133	SAP130	SA2(hsa)	HIGD2A	SLC1A5
ELL2	GTF3C4	TMTC3	NAPG	TNFAIP2	TLL1	CYB561A3	R3HDM4	COLGALT1
MIER1	TMPK(hsa)	WIPF1	NAB1	HIST1H3I	PABPC1	EP300	ZNF524	PCBD1
EEF2K	ANXA3	EME1	RPLP1	PFN2	TBC1D25	POM121	IFI35	DADB-70P7.10-003(hsa)
BAF155(hsa)	HDAC7	NUP98	FAM222B	TSR2	MR1	MIDN	RRM2	SLC39A1
TOB2	ZMYND11	PHACTR4	NOGO(hsa)	WBSCR27	CDYL	SUN1	VGLL4	PTCD3
CDH2	HIST1H2AM	CDA03(hsa)	MT1F	SRK(hsa)	MCMBP	AMOTL2	CAD	FERMT1
C3orf80	LGR4	CEP83	CMTR2	SMAD4	CFL2	BRE	NOH61(hsa)	RAB14
G3BP1	C21orf58	ANKIB1	C7orf49	SLC16A5	ACADVL	SRM300(hsa)	SLC35G2	TFG
E2F1	PTCH1	MAGEB2	UNG	ST6GAL1	RBM47	HDLBP	SLC39A10	MAML1
HSPA1A	GS3786(hsa)	SH3GL1	RBM38	SLC35D1	RPS18	DDAH1	CKAP2	ZNF641
RAB3GAP2	ECK(hsa)	M11S1(hsa)	SPEG	FNDC3B	CDCA7	SLC10A7	CG1(hsa)	TMEM200A
RPS23	AGO3	NRGN	KLF10	SEPHS1	RBBP4	ANKMY1	C21orf2	PON2
PDCD4	DBN1	CHRN4	SNPH	C2CD5	KLHDC3	GAB1	TGIF2	ZFAND3
ARHGEF5	MMP15	C22orf23	SLC25A1	ICMT	ID1	ZNF35	BCX40G17.4-002(hsa)	MGAT4B
MASTL	CABLES2	DCBLD2	SFXN2	RLTPR	GPR3	PPARG	HIST1H2BB	MED22
PCDC5RP(hsa)	RAD51	APH1A	RASSF7	CTNBN1	APBA2	TMEM245	RABEPK	PVRL1
MMS19	PIP5K1C	PPP6C	MPP5	PLA2G12A	MRPL10	ZBTB3	LDLR	STRADA
ZNF318	RAB25	NR4A2	NT5CP(hsa)	DLGAP3	NOL11	ARL5B	SLX4	RPL15
TUFT1	Nbla10545(hsa)	UBL3	SLC35B3	RHNO1	MCPH1	PRIMA1	PDAP1	AMN1
COMMD1	H1F1(hsa)	CCDC14	CCDC85B	BAF170(hsa)	PANX1	KCNAB2	SLC29A3	ATP2C2
TBC1D13	ABCY9	ATP6V1D	TMEM181	KIAA0153(hsa)	TERT	PIGT	TMEM25	PLA2G15

ASB1	SAC3D1	AAGAB	G6PD	RP4-657E11.7-008(hsa)	NYAPI	CNTNAP3B	IL17RC	PRMT3
PRSS3	KIAA1522	GYG(hsa)	RP11-244N20.4-002(hsa)	SLC10A1	HIST2H2AA(hsa)	TFCP2	DONSON	PTGES3
FAM167A NPDC1	DHCR24 CEP57L1	FAM127B FZR1	NECAP2 USP12	THOC6 VTI1B	ZNF426 KLHL7	NANOS1 NOTCH3	GDPD5 TXNL4B	ZBTB47 MARCH3
PRR22	PRRG4	FAM86B1	INSIG1	NTMOD(hsa)	NEO1	SLC44A1	RPRD1A	TTC6
RTTN MORF4L1	NINJ1 ZNF681	KIFC2 DNAJB6	H2AFP(hsa) FAM104A	RAE1 CRY2	ARMCX3 IPO12(hsa)	CCDC169 DNAJC21	PER2 TFE3	ATP5SL SNRNP70
CDON	49N14.8-004(hsa)	RAVER2	MARC2	MSH6	QRSL1	SAMD10	MYL6	RAPH1
LDHD CRYAA ADAM10 NAT6	IMPDH1 TTLL12 CLCN3 LENG8	AGO2 MCM5 LIN28B IL21R	DFFA TBC1D10A CBR3 PAQR4	C6orf1 TUBB3 RNF25 ASNS	AFAR1(hsa) TEAD1 PKX LRRC8C	NCAPH TAX1BP1 GNAQ BCCIP	H2BFF(hsa) SH2D2A DCAF4 CHRNA10	UBE2C PTPRH HSPB4(hsa) FADS3
CAPN2	PRSS8	IMP4	CBFB	SNRPA	hCG_2018597(hsa)	FAM73A	NUP155	GCNT2
CXCL16	ATMIN	PKLR	PRADC1	RRP8	BAZ2A	PPP2CB	MOB3C	XXbac-BPG296P20.4-010(hsa)
EMP1 HIST1H3A	CDKAL1 AMPD3	AFF4 FBXO6	GCH1 SIDT2	RHBDF1 NEDD8	CHIC1 SMARCC1	RPUSD3 H1F5(hsa)	HK1 PP781(hsa)	BAD RPI(hsa)
VASH2	RPSA	ANKRD17	TP53	WDR76	STRN3	CDK17	ASCT2(hsa)	RPA2
FBXO32	ATAD2	STAG2	BMP1	RNF208	HIST1H2AA	ZNF780A	PARD3	PPP1R3E
HIST1H2AJ	PWP2	TIMM8A	RP1-71L16.2.1	MAPRE2	SKI	TRMT10B	HEATR5A	DEF8
ATP5D UROS OSGIN1 ZNF222	ZNRF1 EIF4E3 TINF2 C11orf30	ATPIF1 NTNG1 FAM203A STT3A	RNF187 EPB41L1 VGL(hsa) EXOC4	CCNE2 DSCC1 AXIN2 TMEM56	NADK ANKRD27 NT5M CSNK2A1	SNF2B(hsa) SELPLG CFL(hsa) TWISTNB	SPC24 DKK1 LRP3 ADARB1	MAF1 USH2A BRE1B(hsa) MTHFSD
ST6GALNAC4	EDEM2	HNRNPA0	NLE1	DAAP-21F2.8-002(hsa)	MOB4	KNSL6(hsa)	ZBTB4	ELK1
EPHB2	C10orf54	C1orf86	RBPMS2	ATP1B3	CFLAR	DKFZp434N101(hsa)	TRIM2	COQ2
FAM53B	AKIRIN2	GRHL2	PLEKHA5	GFPT1	KIAA0839(hsa)	CHML	FIP1L1	CMPK1
FBXO46	TPR	PLA2G6	TMEM140	INPP4A	GLUT3(hsa)	PSMD7	IFI27L1	SLC30A6
CEP152	ANKRD52	DOLPP1	ACS4(hsa)	FASTK	IFT5	CELSR3	GORASP2	ARHGAP22
NFKB1	MAP2K7	IRF2BP2	FGFRL1	SLC25A13	FKBP8	RP11-16N10.1-004(hsa)	HMGCS1	MTDH
SAFB2	NSUN5	KEO4(hsa)	PLA2G10	SMARCC2	GGCX	GLTSCR1	PTPN12	GPR137C
IRF4 EXT1	PVRL2 MOB3A	NA DGCR2	B3GALNT1 TARS2	CCDC163P TAPBP	CDKN2AIP DHX38	ABCA7 SEPT3	H4/D(hsa) OPN1SW	LPGAT1 PRR11
DHPR(hsa)	H4FK(hsa)	RASIP1	UBAC1	RFTN1	AKR7A4(hsa)	CLN6	EXOSC6	ENO2
PCOLCE2	H1F2(hsa)	FBXL2	C10orf11	E2F5	WDTC1	ADTAA(hsa)	BARD1	ZNF428
MANEA	TNXB	GCOM1	AGFG2	TYRP1	TFCP2L1	POLD(hsa)	SMPD1	TNRC6C
PTPRU	SPATA2	SLC38A7	MOCS3	SSF42	JAK3	ALAD	GAREML	ST6GALNAC1
S100A16	ELK3	HIST2H3C	C11orf23(hsa)	ST3GAL2	SLC13A3	MRE11A	LIMA1	N4BP1
NTNG2	TMEM184B	MCFD2	LITAF	HECTD3	NAMPT	RHBDF2	LMF2	ZNF282
TOP3A	PPP2CA	FAM103A1	KNS(hsa)	PIGC	XAP4(hsa)	JDP2	SHANK2	FANCI
MET	SPATA31A7	MYO1C	PPP1R11	C17orf53	RPL5	ARHGAP42	MTAP	MCM10
ATP6V0E1	PITHD1	PRDM11	DDX21	SAP30BP	PRPF38B	TRPM4	WAVE2(hsa)	RNF216
SLC6A6	SLC22A18	TM9SF4	PHF6	STRBP	MTSS1	ATF7IP	PIGF	WDR96
UTP14A	H4/J(hsa)	C9orf16	FAM178A	LARP(hsa)	PLEKHG5	IGFBP2	SGSM2	SYVN1
FSTL3	XK	RP11-265M18.2	PRRC2C	SLC8B1	CPEB2	BRD3	ZFP41	RHBG
TROVE2	INPP5J	BHLHE41	CLEC4M	MRPS30	CNKSR3	ACRBP	RP11-197M22.1-003(hsa)	KIAA1715
SLC10A3	SMIM20	MEF2D	MCTS1	AK9	TMCC1	GPIAP1(hsa)	EIF5A2	ORAI3
SLC39A8	H3F3(hsa)	CDKN2B	CDC42EP1	TIGD6	CAND2	C18orf54	CCNI	MYLK
FGD1 SPRYD4 CBFA2T3	SCPEP1 GABRG3 FLOT1	MTMR9 SRM INTS8	MTURN SEMA3F SEC61A2	C1orf85 TSEN15 GIGYF2	CYSRT1 COMTD1 CDK18	KIAA0030(hsa) TGM2 WDR3	TMEM263 PRODH2 HMGN4	GTF2F1 VPS54 ACCS
FEZ1	SMARCA4	MOB1B	ANXA5	KIAA1207(hsa)	FGF9	S100A3	HNRNPL	D3F15S2(hsa)
hCG_39482(hsa)	GTF3C3	SLC25A20	C9orf69	PIGL	PTPN11	TMEM92	RUFY2	WRN
FANCD2	KIAA0312(hsa)	C20orf193(hsa)	DCTN4	MPHOSPH6	POM121C	GRK6	ERGIC1	SUV39H1
GTF2E2	PLCD3	STAG1	ASH1L	C1orf61	HGS	ANKLE1	PPIG	BAZ1B
H4/C(hsa)	SSX5	MFAP2	MBD3	QARS	TMEM246	GJC1	MAP1A	MCM3
ZNF273	GNPDA1	PTPRN	ADAMTS2	H3F3AP6	MAD2L2	NLRC5	NAV3	PID(hsa)

SSH2	BCL2L13	URI1	S100A2	MRPS25	GCF2(hsa)	RP11-108M9.3	CCNJL	PNISR
UBP1	FAM218A	SRGAP2C	SSX2	DDX11	CDC42SE2	SDHA	CCNK	TMBIM6
HFE2	FGFR4	GPATCH2L	MND1	ALAS2	C2orf49	SEZ6L2	HAUS5	KDM4C
ADCY1	CPEB4	PRP16(hsa)	PCSK7	MAOA	KLK1	MAGI1	ID3	CCNL1
SLC44A5	L3HYPDH	CDCA5	METTL23	C1orf210	FARP2	CNOT1	STAT1	RCH2(hsa)
RRAGD	CALB2	TIP47(hsa)	HLA-DMA	CDV3	RNF181	ZNF281	HIPK1	GINM1
MYB	SP140L	DHX37	SRSF1	PIG1(hsa)	XXyac-R12DG2.2	EFNB1	ENY2	H1FX
CALCOCO2	NOL3	DAP	MYNN	INPP5K	GPS2	PTP4A3	AHNAK	NNT
IGSF9	GAPDH	TRMT61A	PURB	KLHL32	NPNT	RP11-269F19.1-004(hsa)	SEPT6	ZNF703
TOM1L2	INTS3	CTAG2	CSMD2	HYAL3	PHC2	ADCK4	RIMS3	RHOG
HNF4A	HDAC1	CTSD	CCDC97	FAM92A1	COX4I1	UBE2D3	HIST2H2BE	ECE1
NDST1	UBIAD1	ARID4A	ACSS2	Z82214.4-003(hsa)	GAS8	CASP6	TRPM7	CCND3
CDT1	ING3	POLD1	HUS1B	ARL3	YWHAZ	FNDC4	LUZP1	MED8
695O20_B	GALT	STRIP2	LRPPRC	MXI1	CDAN1	DAMA-236L13.16-002(hsa)	PRKDC	SYT16
BBS2	NA	SPHAR	EVL	C1orf131	YKT6	WHSC1	TMEM206	TBRG1
ANO6	MIR1199	FAM86A	LCP1	AXL	DKFZp781H1755(hsa)	COX15	RP11-20123.8	NR2F2
ZDHHC21	AFF1	TJP2	CXCL3	WWC3	EIF4ENIF1	ZNF319	KCTD15	ZMYM3
ARMCX5	COPS7B	TNFSF15	ZNF467	SAMD4A	ERAL1	LOXL1	APIG1	RRAS
SDR39U1	MCM6	KIAA0332(hsa)	ZNF548	KNS2(hsa)	FBXL19	PHF12	SMAD7	CARHSP1
CCNB1	MED21	FAM83A	SREBF2	NUFIP2	CRELD1	DNAL4	ORC6	KIF5B
TOR1A	DKAKD	TNFAIP3	ZNF358	ADNP1(hsa)	C1orf159	TOM1	PRKAR2B	NCOA1
ATP2C1	PLAGL2	KIAA0061(hsa)	ENKD1	POGK	PRKX	EIF4E2	SURF2	LIN37
TTL	TFEB	ELP5	FAM188B	RUNX3	CLAPA2(hsa)	CHMP3	CDC42GAP(hsa)	ST3GAL4
VPS45	PME1(hsa)	DTNB	ZDHHC12	TP73	SLC25A36	HNRNPH2	CIZ1	ACOT8
PINK1	C19orf84	PLEKHH2	TAF12	RAPGEF2	CUL7	TMED6	BVES	SLC27A4
UCK(hsa)	LFXN	THRA	HIF1AN	UCP2	TIGAR(hsa)	DMPK	CYCS	HIST2H2AB
UMPK(hsa)	MTX3	CCSER2	BPG254B15.2-002(hsa)	RAB1B	NTPCR	CREB3L2	MEF2C	SOBP
RIN1	NE2	PI4KB	BTF(hsa)	NFATC2IP	RFX3	ATXN7	GLRX5	GPATCH4
GDAP1	ZNF33B	RAB21	RHOC	MSL1	ZNF708	EPS8R2(hsa)	CEP55	H2AFQ(hsa)
HOXC9	USP1	SIRT5	SENP6	H4FH(hsa)	CPT1(hsa)	TSPYL1	UBE2W	DAXX
NUP62	ACVR1B	IMPD1(hsa)	IL22RA1	MARCH2	REXO2	TFB1M	RBP5	HSJ2(hsa)
UBR1	KIF15	LETM2	SIRT2	TMEM243	SPFH2(hsa)	DHRS13	C8orf2(hsa)	ABCF1
SOCS4	KIF2C	CDK1	ZMIZ2	TRAK1	MBD6	CYB561	TMEM127	PDGFRB
MED13L	LRRC8A	GON4L	ZNF385C	C1orf198	GDI1	EPM2AIP1	hCG_41525(hsa)	PIN4
IL18BP	TNS4	AIM1	ECM1	DYNC1L12	MFS3D3	GIN52	MKNK2	ARHGEF3
MRPS26	p16lnk4a(hsa)	MLLT3	HPSE	ZNF503-AS1	ZNF592	SIX5	PSRC1	ZNF689
BCL9	DDX56	SFT2D2	RECK	CISH	VPS45B(hsa)	CNTNAP3	FANCA	PTPN18
TENC1	UBQLN1	GPR158	CTTN	FABP5	CYP51(hsa)	TCTA	SIGIRR	PHLDA1
NOGOC(hsa)	TMEM16A	TBC1D2	GABPB1	PRO0750(hsa)	PSMB2	PARP1	ZIC5	HOXA13
LPPR4	NR6A1	LAMP3	UBA2	IFRD2	STIM1	GK5	DCLRE1B	WBP11
SRR	CDKN3	TMBIM1	EEF1D	PTPLA	MTA2	SLC9A3R2	HERPUD2	RP11-65F13.2.1
FIGF	TGFA	JOSD2	OSR2	CNNM3	SEMA4C	CTSB	PDE7A	C19orf1(hsa)
CYFIP2	C10orf10	NUP160	CCDC150	OMB5(hsa)	TAF4B	H3F3B	PLK1	ARRB1
RPF1	AP2B1	SLC37A4	VICKZ3(hsa)	PALM3	FAM81A	FOXP2	ZNF367	C21orf33
FGD6	DLG1	SHCBP1	ICAM1	HIF1A	hCG_15646(hsa)	RPL37A	RP11-6D1.6	CYB5R2
CIC	SORT1	SPCS2	NLRX1	PPP1R10	TRIP5(hsa)	WWOX	TSN	ADAM15
COMMD9	HIST1H2BO	TEAD3	RNF40	CLN3	H4/O(hsa)	HNRPUL1(hsa)	GYS1	CD44
RP11-569G9.2-002(hsa)	PHGDH	TMEM109	ZNF207	TREX1	TMPO	SEC24B	ARPC4	AP2M1
C15orf26	DDX38(hsa)	MTFMT	H4/M(hsa)	E2F3	TNK2	SERPINB5	ZFP36L2	TFAM
PAQR5	RSF1	EPN2	ITSN2	POGZ	SRRM2	CLPTM1	RWDD2B	PRKACB
GNA12	TBCK	MSL2	HNRNPK	ARFRP1	RNFT1	MPHOSPH9	SUFU	ARHGEF28
PSMD5	RTFDC1	EIF4EBP1	TNRC15(hsa)	SUSD2	CAPN10	CAPN1	H4/B(hsa)	SERPINA1
HES2	NEURL1B	GSTM1	GRN	DAMC-157M7.11-002(hsa)	PTPRG	SLC22A17	VEGFB	MAP1B
NUMBL	XRCC1	IFT57	SIPA1L1	CYB5D1	CCDC167	F12	C16orf13	CD47
SNRPD2	E2F8	SLC26A6	PP2593(hsa)	APITD1	H2AFR(hsa)	STAMBP	AURKB	H2AFA(hsa)

NUCB2	FACL2(hsa)	LONRF1	STC1	RP11-176F3.6-007(hsa)	TEX261	DLD	ZNF3	C14orf154(hsa)
EV15L	CHD8	MINK1	MIS18BP1	RGMB	GEMIN5	SLC5A2	UPP1	SWI5
RP11-321N4.1-004(hsa)	NRDE2	LLPH	AZIN1	H4FB(hsa)	RPAP1	CERS6	MBLAC1	SOX5
SR140(hsa)	USP20	C15orf38	RIMS4	NRIP3	H4FO(hsa)	TMEM150C	USP11	MIER3
TPD52	SMIM1	CENPQ	GLTP	MCTP2	KLHL15	NA	HIST1H1B	VAMP2
VPS45A(hsa)	APEH	TIFA	RALGPS2	C2CD2	PRIM1	GAPVD1	TMEM5	ADH5
EIF2AK1	TIMMDC1	MFN2	GAPEX5(hsa)	VPS37A	FXR1	DDX39B	NASP	MPV17L2
UBE2E3	CYP51A1	DDX17	VAV2	KRI1	CDCL1(hsa)	G3BP2	CMK(hsa)	CAMTA2
ZNF621	157M7.11-003(hsa)	RAB12	C19orf82	HJURP	MBLAC2	RBBP7	ADK	XYLT1
RFX2	DBNDD1	RFNG	TXNDC16	TMEM97	MTA1L1(hsa)	SEC22A	KHNYN	C17orf80
ST3GAL3	IST1	DCTPP1	H2AFV	GIN51	TSPAN4	C7orf55	NFYC	teag7.648(hsa)
AREL1	MBOAT7	DHFR	ZNF317	FUT2	RASA4	SPATA20	UBE2S	ALDH7(hsa)
SH3BGR1	SEPT1	EGFR	DCAF7	OPHN2(hsa)	CDH24	FBXO27	PLEKHG6	ATG4B
C1orf43	OGT	SSR2	PP13181(hsa)	GDAP2	SENP1	CYTH1	ULK1	FAM134B
PACS1	BTD	AFG3L2	SBF1	CEP41	SLC26A2	PPP2R3B	MAGT1	SLAH2
NELFD(hsa)	C2CD2L	SMTNL2	ZNF253	HIST1H2AG	NXPE1	TRAPP6B	CWC15	DGKH
CD200	RPS15A	KIAA0391	RAB43	ATRIP	HIST1H2AL	FAM214B	C5orf63	NUDT19
ZUBR1(hsa)	OAF	ASPHD2	APOL4	NICN1	H3F3A	ANO10	SRSF3	LHX2
SFN	ZNF804A	SLC2A11	CREB1	MAPK8	H1F3(hsa)	FAM149B1	ARHGEF17	TRIM26
TOMM40	CDC37	DNAJC4	GYG1	ZAP70	LYST	MF	FOSL1	UBR4
TRIP(hsa)	HIST1H1E	TYMK(hsa)	ETV5	MPEG1	EPHA2	ADTAB(hsa)	FUT8	NLGN3
CDS2	PRPF40A	PPP3CC	CDH10	TMLHE	DNM1L	TP53I11	SNX25	NA
ANGEL2	SIAE	P4HB	E1BAP5(hsa)	MIF4GD	My043(hsa)	LRRRC23	MOAP1	SENP5
NUDT12	ALDR1(hsa)	RP11-511I2.1-004(hsa)	ZNF436	TMEM116	CERS5	ZFR	WIPI2	XPO5
RNF38	AKR7(hsa)	KIAA0097(hsa)	SORBS3	ATL2	LARP4	NUTF2	TRAPPC13	NA
KIN	ALDH3A2	PRAF2	PKP2	RP11-517O1.1-006(hsa)	CUX1	VPS33A	H3FH(hsa)	HYPA(hsa)
KIAA0060(hsa)	TTC38	CSTB	FBRSL1	RQCD1	RIMKLB	DNAH14	AIMP2	CDC25A
FER1L3(hsa)	ARHGAP24	RDH13	COL6A1	ZC3H7B	SEC31A	HNRNP1	ALDOA	IRF2BP1
MICALL1	NAP1L1	KPNA2	KIAA1558(hsa)	C8orf37	BACE2	PYGB	FAM65A	FNIP2
MRS2	BLOC1S1	ZYX	SEC63	KTN1	TIGD7	PELL3	PTHLH	EREG
RPS28	LTBR	IER5L	OK/SW-cl.35(hsa)	POLR2F	FAM219A	GSTK1	BCAR3	ENTPD3-AS1
ZBTB38	STX1A	KLF7	MED4	MRJ(hsa)	PSMG1	CD22	LERK2(hsa)	RP3-467K16.3-002(hsa)
ZNF93	GPIP137(hsa)	EVI5	SURF-4(hsa)	PKMYT1	ZC3H14	OAZ2	NR1D2	ICBP90(hsa)
CAMKMT	PVR	TPX2	HSPA1A	DNAJB9	RAB40A	RABGDIA(hsa)	SUSD3	C2orf43
NAT16	PIK3R2	GGH	SEMA4G	HERC2	RNASE4	FANCG	LAMP1	RP11-1149O23.3
RIPK2	PLEKHF1	FAM174A	FAM76B	PAG1	LDHA	DCP1B	NIPSNAP1	TGFB3
MED25	ARL2BP	TMOD3	HEATR3	CSNK1A1	CTNNB(hsa)	RDR(hsa)	HOXC4	TIMP1
GLIS2	SH3RF2	ELOVL3	FRG1	CREBRF	LZTS2	FAM210A	NT5B(hsa)	TRIM28
AIM1L	ARHGEF12	KRTDAP	SZT2	CGGBP1	GLCE	IRGQ1(hsa)	FGFR2	MSX2
PKN3	SGPL1	TRAPP4	TRIM41	HME1(hsa)	FAM3C	EPHB6	METTL3	YY1AP1
C1orf27	REEP3	KIAA1578(hsa)	BM28(hsa)	CEP68	FBXO9	DGAT1	UBXN2B	RXRA
PEX19	SLAMF1	RPUSD1	EZH1	hCG_2040048(hsa)	KIAA0642(hsa)	AKAP13	THBD	WHAMM
KSR1	IL2RB	NACC1	FAM122B	CAPN3	RGCC	ESYT2	AK1	ZNF213
FUS	TP53I13	FAM64A	C7orf73	NKD2	CRYL1	GNAI2	HSPA1B	SPRY2
THEM6	FBXO42	SERPINH1	RGMA	CYP4F3	PDRG1	CPA4	PRR19	RPL7
FITM2	ALG1	ZNF226	APOA1BP	RNASEK-C17orf49	GRINA	IGFBP3	STEAP3	MEX3C
KIAA0886(hsa)	SZRD1	ZNF580	ARHGEF10L	RNF24	TMEM59L	PIK3CA	TRIM58	CACNB3
ANXA4	B9D1	NOTCH2	ATG14	MRE11(hsa)	PIP5K1A	H2AFI(hsa)	IQSEC2	ZNF581
NELFCD	TRAF7	ZNF519	AGPAT2	SLC29A1	FAM120C	SLMO1	CDC42SE1	YTHDC1
ITGB8	LMBR1L	GABARA	ZNF576	YPEL3	TNFRSF25	GNB2L1	SERF1B	SCMH1
PGR	YWHAG	CHPT1	ASAP1	RAB1F	CHRAC1	SLC1A4	C11orf68	USH1C
CADM2	NPW	HEATR1	GOSR2	CHCHD10	C6orf62	KIAA1011(hsa)	MGAT5B	R3HDM1
FXYD1	PORCN	CARS	ZDHHC16	LNPEP	SRC	NEU1	ATO8H	H4FA(hsa)

FAM126B	H4/I(hsa)	PTMS	ZBTB46	AFF3	TCOF1	RALGDS	SLC27A2	DSP
PWWP2A	C12orf5	HIST1H3E	RNF10	CXorf38	KLHL23	FASTKD5	ITGA6	NPWBP(hsa)
RHOBTB3	PPPICC	TSPAN12	KIAA1524	DLC1	DNER	RP11-30H12.3-002(hsa)	IGDCC4	SCRIB
WDR7	MCL1	CHMP2A	MAPK11P1L	TIRAP	DUSP8	ZNF211	hCG_2017814(hsa)	RPL10
RTN4R	PTPN4	TMEM132E	GREB1L	POLD3	STC2	LGALS8	NUA(hsa)	RIN3
ASIC1	KIAA1398(hsa)	GLS	EFHD2	RABGGTA	PPAPDC1B	ZNF81	CEP290	H2BFN(hsa)
CDK4	POMT2	PLOD3	EDEM3	CLEC11A	PLAUR	FBXO44	TMEM200B	MECR
PROM2	TMEM37	ID4	cyclinE2(hsa)	LINC00472	SOX6	GRIN2D	CLAPA1(hsa)	ZFAT
JMJD4	SAZD(hsa)	VCL	STK32C	SUPT16H	ICAM3	LSM2	NAPA	IL6R
EPB41L2	BBS1	DHX40	CHP1	DAQB-147D11.2-002(hsa)	CYBB	KIAA0355	ZNF618	ABRACL
COG2	TBL3	ARHGAP26	PPP3CA	FOXN3	hCG_29955(hsa)	LONRF2	TANC2	UBOX5
GPHN	METTL1	USP47	ZBED1	FAM120AOS	ANKFY1	SHMT1	METTL7B	C9orf142
BSDC1	NFKBID	MAG	MLL14	SNAPC5	DDOST	TAF1C	SERINC2	CYB561D2
CXCL8	PTPRR	TLE2	AKT2	MYC	CORO2B	KRT222	EG5(hsa)	COA7
RAC2	FBXL12	IMPDH2	GLUT14(hsa)	PPP6R3	ATF1	GPSM2	EPHA4	KCND3
ZNF879	MRPL34	CTSC	TRIM14	ADAR2(hsa)	PTP4A1	PLXNC1	RRBP1	EFNA1
NUCKS1	H3FL(hsa)	AMOT	CDA	DEDD	SDAD1	C5orf24	DECR2	ELF1
BAIAP3	FAM35A	VAPA	RANBP3	ZDHHC6	PAK4	VPS39	DIXDC1	PRR25
BLM	ZNF639	RHOU	CD320	SMU1	LRRRC28	DDA1	FAM171A1	ZCCHC3
METAP1	RP11-321N4.1-003(hsa)	H4FD(hsa)	AGPAT1	MRPL16	H3FF(hsa)	SPINT1	PDLIM7	RBM15B
RDH11	TAOK2	PLEKHG4B	ATP6V1B2	ACAP3	FGFR1OP2	ASS1	SCNN1A	TXNIP
RAPGEFL1	ZDHHC8	DPAGT1	PCGF5	TATDN2	MESDC2	IL17RE	ST5	LUC7L2
SCD5	UHRF2	C9orf117	UBQLN2	UBE3C	SHOC2	NCDN	VEGFA	HIST1H4J
HIST1H1D	ACTG1	GM2A	RBM8A	KIF4A	DNMT3A	FAM24B	TBX18	KMT2B
TPM1	PCK2	RPP25	SLC7A1	PARVA	TOLLIP	CYP1B1	DAMA-236L13.16-005(hsa)	HIST1H2B0
LSR	TSPAN3	NHLRC2	FOXP4	CENPF	KMT2D	SCD	SYT15	HIST1H4E
RP3-339A18.4-002(hsa)	FOXMI	IKZF4	D7SR(hsa)	IKZF5	SEPN1	HOMER1	PTEN	NEFL
KCTD12	FOXH1	ACTR8	MAWD(hsa)	SON	VPS26B	ACSL4	KIAA0660(hsa)	GGNBP2
PREX1	DISP2	RP3-511B24.2-013(hsa)	MYO1D	HCFC1	LY6G5C	KLHL9	AP2S1	HIST1H4B
ATN1	SMARCA2	ARFGEF2	ARHGAP35	GFAT(hsa)	FSCN1	GRHPR	NUB1	ZNF785
UBAC2	ETS2	KCTD5	SLC2A3	HIST1H2AK	SNF2L4(hsa)	MVD	NFATC3	SOCS7
NOTCH2NL	RR2(hsa)	XBP1	FBXO34	TRIM3	GPALPP1	SGT1(hsa)	APBB2	F8A1
CCDC92	KIAA0324(hsa)	PPP2R5C	ASAP3	EPLG2(hsa)	KIAA0226	CYB5B	PSDR1(hsa)	C2ORF15
WIP1	RABGAP1	ITM2B	TTC28	KOC1(hsa)	SLC25A22	TFIP11	ZC3H4	CT45A1
CTNND1	WDR70	hCG_39606(hsa)	SLC9A3R1	CD46	C1orf56	LGALS1	TTC19	CYFIP1
FAR2	SATB2	NDRG1	C8orf58	NOS3	MPZL2	CHAF1A	CDPF1	ZNF230
LMAN2L	HNRNPD	HSBP1	PTPN13	CTDSPL	LDLRAD3	C14orf28	FGFR1	ZNF2
RP11-51701.1-002(hsa)	PXN	SNAI1	IDI1	MYO18B	POP1	DNA2	SUPT7L	CFHR2
KIAA1324	TM9SF3	B3GALNT2	FOXP1	FBXL17	KDM6A	EDC3	SCARB1	NUDT3
NXPE3	GSPT2	SPATS2L	hCG_2031635(hsa)	FBXO3	NMRAL1	TNFRSF1A	DUSP16	C5orf22
HSPC130(hsa)	DBT	POLR1D	ATM	CD68	EPS8L2	KIF18B	MARCH6	HIST1H2BM
RAD23B	RC3H2	ZNF768	SOGA1	RHOGAP1(hsa)	UBE2K	SREK1IP1	PALLD	S1PR2
SH3PXD2A	SLC2A13	ATAD5	RABGGTB	B3GNT4	H2AFO(hsa)	GUF1	ARC	HIST1H4K
HIST1H2AI	ORC1	SEC61A1	ZSWIM1	MISP	CAMK1	AURKA	RP11-90D4.2	NR4A1
ADCK2	EFL3(hsa)	SPTBN2	CAPZB	MARCH8	KIAA0462(hsa)	ESPN	SIX4	SNX12
H4/H(hsa)	KIAA1321(hsa)	FUT1	LAMC3	MKLN1	hCG_1992160(hsa)	ZNF644	SNED1	CT45A2
ZNF513	NUP210	MGLL	SHKBP1	SEC14L2	NUP50	TATDN3	SGK3	PCGF2
hCG_1994842(hsa)	ZZZ3	CDKN2A	DUSP10	SMIM15	THAP2	KIF2(hsa)	TEX264	CISD3

FRS3	TUBB1	RTKN2	TAGLN2	TCTN1	BCORL1	ZNF512B	SPTBN1	C17orf100
USP25	RNF39	MIEF1	DYX1C1	TXNRD1	MMAB	DKFZp666B209(hsa)	HNRNPUL1	SERPINA3
ZGRF1	ZNF16	KIAA0513	MINOS1	LCN2	H4FE(hsa)	PCDHGA4	CHD6	KLRK1
H2AFJ	MAPKAP1	FAM175B	RFXANK	BCKDK	H4FJ(hsa)	LEPREL2	EIF3G	GTF2I
ACSS1	X104(hsa)	PPP1R12B	TIMM10	NIPSNAP3A	PEA15	DNAJB12	CCDC85C	RASL10B
TKT	ACOX3	RPP30	FURIN	PPM1A	IPO5	KDM7A	HSPA1(hsa)	MYO19
BRD2	TRIM35	H6PD	FLAF1(hsa)	PARP16	CACNA2D4	THOC2	TMEM55A	CXorf65
USP36	PERP	TJP1	ACP6	RAB36	AIF1L	GNP2	LATS1	VAMP3
USP38	GMFB	LOXL3	TES	TOM40(hsa)	RARA	NUP43	HOXB13	TSACC
PXDC1	PMEP1A	KDM2A	HECTD2	ABHD16A	SNAPC1	PLEKHA1	PPP1R1C	TMEM189-UBE2V1
RNASEL	SLC35E4	PGM3	CECR2	HSPA14	CASP9	D4S234E	SLC35F6	SYNRG
ELAVL2	MYOF	CDK5R1	ANKS1A	COPS3	CTC-281B15.1	FAM102A	CENPU	FCGBP
FEM1A	TCF7L1	C1QBP	CEBPB	PRELID1	SH3RF1	LEF1	STYXL1	HIST1H4D
M6PR	PAST1(hsa)	PLGLB2	PERQ2(hsa)	PIGQ	CPLX2	OCLL	APIB1	HIST2H2AA3
HNRNPA1	SMC6	UBE2J1	TICRR	hCG_23463(hsa)	ETHE1	PVT1	DMRT1	ACACA
DICER1	ARPP19	UBC	STK38L	RAD23A	RYR3	MRPL28	KIAA1841	NATD1
TMEM205	WDR27	RRP36	IDH3A	CRBN	STX18	LIN7A	IRAK1	TAF15
FRMD4A	GDF11	NAAA	GNA11	PLEKHO2	SESN2	KMT2A	C17orf97	TFDP2
ACOX1	NABP1	H2AFE(hsa)	ISOC1	DOK3	NARF	ROGDI	UBALD2	TPTE
TMEM141	SERGEF	ZEB1	LLGL2	DEPDC1	RTP(hsa)	FAM222A	IRAK4	NPHP3
ARSDR1(hsa)	TESK2	S100L(hsa)	STRIP1	SFXN5	VPS52	RARG	NFIC	MLLT6
CAP43(hsa)	NKTR	H2AFN(hsa)	LYPD3	SPFH1(hsa)	CDC7	LRRFIP1	DAAM1	CTDSP2
DRG1	NPTXR	TMC8	GTF3C2	SFXN3	RNMTL1	KIAA0368	SPSB3	CWC25
DNM2	FAM127A	ZNF280C	SOSTDC1	RPGRIP1L	MNEI(hsa)	CHCHD6	PLK4	IKBKE
SDC1	CMAS	TMEM164	PNT5(hsa)	CNFN	RAP1GDS1	CDK20	CAP1	ORAI1
E2F2	ETS1	MORN4	ETNK1	KHK	FUK	AKR1A1	H2AFL(hsa)	WBP1
MLF2	RILP	NARS	PEG10	USP46	PPDPF	HSPC272(hsa)	BMP7	ZNF280B
CASP7	BRIP1	PPP5K1	MOB3B	SCAF6(hsa)	C6orf89	ALDH4(hsa)	316M21.1-003(hsa)	HIST1H4A
ATXN7L2	SH3BP2	HEBP1	FAH	TP53INP1	FGF18	C8orf22	ABCA3	BRD4
TPD52L1	PTPN14	OK/SW-cl.73(hsa)	SRRD	LRP8	HIST1H3H	GOLGB1	EMC1	
RCN1	EIF2AK4	HMP(hsa)	GHDC	ELMSAN1	FAM76A	PPP1R21	LRRC49	
RBM12	HS2ST1	TMEM179B	CUEDC1	HIST1H3D	824I19_A.1-011(hsa)	PDE5A	BBX	
SCAI	POLM	BRG1(hsa)	LCORL	MRPS15	RP11-874J12.2	RHBDD2	INF2	
ZBTB10	SYPL1	MTMR2	AKT1S1	ARL17A	CCEP1	UBAP2L	BBS4	
MAMT4	PSME3	GAS2L3	ZNF397	EQTN	AUNIP	MED19	DCAF16	
FAM32A	LRRC8D	OSBPL7	GFPT(hsa)	SLC4A2	KCNC4	ZBTB48	GRHL1	
CAMK4	LINS	QSER1	WSB2	C12orf29	TMED4	NAGS	TAF5	

miR-345-5p

TERF2	CPSF7	ZNF664	LSM5	SPEN	FIGL1	RSBNIL	DGKD	DVL2
C17orf85	PTRF	NT5E	DHODH	GFPT1	SRRM2	STARD9	ZNF106	PSMG4
AK2	CDC25B	BCL2	LIMS1	MYLIP	METTL21A	DMPK	NCKAP1	ZBTB25
NEK7	DHCR24	RNF111	TOP2B	GCN1L1	SEC31A	G3BP2	PSMA4	RNF139
ZEB2	LENG8	BOD1L1	PANK3	CLTA	AQR	FASTKD5	MAN1A1	EIF1
TMED8	PRRC2B	ALDH1L2	EEF1D	SLC19A2	SHOC2	RWDD2A	ACIN1	MGAT4B
DAZAP2	SRP19	DAP	GPR35	RYR2	KMT2D	SCD	XRCC5	AMN1
GUCD1	DLG1	AIM1	MIS18BP1	PPP1R10	IPO4	DNAJB12	RND3	RBM15
LARS2	SKIV2L2	IGF1R	EDEM3	ARFRP1	SESN2	SCAF1	TCF7	AUP1
S100A16	IDS	FMR1	AKT2	F2R	TNFRSF10B	NDC1	PHIP	RTN3
SEN3	NELL2	PPM1E	PCGF5	PPP6R3	CYSLTR1	CTCF	FBXO33	TMBIM6
ADCY1	HTT	GGH	SLC7A1	SON	C16orf72	PKN2	ZNF652	OR51E2
TTC39C	CCND2	PTGR2	RABGGTB	STRN4	DYNLL2	CDKN1A	TTC19	EIF4G2
DNAJC6	TAOK2	GNB1	RPLP2	TIAL1	NF1	UHMK1	FGFR1	AP3M2
ATN1	MOCOS	BMP6	ZBTB37	ZC3H12C	FAIM	ANKHD1-EIF4EBP3	MARCH6	MIER3
GARS	DBT	RHOA	MLEC	ECT2	MALSU1	CNEPIR1	SPTBN1	VAMP2
FAM32A	BACH1	EIF1AX	LARP1	PSMD14	KIAA0100	KIAA0930	MUM1	UBR4
MTHFD2	KIAA0319L	ATP6V1G1	ZC4H2	HIC1	MED28	DONSON	MAPK1	INO80D
STK4	E4F1	GBF1	HDGF	ZC3H13	EIF2S1	VPS28	MTMR3	TXNIP
MMS22L	GSE1	GSTO1	KLHDC10	RAB18	JADE2	TNPO2	FBXW11	GREM1
KIF1B	NFIL3	CHD4	AGO1	GSTP1	GSK3A	BTBD7	RPL27A	SYS1
UBQLN4	GPSM1	SMARCD1	BTG2	PPM1L	SLC39A6	CKS2	TET2	MARCKS
ZNFX1	PERM1	SLC03A1	FBN2	EIF4ENIF1	LMAN1	MPPED2	SYNGR1	PCGF2
BRD8	NHLRC3	CHMP4B	TOP2A	NRP1	PRDM2	CNBP	SART3	MAGIX
UBR5	FBXO4	TMEM145	LPAR1	IPMK	ZNF35	SASH1	RAD9B	MYO18A

miR-200c-3p

TERF2	COP58	ORMDL3	QSER1	EDEM3	MCTP2	KBTBD11	FBXO22	LATS1
RTN4	MSMO1	LMO7	HNRNPU	FAM46A	GDAP2	EIF3J	FN1	THNSL1
RPRD2	ZNF605	FZD6	HSDL1	PPP3CA	ANP32B	C6orf62	MYCN	ALDH1A1
SLC9A2	CCNL2	SOAT1	PPP1R18	DPY19L4	CEP41	MAPRE1	UBN2	CAB39
HSPA13	MCM8	RDX	SPRED2	UBA6	YEATS4	PTP4A1	C22orf39	ATP13A3
ANP32E	GNS	TOB1	VLDLR	CHURC1	DNAJB9	SHOC2	SPTSSA	PHOSPHO2
ADAM9	HNRNPD	INPP5F	UBE2I	PTK2	PPP2R2A	DNMT3A	RAB22A	NUPL1
CCNG1	VAT1L	CTBP2	VEPH1	C9orf41	RNF24	SESN1	LRIF1	RNF168
DUSP4	DENND4B	TMEM167B	KRAS	TTC8	KIDINS220	SIAH1	BAG6	AMOTL1
RAB4A	FBXO30	GAN	EPDR1	NLK	LNPEP	ANKRD46	RBM12B	LATS2
C22orf46	TCF4	WNK1	HEG1	CEBPB	GPR98	PPP1R9B	ZNF92	FBXW11
NEK7	TMED7	GSE1	IP07	MGAT3	QK1	SDE2	UHMK1	PPP2R1B
ZEB2	APC	HOXB5	SEPT7	SEPSECS	ASXL3	SCO1	LHFP	GREB1
MLK4	CRK	PBX1	SETD2	ISOC1	SON	KIF11	BIRC3	ABL2
ZMAT3	FBXW7	B4GALT6	SLC35A4	ARHGAP18	LPL	TNFRSF10B	ATG12	KDR
JARID2	DHX29	NBR1	SERINC1	TUBB4A	DOCK5	SURF4	BDP1	USP33
CASP8A2	UHRF1BP1L	TRPS1	FSTL1	GART	MARCH8	FAM220A	SYNE2	RANBP9
CNOT6	SHC1	MGA	FBXL16	CCDC127	MKLN1	CHD2	NAA16	RAD21
GSKIP	SIRT1	GAL3ST1	SLC16A9	BRCA1	SMIM15	DZIP1	ARF6	KMT2C
FBXL3	NLN	CLCC1	PHF10	ZNF217	PLK2	C16orf72	USP9X	CDK16
NTRK2	RUNX1	NET1	TCP1	ITGAV	MYO9A	FAM199X	MBNL1	ADCY9
PKIA	ABCC1	TMEM64	CPD	STK17B	WSB1	ST7	PRC1	HELLS
UBFD1	CLCN3	KLHL20	MSN	ZNF697	TP53INP1	TSC22D2	NFIA	BTG1
COA4	PAK2	SLC22A25	ZCCHC2	TRIM59	ELMSAN1	PPM1F	TBP	PCDH9
SLMAP	ATMIN	SMARCAD1	NUDCD1	TMX4	SERPINI1	BTAFA1	GPM6A	CAPRIN2
TSC1	AKIRIN2	PTDSS1	NAP1L5	PSMB4	SNX1	CLASP1	CNEP1R1	BAP1
PIM2	ANKRD52	BCL2	LBR	CCDC43	TMBIM4	ZC3H11A	EDNRA	MRPL15
RBM27	COX11	CDKN1B	TAOK1	PMAIP1	GLI3	ADNP	ALG13	PARD6B
PEAK1	SPATA2	SRGAP1	RBAK	CDH1	ARPC2	HSPA8	EIF4EBP2	SERBP1
ARL6IP5	MTUS1	DDB2	KIAA0101	RAB11FIP2	RELN	FIGN	PPM1B	FNBP4
UGCG	PPP2CA	STYX	CANX	PITPNM3	BLOC1S5-TXNDC5	CCNY	MORC3	RAP1B
ERBB2IP	SETD7	MED13	CDR2	KIAA1432	NMD3	KDSR	BCL11B	KLF6
TNPO1	LRRC8B	TUBB	SMG8	DDIT4	PCBP1	CDK13	NOL8	FSD1L
UBE2Z	ZNF431	SLC31A1	KBTBD6	SFXN1	ANKRD42	RANBP2	HMGCS1	RANBP6
GLG1	CPEB4	XPOT	TIPARP	NFAT5	KANK1	SRP72	PTPN12	KIAA1279
POMZP3	GAPDH	DDX6	SIKE1	MFSD9	STX17	FAM13B	EXOSC6	PKD2
ZNF638	ADAR	RALBP1	CWC27	CHMP2B	VIM	MDM4	BCOR	RNF139
PDCD4	ZNF131	SH3GL1	ALDH6A1	PIKFYVE	TMED10	OSTM1	CREG1	CBX5
UBE2R2	SUGP2	HIPK3	FAM60A	DPPA4	REL	B3GALTL	LIMA1	KLF4
TM4SF1	USP31	DLG5	NCOA3	TET3	FRMD6	KRT80	CUL3	TBL1XR1
OTUD3	TCF7L2	PLD1	DDX60	ICA1	ANKRD44	TAF7	BTBD7	WDR37
SPPL3	PLAGL2	MYZAP	LPP	CHN2	EIF2S3L	USP42	TMEM263	C14orf132
PPP2R5E	ZYG11B	CAND1	TMEM123	AP1S2	LPIN2	NMT1	ATP2A2	DUSP1
FEM1B	USP1	PXYLP1	GIGYF1	YIF1B	TTC3	SLC20A1	HIPK1	SPOPL
SMC1A	UBQLN1	AGO2	SKP1	NAV2	E-cadherin(hsa)	LAMC1	AHNAK	SECISBP2L
TROVE2	DLG1	KIAA2018	ANLN	PAN2	DBR1	RPS6KA3	YES1	MTSS1L
ZBTB11	HOXD13	EPG5	NSD1	LARP1B	ZMYM2	ERC1	NRIP1	PRRC2A
CNOT11	SMURF2	MCFD2	RASSF2	RSU1	FLT1	LMAN1	ZBTB34	RAB5B
ID2	RNF103	LMNB1	PLEKHA8	PLCG1	KANK2	VMA21	KCTD15	AKAP11
SLC30A5	RSF1	ZNF302	CMTR2	PHC3	ZBTB5	PROSER1	RGL1	MAP7D1
PACRGL	VAC14	TNKS2	RPS6KA5	TOMM5	SLC38A2	DES11	LEPR	BAG5
RNF2	CSNK1G3	GOLT1B	MFHAS1	NCOR2	EIF4B	PRDM2	GLRX5	GOLIM4
MED13L	PURA	ATP1B1	RHOT1	SLC16A14	RNF19A	GAB1	PLEKHH1	NIN
WNK3	OGT	ELMO2	TUBA1A	STX16	ARMC9	ZCCHC14	UBE2W	ZNF669
DDX3Y	ZNF597	ARID4A	MITF	PDCD10	ABHD5	DCUN1D1	VMP1	SYVN1
NDFIP2	SOWAHC	CCDC117	NUAK1	JUN	ZC3H13	S100BPB	RAN	KIAA1429
TPD52	ZNF43	EFR3B	DDX21	ZNF711	DENND6A	TWISTNB	MKNK2	VKORC1L1
MXD3	HTT	FBLN5	EXOSC3	CRTAP	NOL4L	ATF7IP	KRR1	ARHGAP12
SSR1	ARL2BP	RPP14	ABHD17B	WEE1	SMAD5	YIPF5	GD12	BCL2L11
GATM	NEDD4L	NUP160	HDAC4	ATP6AP2	GALK2	ZNF281	TSN	GTF2E1
ZBTB38	YWHAG	ASH1L	FANCM	TRIM33	WHSC1	ZFP36L2	TSN	NAPIL2
KSR1	SEC23A	SHCBP1	TOP2B	TXLNA	ATP11A	PHF12	C9orf78	HCCS
FUS	MCL1	IGIP	PANK3	CCND1	MMD	EIF4E2	OSBPL8	GPATCH4
SAR1B	PTPN4	CD164	SRSF1	WDR82	CPT2	CFH	NEDD1	XIAP
NUCKS1	TGS1	TIFA	MYNN	FNDC3B	ZFPM1	ILDR1	CWC15	ERII
MGST1	ZDHHC20	DNAJC5	PURB	EFR3A	SFPQ	RIN2	CMTM6	MIER3
PREX1	CDK2	UGP2	LRPPRC	ZNF678	ITPR1	BRD1	CTDSP2L2	RAB34
SMAD2	RAB7A	KPNA2	TAF12	LPAR1	CDYL	DLD	UHRF1BP1	PPP1R3D
SH3PXD2A	ALDH1A3	EV15	SENP6	B3GNT1	CFL2	CERS6	SLC35B4	KIAA1430
BNIP3	MKL2	TMOD3	MTRNR2L4	TUBA1C	CDCA7	DDX39B	PTAR1	PPP1CB
USP25	EEA1	TARDBP	RECK	PVRL4	BAZ2A	UTP23	MOB1A	C2orf69
CBL	TM9SF3	SERPINH1	GABPB1	CTNNA1	STRN3	KIAA0040	CDC42SE1	SYNCRIP
DICER1	TOMM20	KPNA4	ARIH1	CCNE2	CDKN2AIP	SUZ12	SPIN1	GRIA3
TPD52L1	SNX30	NOTCH2	IARS2	GFPT1	TMEM185B	HNRNPH1	PRKRA	MEX3C
RBM12	LMBR1	SQSTM1	IFIH1	SMARCC2	ZFAND6	SNX13	SUCO	TRAPPCC8
PAM	GMFB	TAF4	MED1	MRPS30	NPNT	LGALS8	ZFPM2	YTHDC1
MAST4	TCF7L1	KLF11	ITSN2	SBNO1	ERIC1	GALNT2	ZNF618	INO80D
AMFR	ARPP19	CNIH4	SLC25A38	FEZ2	SLC25A36	CEP57	XPO1	ZFAT
REPS1	BDKRB2	TIMP2	AZIN1	ARL6IP1	ARL5A	C5orf24	TRIM71	FHOD1
SCAF4	PITG1IP	ITM2B	TXNDC16	USP5	BHLHE22	SCD	DIXDC1	GSPT1
IP6K1	FAM127A	NRG1	H2AFV	NPEPPS	ZNF280D	UBE2G1	GPBP1	EFNA1
CRKL	ETS1	ASPH	NFYB	SPK2	RAP2C	NGRN	CPEB3	SOC57
ARHGAP19	NRBP1	RHOA	TEX2	WWC3	KLHL15	SREK1IP1	ZNF652	DACHI
CD59	HUWE1	SPATS2L	SBF1	BLOC1S6	NRS5A2	ZNF512B	ZC3H4	MARCKS
STK4	FRS2	ENSA	YME1L1	LRRC58	PPIL4	KDM7A	FGFR1	SYNRG
TET1	CBX4	MIEF1	RYK	FAM8A1	RCHY1	ENPP4	MARCH6	ACACA
TPCN1	NRBF2	CHD7	DAP3	PPP1R10	SLC26A2	KMT2A	FDPS	
RASA2	BCL9L	CDK5R1	ANKRD40	HELZ	TBK1	VEZF1	DCTN6	

ZNF673	ALG8	ZEB1	KLF13	PM20D2	JAZF1	LIMK1	HPS5
TRIM52	PTPRD	PSAP	ASAP1	E2F3	EPHA2	GEMIN2	PI4K2B
ELK4	CAMSAP2	COPS2	GREB1L	MXD4	ASCC3	DHX9	ERRF1
CLIC4	ZNF121	HIC2	ACVR2B	PAIP2	CUX1	DERL1	ATL3

miR-10a-3p

CCNT2	SMAD2	KATNBL1	RAB1A	CREB1	CYB5D1	LYST	ICK	USP3
B2M	DICER1	GAB3	QSER1	MED4	ATL2	DDX5	PLAG1	HOXA11
KIAA0754	RBM12	BRIP1	TCF19	GREB1L	PPAP2B	DNM1L	PUM2	LSM14B
C16orf52	TMEM33	SYPL1	ZBTB6	EIF5	DNAJC13	C6orf62	AHR	NME1
PFN1	POLI	BACH1	CDK6	TES	LNPEP	PRKAA1	PIAS4	VEGFA
AK2	PDK4	NOD2	KIF23	STK38L	STAU1	ANKFY1	RSBN1L	SPTBN1
RBM14	DIEXF	GLMN	DDX3X	MOB3B	POLD3	ATF1	SPATA6	FOXO1
HOXB7	HP1BP3	PCTP	COPB1	PISD	SRPK1	IPO5	FREM3	MRPS36
ADAM9	THUMPD3	CAMSAP2	INIP	WSB2	QKI	SESN1	MZT1	RNF168
SLC38A1	CLIC4	FICD	NID1	GART	FBXO3	MCUR1	AKAP5	MAPK6
MED29	HOXB4	FZD6	C12orf75	TFDP2	MKLN1	CDC7	ZNF564	FBXW11
EGR1	MSMO1	UBE2E2	PHF10	BRCA1	PPM1A	EBAG9	G3BP2	ABL2
FOS	KIF1B	TRIP11	ADD3	LARP1	SRSF6	TRIO	BRPF1	GAS1
MTA3	CNCL2	CHUK	CCDC71L	PLCB1	C21orf91	RDH10	SH3BP5L	DNAJC27
DARS2	ZNF83	TMEM64	HPS3	DOCK10	PPP1R14C	INTS6	ATP6V1C1	MGAT4A
BRWD3	HNRNPA3	ZNF664	SLCO3A1	CNIH1	ITPR1P2	TSC22D2	SCD	PARD6B
PKHD1L1	C5orf42	TNFRSF11A	APP	DDX18	PLEKHA3	TXLNG	SDC2	MRPL49
ARL4A	VANGL1	FOKK1	MAT2B	PMAIP1	PCBP1	SSX2IP	SREK1IP1	TOP1
PAGR1	PTCH1	HBP1	KIAA2026	ANP32A	SLC16A1	CCDC50	ZNF644	BRWD1
ZBED5	DBN1	SLC31A1	KIAA0101	KIAA1432	CLPX	HMG20A	OCRL	KLF4
PEAK1	FCHSD2	MACF1	PLAGL1	NFAT5	SKIL	RANBP2	MALT1	SLAIN1
ENC1	HLTF	SQLE	PDS5A	PIKFYVE	ATRX	HINT3	XPO4	PIAS1
TNPO1	ANKRD52	COL19A1	TMEM38B	PPP1R12A	VCP	SSR3	ZNRF2	ZNF91
ZNF638	SAMD8	GLUD1	KIAA1109	AGO1	TTC3	OSTM1	SLC7A2	IREB2
TGFBR1	CYTH2	AFF4	RFX7	SND1	IRF3	FN3KRP	TMEM45A	PTGES3
MACC1	SETD7	IBTK	FJX1	MAPK9	PSMD14	FNIP1	UHMK1	TSPAN13
KIAA1731	CEBPZ	CSDE1	HK2	PCNX	GDE1	BTF3L4	BIRC3	ARHGAP5
IRF4	HABP4	STAG1	AGPAT5	FMNL2	RNF19A	C19orf10	HIAT1	AKAP11
PDHX	ING3	RNF217	LPP	BTG2	EIF4G1	AKIRIN1	TNRC6A	MDM2
FEM1B	USP31	SETD5	GIGYF1	PHC3	RAB18	ZNF451	RNF170	SLC39A14
ARID3A	FKTN	SFT2D2	RCN2	B4GALT1	DENND6A	ARHGAP29	NFIA	SLC30A6
MET	UBQLN1	ZNF280A	CMTR2	PNN	CSRNP3	GFM1	PAN3	NIPA1
ATP6V0E1	ATG2B	AGFG1	UNG	PPP1R15B	FOSL2	NDUFB2	SESN3	HMSD
DENND4A	PID1	RAB12	ZNF680	ABHD17B	ELOVL5	LMAN1	ACTR3B	BMPR2
ZNF616	TAF2	PABPC4	INSIG1	FBXO28	STAM2	PRKAR1A	ANKEF1	BCL2L11
PHF20L1	TEFM	DSE	ZNF354B	CCND1	HIST1H4H	VMA21	ZNF483	KIF5B
ANO6	ARHGEF12	PRAF2	LRIG2	SMAD4	ATIC	SUMO3	ZBTB1	LMO4
CUTC	MCL1	UGP2	PDE4D	CTNNB1	PCMTD2	PROSER1	PHF13	PLS3
PSMD5	RAP1A	TPX2	DDX21	ANXA7	TEAD1	EP300	RASSF8	DGKH
CHRM5	CP51	LY75	ACBD3	WDR44	AEN	MIDN	AHNAK	PPP1CB
SSR1	ZDHHC5	PRR5L	SREBF2	GFPT1	USO1	PRDM2	YES1	NDEL1
CAMKMT	SMARCA2	TARDBP	ZXDB	ASPM	DOCK4	DDAH1	PRKDC	F11R
RIPK2	ETS2	TXNDC11	RPS8	PBX3	IPMK	SLC10A7	JADE1	
PGAP1	HOXA9	RDH14	CTTN	AXL	SLC9A9	BTG3	TRRAP	
LAMB1	RC3H2	RHOA	RNF149	NUFIP2	DLGAP5	TMEM245	PDZD8	
CXCL8	CFDP1	POLR1D	TRIP12	ABCC9	ADAM22	THTPA	U2AF1	
CCT2	KAT6B	FEM1C	ZNF317	TRAK1	TFPI2	ARL5B	SNX5	
KDM5C	PDE10A	H6PD	DCAF7	PAICS	RCHY1	MPRIP	CLSTN1	

Table A4. Complete output from DIANA-miRPath v.3

Table A4. Complete output from DIANA-miRPath v.3 when using the miRNA signature (miR-34a-5p, miR-345-5p, miR-200c-3p, miR-10a-3p) as input, from both approaches: MicroT-CDS (*in silico* miRNA target prediction algorithm) and TarBase (experimentally supported approach). The columns show the influenced KEGG pathways, *p*-values after Benjamini-Hochberg correction, number of targeted genes and number of associated miRNAs from the signature. Significant *p*-values are highlighted in bold.

KEGG pathway	<i>p</i> -value	#genes	#miRNAs
MicroT-CDS			
Mucin type O-Glycan biosynthesis	1.184275e-12	5	2
Glycosphingolipid biosynthesis - lacto and neolacto series	3.884874e-10	4	2
Biotin metabolism	0.0006064075	1	1
Proteoglycans in cancer	0.0007940732	22	1
ErbB signaling pathway	0.0008384294	16	1
MicroRNAs in cancer	0.00138567	20	1
Thyroid hormone signaling pathway	0.002132528	16	2
Phosphatidylinositol signaling system	0.00647907	12	2
Neurotrophin signaling pathway	0.009801489	22	1
Renal cell carcinoma	0.01097907	13	1
Glycosaminoglycan biosynthesis - heparan sulfate / heparin	0.01113265	4	1
Lysine degradation	0.01605634	5	2
Hippo signaling pathway	0.04556428	9	1
Axon guidance	0.04746173	13	1
TGF-beta signaling pathway	0.05008158	8	1
Glioma	0.06553687	7	1
Circadian rhythm	0.06948476	5	1
Sphingolipid signaling pathway	0.07745415	12	1
Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate	0.1093001	2	1
Choline metabolism in cancer	0.1191737	12	1
MAPK signaling pathway	0.1518697	28	1
Sphingolipid metabolism	0.1821781	6	1
ECM-receptor interaction	0.2101148	3	1
FoxO signaling pathway	0.236839	17	1
Oocyte meiosis	0.248682	12	1
Glycosphingolipid biosynthesis - globo series	0.2859095	3	1
Small cell lung cancer	0.3219701	12	1
Carbohydrate digestion and absorption	0.3981785	1	1
SNARE interactions in vesicular transport	0.4719691	5	1
Base excision repair	0.5364044	1	1
Inflammatory mediator regulation of TRP channels	0.5608684	9	1
TarBase			
Pathways in cancer	7.806205e-09	141	3
MicroRNAs in cancer	3.356072e-08	36	1
Proteoglycans in cancer	4.259346e-08	82	4
Adherens junction	4.849975e-08	41	3
Colorectal cancer	6.624356e-06	37	3
Fatty acid biosynthesis	1.571663e-05	4	1
p53 signaling pathway	8.629925e-05	40	2
Endocytosis	0.000155911	80	2
Cell cycle	0.0001862279	52	1
Chronic myeloid leukemia	0.0003003506	37	2
Hippo signaling pathway	0.0005622035	26	2
Metabolism of xenobiotics by cytochrome P450	0.0007820423	2	1
Lysine degradation	0.0007881832	7	1
TGF-beta signaling pathway	0.0009288388	13	2
Prostate cancer	0.001594596	39	2
Hepatitis B	0.002008518	54	2
Oocyte meiosis	0.002446339	16	1
Bladder cancer	0.002960341	22	1
Thyroid cancer	0.003013095	16	1
Pancreatic cancer	0.003759289	33	1
Transcriptional misregulation in cancer	0.004338518	62	1

Viral carcinogenesis	0.004834794	74	2
Bacterial invasion of epithelial cells	0.00518036	36	2
Ubiquitin mediated proteolysis	0.006448268	22	1
Melanoma	0.007508105	30	1
Non-small cell lung cancer	0.007831112	26	1
Fatty acid metabolism	0.008055732	14	1
Steroid biosynthesis	0.008281795	1	1
Other types of O-glycan biosynthesis	0.01126346	13	1
Protein processing in endoplasmic reticulum	0.01302932	17	1
Regulation of actin cytoskeleton	0.014233	71	1
Glioma	0.01423311	26	1
FoxO signaling pathway	0.01449044	12	1
Thyroid hormone signaling pathway	0.01501771	44	1
Endometrial cancer	0.01737389	22	1
Small cell lung cancer	0.03340758	13	1
HTLV-I infection	0.04337413	81	1
Glycosphingolipid biosynthesis - lacto and neolacto series	0.04423077	9	1
Shigellosis	0.05387291	29	2
DNA replication	0.08411226	17	1
Renal cell carcinoma	0.09253995	26	1
Ras signaling pathway	0.1004746	24	1
Central carbon metabolism in cancer	0.1017866	27	1
PI3K-Akt signaling pathway	0.1389146	29	1
MAPK signaling pathway	0.140083	76	1
Huntington's disease	0.1587988	2	1
Wnt signaling pathway	0.1749672	14	1
Alcoholism	0.2882482	60	1
RNA transport	0.2884383	16	1
Neurotrophin signaling pathway	0.3112592	15	1
Progesterone-mediated oocyte maturation	0.4438475	31	1
Epithelial cell signaling in Helicobacter pylori infection	0.4488572	7	1
HIF-1 signaling pathway	0.5095467	35	1
Adrenergic signaling in cardiomyocytes	0.52571	10	1

Table A5. Comparison of studies investigating miRNAs from brain samples

Table A5. Comparison of studies investigating miRNAs from brain samples of FTD and/or ALS patients.

	Kocerha et al. 2011[1]	Chen-Plotkin et al. 2012[2]	Hébert et al., 2013[3]	Gascon et al., 2014[4]	Helferich et al. 2018[5]	Jawaid et al. 2019[6]
Disease	FTD	FTD	FTD	FTD	ALS	FTD, ALS
Cohort	Mixed sporadic/genetic	Mixed sporadic/genetic	Not mentioned	Sporadic	Mixed sporadic/genetic	Sporadic
Patients, n= Discovery/replication	32 PGRN+ 8 PGRN-	5 PGRN+ 7 PGRN-	5/14	5	5 C9orf72+ 1 SOD1+ 16 sporadic	10 ALS 9/12 FTD
Methods of analysis	Microarray	Microarray	Deep sequencing, qRT-PCR	qRT-PCR	qRT-PCR	qRT-PCR
Major deregulated miRNAs	miR-922 miR-516a-3p miR-571 miR-548b-5p miR-548c-5p	miR-132 miR-212	miR-132-3p	miR-124	miR-1825	miR-183/96/182

Figure A1. Stratified nested cross-validation

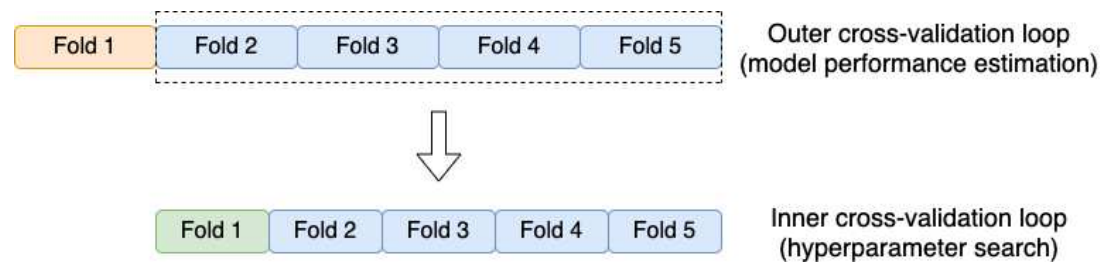


Figure A1. Stratified nested cross-validation scheme, with 5-fold outer and inner cross-validation. The outer cross-validation loop splits the whole dataset into five folds, using four folds as training data and one as test data at each of its iterations. Model performance is estimated averaging the ROC AUC using all five folds as test data. The inner 5-fold cross-validation loop splits the training data into four training folds and one validation fold at each of its iterations. For every outer loop iteration, one hyperparameter is chosen based on the highest average ROC AUC over all five validation folds.

Figure A2. Expression heatmap of miRNA signature

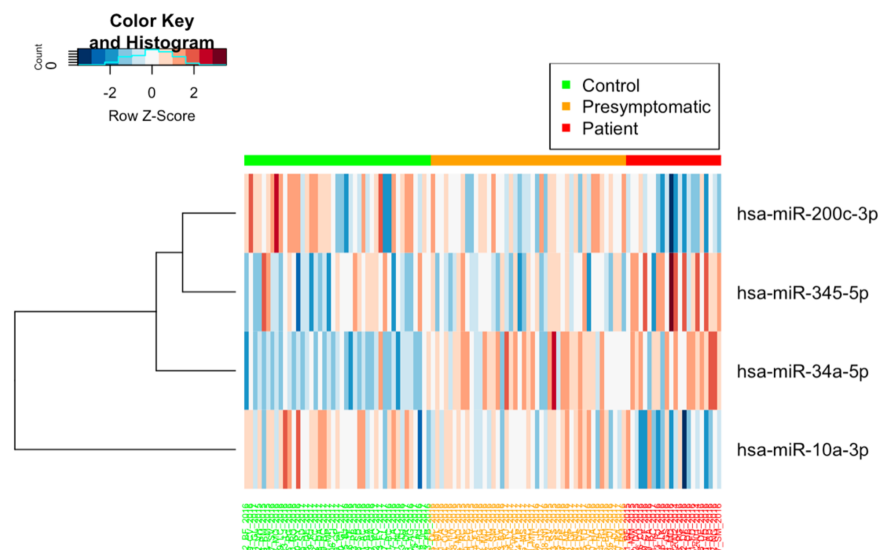


Figure A2. Expression heatmap and hierarchical clustering of the four miRNAs identified as differentially expressed. Rows represent miRNAs and columns represent individuals ordered by clinical status (control, presymptomatic and patient from left to right). The \log_2 expression levels of each miRNA are rescaled to have a mean of 0 and a standard deviation of 1, and z-scores are indicated by color: shades of blue indicate low-expression values, white indicates mean expression and shades of red indicate high-expression values. Dendrogram added to the left side clusters the rows according to the miRNA expression means.

Figure A3. Bootstrapped ROC AUC scores

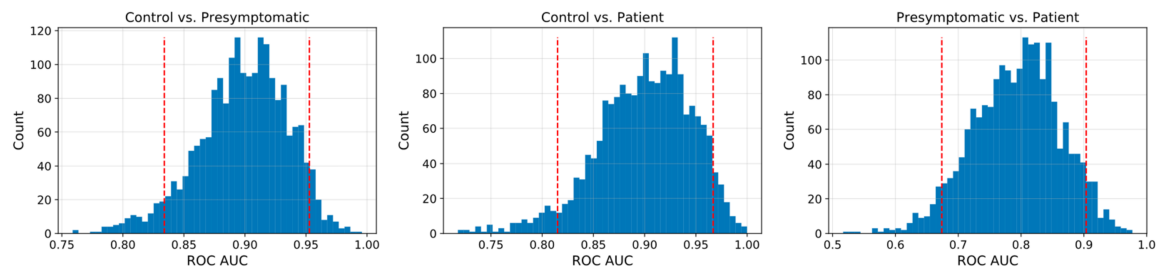


Figure A3. Logistic regression bootstrapped ROC AUC scores obtained with 2000 bootstrap samples for each pairwise comparison, using as features the expression levels of the miRNA signature (miR-34a-5p, miR-345-5p, miR-200c-3p and miR-10a-3p). The red dashed lines indicate the 5th and 95th percentiles (empirical 90% confidence intervals): [0.83, 0.95] for control vs. presymptomatic, [0.82, 0.97] for control vs. patient and [0.67, 0.90] for presymptomatic vs. patient.

Figure A4. ROC AUC scores with 100 different fold splits

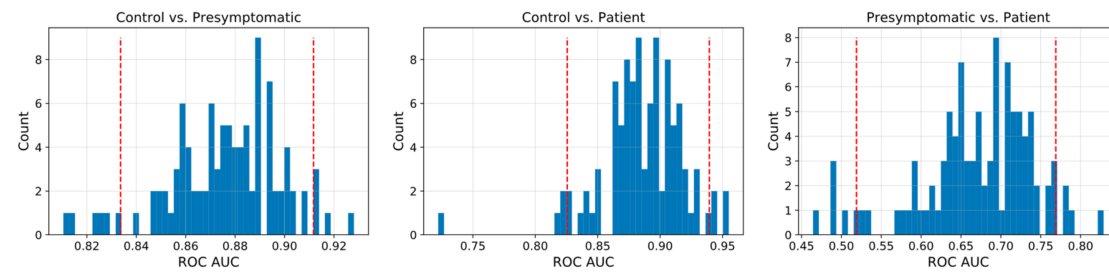


Figure A4. Logistic regression ROC AUC scores obtained with 5-fold cross-validation with 100 different fold splits, using as features the expression levels of differentially expressed miRNAs computed with only the outer cross-validation loop training data (four out of five folds) at each iteration. The red dashed lines indicate the 5th and 95th percentiles (empirical 90% confidence intervals): [0.83, 0.91] for control vs. presymptomatic, [0.83, 0.94] for control vs. patient and [0.52, 0.77] for presymptomatic vs. patient.

Figure A5. Presymptomatic subjects probability scores

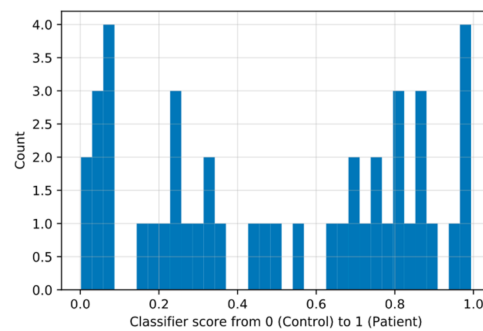


Figure A5. Logistic regression probability scores for all presymptomatic subjects (N=45), when model was trained with the expression levels of differentially expressed miRNAs in controls (N=43) and patients (N=22). Scores near 0 indicate that the subject has a miRNA profile similar to controls; scores close to 1 mean that the individual has a miRNA profile similar to patients.

Figure A6. Heatmap of the level of enrichment in KEGG pathways

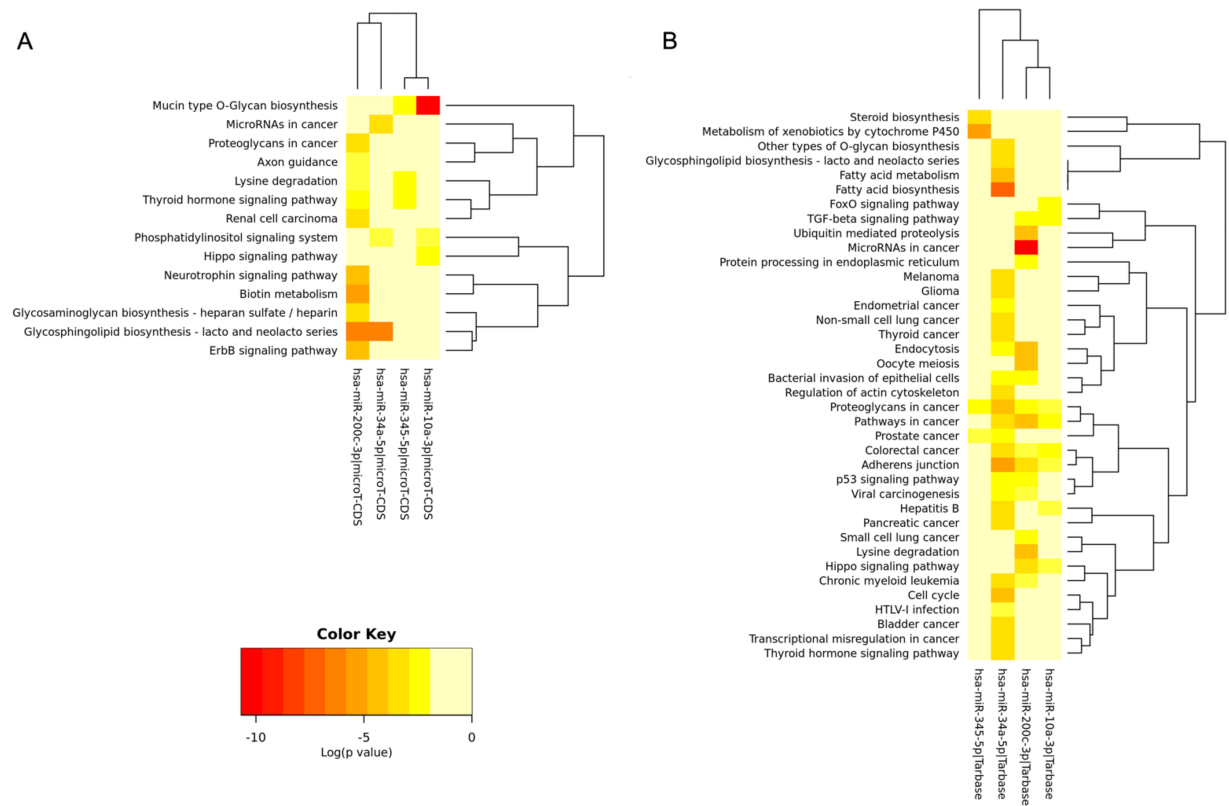


Figure A6. Heatmaps depicting the level of enrichment in KEGG pathways for the four differentially expressed miRNAs, as computed by the *in silico* target prediction algorithm (A) and the experimentally supported approach (B). Pathways with similar enrichment patterns are clustered together.

SUPPLEMENTARY REFERENCES

- 1 Kocerha J, Kouri N, Baker M, *et al.* Altered microRNA expression in frontotemporal lobar degeneration with TDP-43 pathology caused by progranulin mutations. *BMC Genomics* 2011;**12**:527. doi:10.1186/1471-2164-12-527
- 2 Chen-Plotkin AS, Unger TL, Gallagher MD, *et al.* TMEM106B, the Risk Gene for Frontotemporal Dementia, Is Regulated by the microRNA-132/212 Cluster and Affects Progranulin Pathways. *J Neurosci* 2012;**32**:11213–27. doi:10.1523/JNEUROSCI.0521-12.2012
- 3 Hébert SS, Wang W-X, Zhu Q, *et al.* A Study of Small RNAs from Cerebral Neocortex of Pathology-Verified Alzheimer's Disease, Dementia with Lewy Bodies, Hippocampal Sclerosis, Frontotemporal Lobar Dementia, and Non-Demented Human Controls. *J Alzheimers Dis JAD* 2013;**35**:335–48. doi:10.3233/JAD-122350
- 4 Gascon E, Lynch K, Ruan H, *et al.* Alterations in microRNA-124 and AMPA receptors contribute to social behavioral deficits in frontotemporal dementia. *Nat Med* 2014;**20**:1444–51. doi:10.1038/nm.3717
- 5 Helferich AM, Brockmann SJ, Reinders J, *et al.* Dysregulation of a novel miR-1825/TBCB/TUBA4A pathway in sporadic and familial ALS. *Cell Mol Life Sci* 2018;**75**:4301–19. doi:10.1007/s00018-018-2873-1
- 6 Jawaid A, Woldemichael BT, Kremer EA, *et al.* Memory Decline and Its Reversal in Aging and Neurodegeneration Involve miR-183/96/182 Biogenesis. *Mol Neurobiol* 2019;**56**:3451–62. doi:10.1007/s12035-018-1314-3