Understanding Competitive Endogenous RNA Network Mechanism in Type 1 Diabetes Mellitus Using Computational and Bioinformatics Approaches

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Background: Type 1 diabetes mellitus (T1DM), an autoimmune disease with a genetic tendency, has an increasing prevalence. Long non-coding RNA (lncRNA) and circular RNA (circRNA) are receiving increasing attention in disease pathogenesis. However, their roles in T1DM are poorly understood. The present study aimed at identifying signature lncRNAs and circRNAs and investigating their roles in T1DM using the competing endogenous RNA (ceRNA) network analysis.

Methods: The T1DM expression profile was downloaded from Gene Expression Omnibus (GEO) database to identify the differentially expressed circRNAs, lncRNAs, and mRNAs. The biological functions of these differentially expressed circRNAs, lncRNAs, and mRNAs were analyzed by the Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis. Targeting relationships of circRNA-miRNA, lncRNA-miRNA, and miRNA-mRNA were predicted, and the circRNA-lncRNA-miRNA-mRNA ceRNA regulatory network was established. Finally, qRT-PCR was applied to identify the effect of hsa_circ_0002202 inhibition on the IFN-I induced macrophage inflammation.

Results: A total of 178 circRNAs, 404 lncRNAs, and 73 mRNAs were identified to be abnormally expressed in T1DM samples. Functional enrichment analysis results indicated that the differentially expressed genes were mainly enriched in extracellular matrix components and macrophage activation. CeRNA regulatory network showed that circRNAs and lncRNAs regulate mRNAs through integrate multiple miRNAs. In addition, in vitro experiments showed that hsa_circ_0002202 inhibition suppressed the type I interferon (IFN-I)-induced macrophage inflammation.

Conclusion: In the present study, the circRNA-lncRNA-miRNA-mRNA ceRNA regulatory network in T1DM was established for the first time. We also found that hsa_circ_0002202 inhibition suppressed the IFN-I-induced macrophage inflammation. Our study may lay a foundation for future studies on the ceRNA regulatory network in T1DM.

Keywords: type 1 diabetes mellitus, ceRNA network, peripheral blood mononuclear cell, macrophage

Introduction

Type 1 diabetes mellitus (T1DM), also known as insulin-dependent diabetes mellitus, is a chronic autoimmune disease characterized by impaired islet function and decreased insulin secretion.1,2 The cause of T1DM involves various factors, including epigenetic, individual genetics, and environmental triggers.3–6 T1DM is diagnosed at all ages.7,8 Among them, approximately 78,000 young people are diagnosed with T1DM annually worldwide.9 Moreover, recent studies revealed...
that the incidence of T1DM is on the rise at the age of 10–14, and the number of children and adolescents with T1DM worldwide is estimated to continue to increase.10,11

Patients with T1DM usually suffer from the disease for a longer time, which requires them to inject insulin daily and perform continuous blood glucose monitoring, resulting in huge lifetime costs and time requirements.12 At the same time, T1DM has serious complications such as ketoacidosis, heart disease, stroke, kidney failure, and blindness.13–17 These long-term effects are likely to spread to other areas of the patients’ lives, which will cause economic impact and social burdens.12,18 Thus, it is necessary to diagnose T1DM early. However, the traditional diagnostic methods of diabetes are no longer satisfactory.19 Therefore, it is urgent to understand the etiology and pathogenesis of T1DM for more effective diagnosis and treatment.

Through the recent researches on the post-transcriptional regulatory mechanism, non-coding RNA (ncRNA), which does not have traditional RNA functions in protein translation, was discovered.20 Among them, the long non-coding RNA (lncRNA) is a kind of linear non-coding RNA with a length of more than 200 nucleotides,21 and circular RNA (circRNA) is a kind of endogenous non-coding RNA with a closed-loop structure.22 Previous studies have shown the vital roles of various lncRNAs and circRNAs in T1DM. lncRNA Lnc13 is up-regulated in β-cells and contributes to the pathogenesis of T1DM by increasing pancreatic β-cell inflammation.23 Ding et al reported that lncRNA MALAT1 induces the dysfunction of β-cells in T1DM.24 Another study by Zhang et al found that circRNA circPPM1F modulates M1 macrophage activation and pancreatic islet inflammation in T1DM.25 Therefore, examining the expression of lncRNAs and circRNAs and exploring their underlying mechanism in T1DM opens avenues to a better understanding of the T1DM pathogenesis.

Both lncRNA and circRNA can act as microRNA (miRNA) sponges to compete with the same corresponding miRNA response element (MRE), thus controlling subsequent miRNA post-transcriptional regulation and forming competitive endogenous RNA (ceRNA) regulatory network.26–28 The ceRNA regulatory networks in diabetes have been widely reported.29–32 While in T1DM, few studies regarding the ceRNA regulatory network were reported. Li et al and Luo et al identified the circRNA-miRNA-mRNA network in T1DM via bioinformatic analysis.32,33 Shi et al reported the lncRNA-miRNA-mRNA regulatory networks in T1DM.34 Thus, further studies aimed at clarifying ceRNA-based molecular mechanisms in T1DM are needed to provide potential opportunities for better understanding the pathogenesis and treatment of T1DM.

With the popularization of high-throughput sequencing, bioinformatics analysis has been widely used in multiple disease research. Researchers can analyze data from various public databases and explore the regulatory mechanism underlying the disease. Here, we identified the differentially expressed circRNAs (DEcircRNAs), lncRNAs (DElncRNAs), mRNAs (DEmRNAs) in T1DM using expression profile GSE133225 and GSE133217 downloaded from the Gene Expression Omnibus (GEO) database.35 Subsequently, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analyses were performed to detect the function of these differentially expressed genes. Then, the circRNA-miRNA, lncRNA-miRNA, and miRNA-mRNA interaction were predicted, and the circRNA-lncRNA-miRNA-mRNA ceRNA regulatory network was constructed. This is the first time to construct the ceRNA regulatory network by comprehensive screening of circRNA, lncRNA, miRNA, and mRNA in T1DM.

Materials and Methods

Data Sources
Two individual cohorts from the GEO database (http://www.ncbi.nlm.nih.gov/geo/) were included in this study. One is the circRNA, lncRNA, and mRNA expression profile GSE133225, and the other one is the miRNA expression profile GSE133217. Both expression profiles were provided by Zhang Caiyan and Zhou Yufeng,25,36 and included 4 peripheral blood mononuclear cells (PBMCs) samples from T1DM patients and 4 PBMCs samples from healthy volunteers.

Summary of Statistical Analysis
In the current study, we first analyzed the circRNA, lncRNA, miRNA, and mRNA expression using the microarray GSE133225 and GSE133217. Next, according to the filtrate threshold (P value < 0.05 and log2 (fold change) > 1), the differentially expressed circRNA, lncRNA, and mRNA were screened out. GO and KEGG enrichment analyses were performed to better comprehend the mechanisms of T1DM. Then, the target prediction was performed with the online web tools Circinteractome,
LncBase, and starBase, and the circRNA-lncRNA-miRNA-mRNA interaction network was established. Finally, circRNA hsa_circ_0002202 was selected for further verification. A brief workflow was shown in Figure 1.

**Differential Expression Analysis**

R software (Ver. 3.5.0, [https://www.r-project.org/](https://www.r-project.org/)) was employed for microarray analysis. The “affy” package was used for normalizing microarray expression profiles as described before. Then, empirical Bayes moderated t-test in the “limma” package was applied to screen the differentially expressed genes (DEGs) between T1DM samples and normal samples with \( P \) value < 0.05 and \( \log_2 \) (fold change) > 1 as the threshold. The code for the differential expression analysis was shown in Supplementary File 1.

**Functional and Pathway Enrichment Analysis of Differentially Expressed circRNAs, lncRNAs, and mRNAs**

To better comprehend the mechanisms of T1DM, GO ([http://www.geneontology.org/](http://www.geneontology.org/)) analysis and KEGG ([http://www.kegg.jp/](http://www.kegg.jp/)) pathway analysis of the differentially expressed circRNA, lncRNA, and mRNAs was performed.

![Figure 1](image-url) The analysis flow chart of this study.
conducted with the “clusterProfiler” package\textsuperscript{39} using $P < 0.05$ (adjusted using Benjamin and Hochberg method) as the threshold. Specifically, GO analysis is used to construct gene annotation base on biological processes (BP, a biological objective to which the gene or gene product contributes), cellular components (CC, the place in the cell where a gene product is active), and molecular functions (MF, the biochemical activity (including specific binding to ligands or structures) of a gene product),\textsuperscript{40} and KEGG analysis is used to interpret the potential functions and pathways.\textsuperscript{41} The code for the enrichment analysis was shown in Supplementary File 2. For the enrichment analysis for differentially expressed circRNAs, we used their parental genes. For the enrichment analysis for differentially expressed lncRNAs, we used their associated genes.

Construction of circRNA-LncRNA-miRNA-mRNA ceRNA Regulatory Network

The expression correlation of differentially expressed circRNAs, lncRNAs, and miRNAs was calculated using Pearson correlation coefficients with the “psych” package (https://cran.r-project.org/web/packages/psych/). The code for the correlation analysis was shown in Supplementary File 3. circRNA-mRNA and LncRNA-mRNA with $r > 0.7$ and $P < 0.05$ were selected for further study. Then, the Circinteractome web tool (https://circinteractome.nia.nih.gov/) was applied to predict the circRNA-miRNA interactions. LncBase web tool (http://carolina.imis.athena-innovation.gr/diana_tools/web/index.php?r=lncbasev2/index) was applied to predict the miRNA-mRNA interactions. Finally, a circRNA-LncRNA-miRNA-mRNA interaction network visualized by Cytoscape software\textsuperscript{42} based on the ceRNA theory.

Cell Culture and Treatment

Human THP-1 cell line from Procell Life Science&Technology Co., Ltd. (Wuhan, China) was cultured in the RPMI-1640 medium supplied with 10% fetal bovine serum (FBS, Gibco, Gaithersburg, MD, USA) and 1% penicillin-streptomycin (Gibco) at 37°C with 5% CO\textsubscript{2}. Then, according to a previous study,\textsuperscript{36} THP-1-derived macrophages were induced by treating with 50 ng/mL phorbol 12-myristate 13-acetate (PMA) for 48 h. Cell transfection was performed using Lipofectamine 3000 reagent (Invitrogen, USA) with the chemically synthesized circRNA small interfering RNAs (si-circ, sequence: 5’-AGTACAAACATTCAAGTGATT-3’), and small interfering RNAs negative control (si-NC, sequence: 5’-UUCUCCGAACGUGUCACGUTT-3’). After 48 h of transfection, the macrophages were treated with type I interferon (IFN-I, 1000 units/mL, PBL Assay Science, USA) to induce the inflammation.

Quantitative Real-Time PCR (qRT-PCR)

Total RNA was extracted from cells with Trizol (Invitrogen, USA). Next, cDNA was reverse transcribed with PrimeScript First Strand cDNA Synthesis Kit (Takara, Japan). Then, the qRT-PCR reaction was performed with SYBR\textsuperscript{®} Premix Ex Taq™ II (Takara, Japan) on the LightCycler 96 PCR system (Roche, Rotkreuz, Switzerland). β-actin was selected as the internal control according to the geNorm\textsuperscript{43} and normFinder\textsuperscript{44} algorithms. The level of RNA was quantified by the $2^{-\Delta\Delta CT}$ method. Primers were displayed in Table 1.

Nuclear and Cytoplasmic Separation

In brief, nuclear and cytoplasmic RNAs were extracted using the PARIS kit (Invitrogen, Carlsbad, CA, USA). Then, the RNA extractions were subjected to qRT-PCR.

Table 1 Primers Used for qRT-PCR

| Name                  | Sequence (5’-3’)                                                                 |
|-----------------------|---------------------------------------------------------------------------------|
| IFIT1 forward         | GCCCTGCTGAAGTGTTGAGGAA                                                          |
| IFIT1 reverse         | ATCCAGCGGATACCCGAGAAGGCATC                                                      |
| IFIH1 forward         | GACTCGGGATATCCTGAGGAGG                                                         |
| IFIH1 reverse         | GCTCTACCCCTCACTGACCC                                                           |
| iNOS forward          | GTGCCGAGATTGTAGCCTGTAGC                                                         |
| iNOS reverse          | GTTGAGAAGATGAGTCTGACCC                                                         |
| CXCL10 forward        | GCCCTCGCACTCATCCGTTAGG                                                         |
| CXCL10 reverse        | ATCCGCTGTGAGGTTGAGG                                                           |
| hsa_circ_0002202 forward | GCCCTTCTGCACTCATCCGTTAGG                                                      |
| hsa_circ_0002202 reverse | GCCCTTCTGCACTCATCCGTTAGG                                                      |
| GAPDH forward         | GACTCGGGATATCCTGAGGAGG                                                         |
| GAPDH reverse         | GCTCTACCCCTCACTGACCC                                                           |
| hsa_circ_0002202 forward | GCCCTCCTGCCCATACCCGTTAGG                                                      |
| hsa_circ_0002202 reverse | GCCCTCCTGCCCATACCCGTTAGG                                                      |
| β-actin forward       | GCTCTACCCCTCACTGACCC                                                           |
| β-actin reverse       | GCTCTACCCCTCACTGACCC                                                           |
| β-tubulin forward     | ATCCGCTGTGAGGTTGAGG                                                           |
| β-tubulin reverse     | GCCCTCCTGCCCATACCCGTTAGG                                                      |
| 18S rRNA forward      | GCCCTCCTGCCCATACCCGTTAGG                                                      |
| 18S rRNA reverse      | GCCCTCCTGCCCATACCCGTTAGG                                                      |
| β-tubulin forward     | ATCCGCTGTGAGGTTGAGG                                                           |
| β-tubulin reverse     | GCCCTCCTGCCCATACCCGTTAGG                                                      |
| U6 forward            | GCTCTACCCCTCACTGACCC                                                           |
| U6 reverse            | GCTCTACCCCTCACTGACCC                                                           |

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3868

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3868

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U6 was used as the internal control of the nucleus, and 18S rRNA was used as the internal control of the cytoplasm.

Statistical Analysis
The qRT-PCR experiments were performed in triplicate, and the results were shown as mean ± SD. Statistical difference was analyzed using one-way ANOVA with GraphPad Prism (Ver. 8.0, GraphPad Software, Inc). P < 0.05 was considered to be statistically significant.

Results

Identification of Differentially Expressed circRNA in T1DM and Healthy Patients
By analyzing the circRNA expression in microarray GSE133225 (Figure 2A and B), we identified 178 differentially expressed circRNAs (DEcircRNAs, 77 up-regulated and 101 down-regulated) (Table 2). We also analyzed the chromosomal positions of these DEcircRNAs, and the top 5 chromosomes are as follows: chr1 (18, 10.11%), chr2 (15, 8.43%), chr3 (12, 6.74%), chr7 (12, 6.74%) %, chr10 (11, 6.18%). Functional enrichment analysis of DEcircRNAs was performed using the “clusterProfiler” tool. The results showed that the most significantly enriched GO terms were related to collagen fibril organization (GO: 0030199), membrane raft (GO: 0045121), and extracellular matrix structural constituent conferring tensile strength (GO: 0030020) (Figure 2C and Table 3). For the KEGG pathway analysis, the DEcircRNAs were enriched in protein digestion and absorption (hsa04974) (Table 4).

Identification of Differentially Expressed lncRNA in T1DM and Healthy Patients
Similarly, we analyzed the lncRNA expression with the microarray GSE133225. As shown in the volcano plot (Figure 3A) and heatmap (Figure 3B), 404 differentially expressed lncRNAs were screened (DElncRNAs, 199 up-regulated and 205 down-regulated) (Table 5). Meanwhile, the top 5 chromosomal positions of these DElncRNAs are as follows: chr1 (34, 8.42%), chr2 (29, 7.18%), chr17 (25, 6.19%), chr3 (25, 6.19%), chr10 (24, 5.94%). The GO enrichment analysis results showed that the DElncRNAs were enriched in macrophage activation (GO:0042116) and microvillus (GO:0036122) (Figure 3C and Table 6).

Identification of Differentially Expressed mRNA in T1DM and Healthy Patients
Subsequently, the differentially expressed mRNAs between the normal and T1DM groups were analyzed. As the volcano plot (Figure 4A) and heatmap (Figure 4B) indicated, there were 73 differentially expressed mRNAs (DEmRNAs, 31 up-regulated and 42 down-regulated) (Table 7). Most of them were located at chr2 (7, 9.59%), chr7 (6, 8.22%), chr17 (5, 6.85%), chr20 (5, 6.85%), chr12 (4, 5.48%). In addition, GO enrichment analysis showed that the DEmRNAs were enriched in prostaglandin receptor activity (GO:004955), prostanoid receptor activity (GO:004954), and BMP binding (GO:0036122) (Figure 4C and Table 8).

The circRNA-lncRNA-miRNA-mRNA Network in T1DM
Due to the large number of differentially expressed circRNAs and lncRNAs, we further analyzed their correlation with the DEmRNAs expression and constructed the circRNA-lncRNA-miRNA-mRNA network using r>0.7 as the screening criteria (Figure 5). Meanwhile, according to the ceRNA hypothesis, lncRNA and circRNA can function as miRNA sponges that bind to miRNA and inhibit the regulation of miRNAs on its target mRNAs, thereby indirectly regulating gene expression. Thus, we predicted the miRNAs targeting the DEcircRNAs and DElncRNAs and analyzed their expression using the dataset GSE133217 (Table 9). After screening, the circRNA-lncRNA-miRNA-mRNA network was visualized using Cytoscape software (Figure 6). For example, hsa_circ_0002202 was identified as ceRNA of miR-495-3p, miR-668-3p, miR-508-3p, and miR-487a-3p, which targeted GREM2. lncRNA LINC01007 regulated HSPB8 by competing for miR-33b-5p, miR-1321, and miR-455-3p.

Hsa_circ_0002202 Inhibition Suppressed the IFN-I-Induced Inflammation
To confirm our above discovery and conceive future study designs, we chose hsa_circ_0002202 with more miRNA targets for in vitro experiments. We first used the geNorm and normFinder algorithms to select the reference gene for normalization. As shown in Supplementary Figure 1, β-actin was the most stable reference gene. Then, subcellular distribution analysis...
Figure 2: The differentially expressed circRNAs in T1DM and healthy patients. (A) Volcano plot of DEcircRNAs between normal and T1DM groups. Red and green indicate up- and downregulation, respectively. (B) Heatmap of DEcircRNAs between normal and T1DM groups. Red color represents increased expression, and green color represents decreased expression. The darker the color, the greater the difference of circRNA expression. (C) Enrichment analysis of the DEcircRNAs in the categories biological process, cellular component, and molecular function.
| circRNAs       | Log2FoldChange | Regulation | P-value     | P-adj     |
|---------------|---------------|------------|-------------|-----------|
| hsa_circ_0060875 | 2.1258337     | Down       | 9.90×10^{-5} | 0.36011603 |
| hsa_circ_0091120 | -1.8970129    | Down       | 0.00502998  | 0.61872814 |
| hsa_circ_0018219 | -1.8216577    | Down       | 0.03718813  | 0.6896574  |
| hsa_circ_0083266 | -1.8178634    | Down       | 0.01012685  | 0.6404092  |
| hsa_circ_0081949 | -1.7877271    | Down       | 0.04837352  | 0.69864211 |
| hsa_circ_0017702 | -1.7544117    | Down       | 0.00777686  | 0.6371225  |
| hsa_circ_0089817 | -1.7206724    | Down       | 0.00023941  | 0.36707996 |
| hsa_circ_0061761 | 1.6671013     | Down       | 0.03278591  | 0.6886992  |
| hsa_circ_0043949 | 1.6515359     | Down       | 0.00163728  | 0.49940512 |
| hsa_circ_0026805 | 1.6449812     | Down       | 0.03133761  | 0.6886992  |
| hsa_circ_0066856 | -1.5895376    | Down       | 0.00030271  | 0.36707996 |
| hsa_circ_0010600 | -1.5588221    | Down       | 0.00021508  | 0.36707996 |
| hsa_circ_0089863 | -1.3576906    | Down       | 0.00085911  | 0.43375667 |
| hsa_circ_0012945 | -1.5426338    | Down       | 0.00031327  | 0.63707996 |
| hsa_circ_0087118 | -1.5293394    | Down       | 0.01309075  | 0.6461669  |
| hsa_circ_0025477 | -1.5269283    | Down       | 2.49×10^{-5} | 0.27197545 |
| hsa_circ_0035318 | 1.4846081     | Down       | 0.02228095  | 0.67318317 |
| hsa_circ_0011345 | 1.4808367     | Down       | 0.00116665  | 0.47332912 |
| hsa_circ_0029046 | 1.4680823     | Down       | 1.66×10^{-5} | 0.27163735 |
| hsa_circ_0070052 | 1.4651817     | Down       | 0.00043961  | 0.37883821 |
| hsa_circ_0055707 | 1.4461302     | Down       | 0.01391048  | 0.6461669  |
| hsa_circ_0018927 | 1.4114948     | Down       | 0.0203531   | 0.66887334 |
| hsa_circ_0053289 | 1.3992471     | Down       | 0.00193263  | 0.49940512 |
| hsa_circ_0055713 | -1.3964091    | Down       | 0.01169841  | 0.6461669  |
| hsa_circ_0092322 | -1.3886845    | Down       | 1.32×10^{-5} | 0.27163735 |
| hsa_circ_0045848 | 1.3854297     | Down       | 0.04413029  | 0.69594076 |
| hsa_circ_0069584 | -1.3853501    | Down       | 0.01824692  | 0.65662851 |
| hsa_circ_0008441 | -1.3733694    | Down       | 0.00074912  | 0.44105722 |
| hsa_circ_0073007 | 1.3518705     | Down       | 0.04300145  | 0.69594076 |
| hsa_circ_0030977 | -1.3421675    | Down       | 0.03991266  | 0.69072451 |
| hsa_circ_0088254 | -1.3367378    | Down       | 0.00795582  | 0.63723776 |
| hsa_circ_0012093 | -1.312721     | Down       | 0.03432713  | 0.6886992  |
| hsa_circ_0034676 | -1.311979     | Down       | 0.0072544   | 0.6371225  |
| hsa_circ_0082293 | -1.2977776    | Down       | 0.00872193  | 0.63723776 |
| hsa_circ_0080325 | -1.2957511    | Down       | 0.0029555   | 0.52887377 |
| hsa_circ_0004712 | -1.2890482    | Down       | 0.01102659  | 0.6461669  |
| hsa_circ_0068381 | -1.270335     | Down       | 0.01699615  | 0.65626057 |
| hsa_circ_0042502 | -1.2651427    | Down       | 0.03467318  | 0.6886992  |
| hsa_circ_0025413 | -1.2635234    | Down       | 0.0184742   | 0.6573827  |
| hsa_circ_0068488 | -1.2549415    | Down       | 0.02684532  | 0.6886992  |
| hsa_circ_0072670 | -1.24989      | Down       | 0.00188517  | 0.52606124 |
| hsa_circ_0078706 | -1.240986     | Down       | 0.02179647  | 0.67318317 |
| hsa_circ_0025473 | -1.2401025    | Down       | 0.00671056  | 0.6371225  |
| hsa_circ_0080593 | -1.2388893    | Down       | 0.0129599   | 0.6461669  |
| hsa_circ_0082426 | -1.236374     | Down       | 0.02682174  | 0.6886992  |
| hsa_circ_0002456 | -1.2308499    | Down       | 0.0340347   | 0.6886992  |
| hsa_circ_0035624 | -1.229398     | Down       | 0.01432306  | 0.6461669  |
| hsa_circ_0027593 | -1.2143428    | Down       | 0.01510762  | 0.6461669  |
| hsa_circ_0033522 | -1.2109569    | Down       | 0.00530799  | 0.61994831 |
| hsa_circ_0070813 | -1.2004595    | Down       | 0.04540634  | 0.69594076 |
| hsa_circ_0089089 | -1.197761     | Down       | 0.03000448  | 0.6886992  |

(Continued)
| circRNAs          | Log2FoldChange | Regulation | P-value  | P-adj    |
|------------------|----------------|------------|----------|----------|
| hsa_circ_008732  | −1.1974429     | Down       | 0.0014563 | 0.49940512 |
| hsa_circ_0083243 | −1.1873178     | Down       | 0.00020845 | 0.36707996 |
| hsa_circ_0044570 | −1.1776689     | Down       | 0.00506876 | 0.61872814 |
| hsa_circ_0051957 | −1.1766531     | Down       | 0.018845 | 0.66175152 |
| hsa_circ_0070872 | −1.1753034     | Down       | 0.00571746 | 0.6277625 |
| hsa_circ_0003146 | −1.1698955     | Down       | 0.03610804 | 0.6896574 |
| hsa_circ_0088267 | −1.1654894     | Down       | 0.0060454 | 0.62927103 |
| hsa_circ_0020296 | −1.1650009     | Down       | 0.00111814 | 0.47332912 |
| hsa_circ_0012285 | −1.153328      | Down       | 0.00252476 | 0.61994831 |
| hsa_circ_0086765 | −1.1459122     | Down       | 0.00649551 | 0.6461669 |
| hsa_circ_0084641 | −1.1438333     | Down       | 0.00053871 | 0.01025776 |
| hsa_circ_0015060 | −1.1429878     | Down       | 0.00053871 | 0.01025776 |
| hsa_circ_0065173 | −1.1388487     | Down       | 0.00755684 | 0.6371225 |
| hsa_circ_0043616 | −1.132645      | Down       | 0.0369064 | 0.6896574 |
| hsa_circ_0047903 | −1.1276276     | Down       | 0.01716979 | 0.65626057 |
| hsa_circ_0018827 | −1.1202055     | Down       | 0.0018818 | 0.36707996 |
| hsa_circ_0015069 | −1.1175352     | Down       | 0.04417262 | 0.69594076 |
| hsa_circ_0032813 | −1.1131832     | Down       | 0.0085541 | 0.63723776 |
| hsa_circ_0019143 | −1.112285      | Down       | 0.04029593 | 0.69072451 |
| hsa_circ_0008537 | −1.1053958     | Down       | 0.00053611 | 0.41025776 |
| hsa_circ_0002529 | −1.1048341     | Down       | 0.0125173 | 0.6461669 |
| hsa_circ_0046840 | −1.0988722     | Down       | 0.0035777 | 0.36707996 |
| hsa_circ_0028284 | −1.0905105     | Down       | 0.04120974 | 0.69432323 |
| hsa_circ_0019432 | −1.0725782     | Down       | 0.00295458 | 0.52887377 |
| hsa_circ_0047303 | −1.0705012     | Down       | 0.0068965 | 0.6371225 |
| hsa_circ_0072137 | −1.0684678     | Down       | 0.01800286 | 0.65626057 |
| hsa_circ_0024130 | −1.0663774     | Down       | 0.0205363 | 0.6691564 |
| hsa_circ_0022919 | −1.0578978     | Down       | 0.0093951 | 0.63723776 |
| hsa_circ_0022238 | −1.0545557     | Down       | 0.02150931 | 0.67318371 |
| hsa_circ_0086805 | −1.0531799     | Down       | 0.01662828 | 0.6547198 |
| hsa_circ_0077069 | −1.0513113     | Down       | 0.02550238 | 0.68798091 |
| hsa_circ_0057374 | −1.0509624     | Down       | 0.00039234 | 0.36707996 |
| hsa_circ_0069321 | −1.0491406     | Down       | 0.00507185 | 0.61872814 |
| hsa_circ_0007471 | −1.0383975     | Down       | 0.01103246 | 0.6461669 |
| hsa_circ_0032858 | −1.0382432     | Down       | 0.0058831 | 0.62927103 |
| hsa_circ_0033892 | −1.0300829     | Down       | 0.04029593 | 0.69072451 |
| hsa_circ_0024575 | −1.023773      | Down       | 0.04526006 | 0.69594076 |
| hsa_circ_0083836 | −1.0232697     | Down       | 0.00482139 | 0.60677969 |
| hsa_circ_0064419 | −1.020977      | Down       | 0.00012256 | 0.3648499 |
| hsa_circ_0030657 | −1.0226422     | Down       | 0.00883236 | 0.63723776 |
| hsa_circ_0087729 | −1.0196745     | Down       | 0.03005932 | 0.6886992 |
| hsa_circ_0020964 | −1.0153533     | Down       | 0.02651006 | 0.6886992 |
| hsa_circ_0078325 | −1.0146273     | Down       | 0.0142381 | 0.6461669 |
| hsa_circ_0068030 | −1.0135546     | Down       | 0.00881102 | 0.63723776 |
| hsa_circ_0087884 | −1.0107733     | Down       | 0.02874001 | 0.6886992 |
| hsa_circ_0067127 | −1.0102228     | Down       | 0.03491637 | 0.6886992 |
| hsa_circ_0077292 | −1.0098441     | Down       | 0.03166391 | 0.6886992 |
| hsa_circ_0050829 | −1.0079665     | Down       | 0.00046365 | 0.38552675 |
| hsa_circ_0088545 | −1.0038141     | Down       | 0.02816448 | 0.6886992 |
| hsa_circ_0066559 | −1.0001944     | Down       | 0.00562765 | 0.62317278 |

(Continued)
Table 2 (Continued).

| circRNAs            | Log2FoldChange | Regulation | P-value   | P-adj     |
|---------------------|----------------|------------|-----------|-----------|
| hsa_circ_0030691    | 1.0075362      | Up         | 0.03650781| 0.6896574 |
| hsa_circ_0073355    | 1.00406779     | Up         | 0.01584992| 0.6461669 |
| hsa_circ_0060973    | 1.0052219      | Up         | 0.01129814| 0.6670996 |
| hsa_circ_0071490    | 1.0037299      | Up         | 0.02198034| 0.6731831 |
| hsa_circ_0073332    | 1.01653192     | Up         | 0.00029189| 0.3670996 |
| hsa_circ_0041267    | 1.02731163     | Up         | 0.04826044| 0.6986421 |
| hsa_circ_0034557    | 1.02903097     | Up         | 0.04563388| 0.6959407 |
| hsa_circ_0014206    | 1.03151729     | Up         | 0.00754327| 0.6371225 |
| hsa_circ_0034188    | 1.03292459     | Up         | 7.23×10⁻⁵  | 0.36011603|
| hsa_circ_0084862    | 1.04447426     | Up         | 0.03297313| 0.6886992 |
| hsa_circ_0043575    | 1.04451466     | Up         | 0.00606669| 0.6291703 |
| hsa_circ_0066752    | 1.05303312     | Up         | 0.00123282| 0.48639953|
| hsa_circ_0018918    | 1.0536996      | Up         | 0.03876368| 0.6896574 |
| hsa_circ_0030816    | 1.06017092     | Up         | 0.01231415| 0.6461669 |
| hsa_circ_0002308    | 1.06451001     | Up         | 0.00139462| 0.49940512|
| hsa_circ_0057940    | 1.06723667     | Up         | 0.0355786 | 0.6886992 |
| hsa_circ_0003310    | 1.07580527     | Up         | 0.0121094 | 0.6869574 |
| hsa_circ_0003130    | 1.0780832      | Up         | 0.01833869| 0.6537827 |
| hsa_circ_0004607    | 1.09052865     | Up         | 0.0026797 | 0.52887377|
| hsa_circ_0074026    | 1.10437363     | Up         | 0.00887386| 0.63723776|
| hsa_circ_0013280    | 1.11294406     | Up         | 0.02142065| 0.67318317|
| hsa_circ_0000324    | 1.11328742     | Up         | 0.02004466| 0.663805  |
| hsa_circ_0011437    | 1.11571417     | Up         | 0.00203065| 0.52606124|
| hsa_circ_0003162    | 1.12089099     | Up         | 0.0121094 | 0.6869574 |
| hsa_circ_0006561    | 1.12140856     | Up         | 0.02296689| 0.67670006|
| hsa_circ_00019321   | 1.12534202     | Up         | 0.01003317| 0.64004092|
| hsa_circ_00066588   | 1.13259964     | Up         | 0.00644124| 0.6371225 |
| hsa_circ_0008846    | 1.13350867     | Up         | 0.04980974| 0.69965823|
| hsa_circ_00048941   | 1.13392642     | Up         | 0.0073921 | 0.6371225 |
| hsa_circ_0013276    | 1.1352225      | Up         | 0.01594875| 0.65471981|
| hsa_circ_00084803   | 1.13561704     | Up         | 0.00291642| 0.52887377|
| hsa_circ_0009718    | 1.14501876     | Up         | 0.0113062 | 0.47332912|
| hsa_circ_00052890   | 1.14899657     | Up         | 0.0101269 | 0.47332912|
| hsa_circ_00052578   | 1.15746251     | Up         | 0.00204063| 0.52606124|
| hsa_circ_0004247    | 1.16577189     | Up         | 0.03834653| 0.6896574 |
| hsa_circ_0006366    | 1.17060861     | Up         | 0.02336843| 0.67886043|
| hsa_circ_0004970    | 1.17164435     | Up         | 0.00191073| 0.52606124|
| hsa_circ_0003760    | 1.19544727     | Up         | 0.00830217| 0.63723776|
| hsa_circ_00077040   | 1.19660605     | Up         | 0.00388828| 0.36707996|
| hsa_circ_00064649   | 1.2032629      | Up         | 0.00363496| 0.63530743|
| hsa_circ_00057921   | 1.22298163     | Up         | 0.00658344| 0.6371225 |
| hsa_circ_00010167   | 1.22782484     | Up         | 0.01705561| 0.65626057|
| hsa_circ_0002626    | 1.23796418     | Up         | 0.04850693| 0.69864211|
| hsa_circ_0004814    | 1.24697128     | Up         | 0.10190214| 0.66175152|
| hsa_circ_0007356    | 1.24865998     | Up         | 0.0053345 | 0.61194831|
| hsa_circ_00045123   | 1.24884849     | Up         | 0.02530036| 0.68798901|
| hsa_circ_00069213   | 1.25118583     | Up         | 0.00366065| 0.58881715|
| hsa_circ_00079548   | 1.25190508     | Up         | 0.01484117| 0.6461669 |

(Continued)
illustrated that hsa_circ_0002202 is mainly located in the cytoplasm in THP-1-derived macrophages, with the remaining proportion in the nucleus (Figure 7A). Transfection of si-circ significantly decreased hsa_circ_0002202 expression in THP-1-derived macrophages (Figure 7B). Afterward, qRT-PCR results showed that hsa_circ_0002202 knockdown significantly suppressed the expression of IFIT1, IFIH1, CXCL10, and iNOS under IFN-I stimulation, suggesting an inhibitory effect of hsa_circ_0002202 knockdown on IFN-I-induced inflammation (Figure 7C).

Discussion

Despite great efforts to find treatment strategies, T1DM is still a terrible threat to human health, and its prevalence is still rising worldwide. To better understand the exact mechanisms of T1DM and promote the discovery of new biomarkers, we analyzed the gene expression data from GEO public database. Furthermore, we established a circRNA-lncRNA-miRNA-mRNA ceRNA regulatory network in T1DM, which elucidated the underlying pathogenesis of T1DM.

The post-transcriptional regulation of gene expression mediated by the ceRNA regulatory network during the diseases process has attracted wide attention from researchers. In diabetes and diabetic complications, the ceRNA regulatory network in pathophysiological processes has been widely reported. For example, lncRNA MT1P3 promoted p2y12 expression by sponging miR-126 to promote platelet activation and aggregation in type 2 diabetes. IncRNA H2k2/miR-449a/b/Trim11 signaling pathway promotes mesangial cell proliferation in diabetic nephropathy. Hsa_circ_010567/miR-141/TGF-β1 axis promotes myocardial fibrosis in diabetic mice. The complex interaction network of multiple factors may be more theoretically meaningful for revealing the internal mechanism of T1DM. But few studies focused on the ceRNA

| circRNAs          | Log2FoldChange | Regulation | P-value   | P-adj     |
|-------------------|----------------|------------|-----------|-----------|
| hsa_circ_0090098  | 1.25536841     | Up         | 0.02596742| 0.6886992 |
| hsa_circ_0030624  | 1.25599738     | Up         | 0.03651889| 0.6895674 |
| hsa_circ_0069324  | 1.26605445     | Up         | 0.00060556| 0.42191899|
| hsa_circ_0060335  | 1.28618107     | Up         | 0.00081571| 0.44105722|
| hsa_circ_0058206  | 1.32621611     | Up         | 0.01802886| 0.65826057|
| hsa_circ_0056882  | 1.34999287     | Up         | 0.03545574| 0.6886992 |
| hsa_circ_0013437  | 1.36386499     | Up         | 0.01654656| 0.65471981|
| hsa_circ_0046700  | 1.37107512     | Up         | 0.0439923  | 0.69594076|
| hsa_circ_0057436  | 1.37970777     | Up         | 0.00977977| 0.4732912 |
| hsa_circ_0048871  | 1.42092532     | Up         | 0.0407976 | 0.69077151|
| hsa_circ_0009443  | 1.48425272     | Up         | 0.00287515| 0.52887377|
| hsa_circ_0060450  | 1.51788173     | Up         | 0.01218226| 0.6461669 |
| hsa_circ_0060456  | 1.55691545     | Up         | 0.04257115| 0.69594076|
| hsa_circ_0026352  | 1.61091952     | Up         | 0.0312629 | 0.6886992 |
| hsa_circ_0056621  | 1.65069395     | Up         | 0.01137623| 0.6461669 |
| hsa_circ_0057880  | 1.65520964     | Up         | 0.01050849| 0.64298015|
| hsa_circ_0073340  | 1.72721874     | Up         | 0.00133111| 0.49533889|
| hsa_circ_0029674  | 1.74098979     | Up         | 0.00229149| 0.52887377|
| hsa_circ_0021068  | 1.79691824     | Up         | 0.00294272| 0.52887377|
| hsa_circ_0053947  | 1.80953972     | Up         | 0.02793328| 0.6886992 |
| hsa_circ_0002202  | 1.89669617     | Up         | 0.00079917| 0.44105722|
| hsa_circ_0079556  | 1.94764347     | Up         | 0.00845628| 0.63723776|
| hsa_circ_0015729  | 2.96958438     | Up         | 0.02245883| 0.67318317|
| hsa_circ_0092238  | 3.03036764     | Up         | 0.02362915| 0.6786653 |
| hsa_circ_0092236  | 3.45575278     | Up         | 0.03065391| 0.6886992 |
| hsa_circ_0092221  | 4.29199121     | Up         | 0.03950529| 0.6896252 |

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regulatory networks in T1DM. Meanwhile, previous studies on T1DM ceRNA regulatory networks only discussed the role of either lncRNA or circRNA, and did not consider both of them simultaneously. Therefore, this study was systematic and comprehensive for revealing the T1DM mechanism.

In the current study, we identified 178 DEcircRNAs, 404 DElncRNAs, and 73 DEmRNAs from the

### Table 3 Results of Gene Ontology (GO) Enrichment Analysis of Differentially Expressed circRNAs

| Ontology | Term | Description | Gene Number | P-adj |
|----------|------|-------------|-------------|-------|
| BP       | GO:0030199 | Collagen fibril organization | 7 | 0.00044787 |
| BP       | GO:0043062 | extracellular structure Organization | 15 | 0.00076629 |
| BP       | GO:0030198 | Extracellular matrix organization | 14 | 0.00076629 |
| BP       | GO:0060840 | Artery development | 7 | 0.00694781 |
| BP       | GO:0071230 | Cellular response to amino acid stimulus | 6 | 0.00694781 |
| BP       | GO:0043200 | Response to amino acid | 7 | 0.01121075 |
| BP       | GO:0001101 | Response to acid chemical | 1 | 0.02282114 |
| BP       | GO:0045176 | Apical protein localization | 3 | 0.02282114 |
| CC       | GO:0045121 | Membrane raft | 11 | 0.00284762 |
| CC       | GO:0098857 | Membrane microdomain | 11 | 0.00284762 |
| CC       | GO:0098589 | Membrane region | 11 | 0.00284762 |
| CC       | GO:0044420 | Extracellular matrix component | 5 | 0.00284762 |
| CC       | GO:0005583 | Fibrillar collagen trimer | 3 | 0.00333723 |
| CC       | GO:0098643 | Banded collagen fibril | 3 | 0.00333723 |
| CC       | GO:0005788 | Endoplasmic reticulum lumen | 10 | 0.00425887 |
| CC       | GO:0031252 | Cell leading edge | 11 | 0.00744841 |
| CC       | GO:0005901 | Caveola | 5 | 0.01094539 |
| CC       | GO:0098644 | Complex of collagen trimers | 3 | 0.01126914 |
| CC       | GO:0005581 | Collagen trimer | 5 | 0.01321773 |
| CC       | GO:0045177 | Apical part of cell | 10 | 0.01358578 |
| CC       | GO:0016324 | Apical plasma membrane | 9 | 0.01385878 |
| CC       | GO:0062023 | Collagen-containing extracellular matrix | 10 | 0.01868493 |
| CC       | GO:0031253 | Cell projection membrane | 9 | 0.02141473 |
| CC       | GO:0044853 | Plasma membrane raft | 5 | 0.02530242 |
| CC       | GO:0031256 | Leading edge membrane | 6 | 0.03027327 |
| CC       | GO:0005844 | Polysome | 4 | 0.03442097 |
| CC       | GO:0005911 | Cell-cell junction | 10 | 0.03442097 |
| CC       | GO:0097470 | Ribbon synapse | 2 | 0.03835081 |
| CC       | GO:0005925 | Focal adhesion | 9 | 0.04505555 |
| CC       | GO:0005924 | Cell-substrate adherens junction | 9 | 0.04570731 |
| CC       | GO:0030055 | Cell-substrate junction | 9 | 0.04581649 |
| MF       | GO:0030020 | Extracellular matrix structural constituent conferring tensile strength | 5 | 0.04674156 |
| MF       | GO:0005201 | Extracellular matrix structural constituent | 8 | 0.0708066 |
| MF       | GO:0140104 | Molecular carrier activity | 5 | 0.0916654 |
| MF       | GO:0019838 | Growth factor binding | 7 | 0.0134742 |
| MF       | GO:0046332 | SMAD binding | 5 | 0.03542754 |
| MF       | GO:0003779 | Actin binding | 11 | 0.04505555 |

**Abbreviations**: BP, biological process; CC, cellular component; MF, molecular function.

### Table 4 Results of KEGG Enrichment Analysis of Differentially Expressed circRNAs

| Term   | Description                        | Gene Number | P-adj  |
|--------|------------------------------------|-------------|--------|
| hsa04974 | Protein digestion and absorption | 7           | 0.009083535 |

regulatory networks in T1DM. Meanwhile, previous studies on T1DM ceRNA regulatory networks only discussed the role of either lncRNA or circRNA, and did not consider both of them simultaneously. Therefore, this study was systematic and comprehensive for revealing the T1DM mechanism.

In the current study, we identified 178 DEcircRNAs, 404 DElncRNAs, and 73 DEmRNAs from the
GSE133225 database. Meanwhile, we analyzed the miRNA chip GSE133217 to construct the interaction network of circRNA, lncRNA, miRNA, and mRNA. This network suggested that circRNA and lncRNA play a central regulatory role in T1DM. One circRNA and lncRNA can be associated with multiple identical miRNAs to regulate more mRNAs synergistically. Among the circRNAs and lncRNAs, circRNA hsa_circ_0002202 and lncRNA AL356740.2–201 (ENST00000601559.1) linked most miRNAs. Here, we selected hsa_circ_0002202 for the in vitro experiment verification. Hsa_circ_0002202 is formed from SMAD4A. A previous study has reported the oncogene role of circSAMD4A in osteosarcoma. Liu et al found that circSAMD4A acts as an adipogenesis promoting factor. In this study, we found that hsa_circ_0002202 was up-regulated in T1DM PBMCs samples, suggesting that hsa_circ_0002202 may take part in the T1DM procession. As the circRNAs show their sponge function in the cytoplasm, we detected

Figure 3 The differentially expressed lncRNAs in T1DM and healthy patients. (A) Volcano plot of DElncRNAs between normal and T1DM groups. Red and green indicate up- and downregulation, respectively. (B) Heatmap of DElncRNAs between normal and T1DM groups. Red color represents increased expression, and green color represents decreased expression. The darker the color, the greater the difference of lncRNA expression. (C) Enrichment analysis of the DElncRNAs in the categories biological process and cellular component.
| IncRNAs                  | Log2FoldChange | Regulation | P-value    | P-adj       |
|-------------------------|----------------|------------|------------|-------------|
| Inc-MARC1-2:1           | -2.571855      | Down       | 0.002228   | 0.49624326  |
| Inc-PSMG1-3:2           | -2.3628597     | Down       | 0.00610319 | 0.55695089  |
| CCND2-AS1-201           | -2.1767994     | Down       | 0.00261656 | 0.51224337  |
| Inc-ANGFPL2-7:1         | -2.1177664     | Down       | 0.00318539 | 0.53930742  |
| AL356740.2–201          | -2.0532982     | Down       | 0.0027546  | 0.51224337  |
| Inc-APBA2-1:3           | -2.0384649     | Down       | 0.00358789 | 0.54892347  |
| Inc-SELH3-10:1          | -1.9247783     | Down       | 0.00065127 | 0.39679443  |
| ENPP7P13                | -1.8523605     | Down       | 0.03454029 | 0.72695785  |
| Inc-MBNL2-2:1           | -1.8516299     | Down       | 0.00108059 | 0.4269515   |
| Inc-CTD-2523D13.1–1-2  | -1.8151432     | Down       | 0.00042329 | 0.33998788  |
| LOC101929733            | -1.8035357     | Down       | 0.01482032 | 0.65467375  |
| AC011287.1–203          | -1.8043227     | Down       | 0.01357893 | 0.63919136  |
| AC013553.4–201          | -1.7883164     | Down       | 0.01251521 | 0.63775317  |
| AL021368.3–201          | -1.7524563     | Down       | 0.02035199 | 0.68302181  |
| Inc-CDSL-1:1            | -1.7425319     | Down       | 0.00420523 | 0.55695089  |
| SEMA6A-AS1-206          | -1.7140352     | Down       | 0.00131451 | 0.4460612   |
| LINC00299-203           | -1.71106       | Down       | 0.00391051 | 0.55546359  |
| Inc-FRZB-2:2            | -1.6847279     | Down       | 0.00324333 | 0.53930742  |
| GGNBPI                  | -1.6719447     | Down       | 0.0166596  | 0.65620897  |
| Inc-UNC5CL-7:1          | -1.6687674     | Down       | 0.00461045 | 0.55695089  |
| Inc-MRPS5-13:1          | -1.6546035     | Down       | 0.00921325 | 0.6151086   |
| Inc-CIorf64-6:1         | -1.6395822     | Down       | 0.01190126 | 0.63705043  |
| AL136979.1–201          | -1.6202871     | Down       | 0.0006092  | 0.39679443  |
| Inc-CNGBI-1:1           | -1.5925938     | Down       | 0.0221688  | 0.6889443   |
| AL021937.6–201          | -1.5827605     | Down       | 0.00032605 | 0.33391458  |
| Inc-RASGRP1-6:1         | -1.5821617     | Down       | 2.33×10⁻⁶  | 0.05960188  |
| Inc-ANO2-4:1            | -1.5733225     | Down       | 0.00170014 | 0.48236519  |
| LINC00471               | -1.5517992     | Down       | 0.01828625 | 0.66352772  |
| AP001363.1–201          | -1.5323863     | Down       | 0.02355621 | 0.69616967  |
| AC011405.1–201          | -1.523797      | Down       | 0.00820535 | 0.65707011  |
| AC108935.1–201          | -1.5001012     | Down       | 0.00635053 | 0.55695089  |
| Inc-TBC1D3C-4:1         | -1.4786853     | Down       | 0.00403532 | 0.55546359  |
| Inc-LIP1-6:1            | -1.4669252     | Down       | 0.00132802 | 0.4460612   |
| Inc-FCHSD2-4:1          | -1.4647594     | Down       | 0.00223289 | 0.49624236  |
| AC104590.1–201          | -1.458406      | Down       | 0.00163683 | 0.47784335  |
| Inc-NDFIP2-8:1          | -1.4500676     | Down       | 0.01442379 | 0.65361455  |
| Inc-AL359878.1–1:1     | -1.4473997     | Down       | 0.04508299 | 0.74859413  |
| Inc-NUP98-2:1           | -1.4448238     | Down       | 0.02667345 | 0.70311657  |
| Inc-DTHDI-2:1           | -1.4441469     | Down       | 0.00161419 | 0.47784335  |
| Inc-DCAF4L-1:1          | -1.4367953     | Down       | 0.02450173 | 0.69781796  |
| AC022296.1–201          | -1.4277172     | Down       | 0.00029813 | 0.33391458  |
| LINC02279-201           | -1.4213164     | Down       | 0.00907281 | 0.6151086   |
| C5orf66-AS1             | -1.4124554     | Down       | 0.00199206 | 0.49624326  |
| Inc-IRF5-2:1            | -1.4087918     | Down       | 0.04752968 | 0.75874445  |
| Inc-FXYD2-1:2           | -1.4016591     | Down       | 0.01605233 | 0.65476375  |
| ENST00000434742         | -1.3965605     | Down       | 0.04268783 | 0.74199998  |
| LINC00710-210           | -1.3926583     | Down       | 0.00459619 | 0.55695089  |
| Inc-RUNX1T1-6:1         | -1.390228      | Down       | 0.04310897 | 0.74348205  |
| Inc-REP15-2:1           | -1.3887183     | Down       | 0.01204392 | 0.63775317  |

(Continued)
Table 5 (Continued).

| lnc-RNAs                   | Log2FoldChange | Regulation | P-value   | P-adj      |
|----------------------------|----------------|------------|-----------|------------|
| Inc-GLCCI1-5:1             | -1.3790449     | Down       | 0.00360051| 0.54892347 |
| Inc-TDRDS-2:2              | -1.3779141     | Down       | 0.00653613| 0.56344961 |
| Inc-TIPARP-1:1             | -1.3745656     | Down       | 1.71x10^-5| 0.219024   |
| NONHSA144810               | -1.3733309     | Down       | 0.04223393| 0.74199989 |
| Inc-C8orf12-1:5            | -1.3670614     | Down       | 0.01262556| 0.63775317 |
| FLJ42393-201               | -1.360109      | Down       | 0.01787249| 0.65667837 |
| AL031186.1--201            | -1.359927      | Down       | 0.00231239| 0.50172959 |
| NONHSA1078217              | -1.3517092     | Down       | 0.03830547| 0.73920545 |
| HSFY1P                     | -1.3512769     | Down       | 0.02395161| 0.69616967 |
| AL365295.1--203            | -1.3483624     | Down       | 0.00642502| 0.55846139 |
| Inc-STBS1A-4-9:1           | -1.3434237     | Down       | 0.04271071| 0.74199989 |
| LINC01461                  | -1.3413799     | Down       | 0.01143714| 0.63705043 |
| Inc-GPR27-16:1             | -1.3407603     | Down       | 0.01648499| 0.65476375 |
| AC005772.1--201            | -1.3381628     | Down       | 0.00051768| 0.37869313 |
| MIR2117                    | -1.3345777     | Down       | 0.00182095| 0.45957527 |
| Inc-GPR180-8:1             | -1.3325294     | Down       | 0.04785484| 0.75909133 |
| Inc-CDH19-1:1              | -1.3297711     | Down       | 0.00373595| 0.55546359 |
| Inc-MYLP1-1:1              | -1.3230214     | Down       | 0.03290443| 0.7208645  |
| Inc-AC006156.1--6:1        | -1.3212148     | Down       | 0.03163903| 0.72031743 |
| LINC00326-202              | -1.3131651     | Down       | 0.0007281 | 0.51224337 |
| Inc-THSD7A-5:1             | -1.3104044     | Down       | 0.01270662| 0.63775317 |
| ALS13320.1--201            | -1.3078099     | Down       | 0.02483242| 0.69822202 |
| LOC100288570               | -1.302538      | Down       | 0.00116144| 0.42609515 |
| OR4F13P                    | -1.3002495     | Down       | 0.00258605| 0.51224337 |
| SKAPI-AS1-201              | -1.2965689     | Down       | 0.03989885| 0.74199989 |
| Inc-ZC3H12B-8:1            | -1.2960126     | Down       | 0.00485753| 0.55695089 |
| Inc-DDX58-6:2              | -1.2919894     | Down       | 0.04664872| 0.75453224 |
| Inc-MRPL9-1:1              | -1.2821415     | Down       | 0.0193777 | 0.67753348 |
| Inc-C6orf195-20:1          | -1.2797904     | Down       | 0.00068424| 0.39679443 |
| LINC00563                  | -1.2751075     | Down       | 0.04014392| 0.74199989 |
| RNU6-693P-201              | -1.2734215     | Down       | 0.00931818| 0.6151086  |
| Inc-SERP2-13:1             | -1.2711219     | Down       | 0.03525604| 0.72695785 |
| Inc-NKD2-3:8               | -1.2692144     | Down       | 0.01741431| 0.65667837 |
| Inc-CSNK1A1-6:1            | -1.2661357     | Down       | 0.03246677| 0.72031743 |
| Inc-TMEM178-6:1            | -1.2653338     | Down       | 0.01654808| 0.65588218 |
| AC010280.1--201             | -1.2633516     | Down       | 0.02288955| 0.69353994 |
| AC011333.1--201             | -1.2601339     | Down       | 0.01734914| 0.65667837 |
| Inc-SRY-12:1               | -1.255766      | Down       | 0.04179039| 0.74199989 |
| LOC101929541               | -1.2543068     | Down       | 0.00422143| 0.55695089 |
| Inc-IQCG-1:1               | -1.2510293     | Down       | 0.00960776| 0.6151086  |
| Inc-TRAF7-1:4              | -1.250778      | Down       | 0.02651159| 0.7025969 |
| AC06805.1--202              | -1.250693      | Down       | 0.01630728| 0.65588218 |
| Inc-WSB1-9:1               | -1.2490003     | Down       | 0.0027697 | 0.33391458 |
| HIPK1-AS1-202              | -1.247658      | Down       | 0.00640044| 0.55880591 |
| Inc-ANKRD65-4:1            | -1.2456674     | Down       | 0.00167491| 0.48182856 |
| Inc-RASD1-2:1              | -1.2336926     | Down       | 0.03531618| 0.72695785 |
| Inc-PTPN12-1:1             | -1.2251669     | Down       | 0.00203611| 0.49624235 |
| Inc-ASAH2B-6:1             | -1.2249331     | Down       | 0.02282058| 0.69285761 |
| Inc-VSTM2B-7:1             | -1.2187025     | Down       | 0.00664315| 0.56471029 |
Table 5 (Continued).

| IncRNAs                      | Log2FoldChange | Regulation | P-value     | P-adj     |
|------------------------------|----------------|------------|-------------|-----------|
| AC009145.3–201               | -1.2150544     | Down       | 0.00669705  | 0.56471029|
| Inc-EXOC4-2:1                | -1.2094249     | Down       | 0.03638874  | 0.73000405|
| Inc-ASFIA-7:1                | -1.2091281     | Down       | 0.04945525  | 0.76055974|
| LOC101927915                 | -1.2090211     | Down       | 0.04151546  | 0.74199989|
| MIR520D                      | -1.2003733     | Down       | 0.01614125  | 0.65476375|
| Inc-RP11-14BO21.3:1–3:1      | -1.1989594     | Down       | 0.03101553  | 0.72031743|
| Inc-VCP1P1-2:1               | -1.1940207     | Down       | 0.01680361  | 0.65667837|
| Inc-MANE4-15:1               | -1.1934022     | Down       | 0.03073549  | 0.71869418|
| AP007216.1–201               | -1.1933507     | Down       | 0.03903039  | 0.74199989|
| Inc-BOC-1:1                  | -1.1894086     | Down       | 0.03214827  | 0.72031743|
| Inc-ALCAM-16:1               | -1.1864006     | Down       | 0.00010229  | 0.23823842|
| AC243965.1–201               | -1.1825172     | Down       | 0.00992456  | 0.61994889|
| Inc-SNRPEP2-1:1              | -1.1779725     | Down       | 0.00505178  | 0.55690589|
| MIR8063                      | -1.1720035     | Down       | 0.03554046  | 0.72695705|
| LINC01497                    | -1.1712102     | Down       | 0.00396132  | 0.55546359|
| AP005202.1–201               | -1.1714525     | Down       | 0.02687222  | 0.7058418 |
| Inc-CASA-14:1                | -1.170243      | Down       | 0.01880508  | 0.66963439|
| TBCID26-AS1-201              | -1.1690859     | Down       | 0.03794326  | 0.73763201|
| Inc-RHOB-6:4                 | -1.164896      | Down       | 0.00952576  | 0.6151086 |
| Inc-TMEM235-3:1              | -1.164461      | Down       | 0.02080375  | 0.68520443|
| Inc-NKAIN3-1:1               | -1.1639521     | Down       | 0.01613077  | 0.65476375|
| Inc-TFAP2A-12:1              | -1.1638797     | Down       | 0.0458381   | 0.75250711|
| NONHSAT080748                | -1.1637059     | Down       | 0.04242998  | 0.74199989|
| Inc-WDR1-2:1                 | -1.1612431     | Down       | 0.01413228  | 0.64612284|
| Inc-STYK1-2:1                | -1.160814      | Down       | 0.03332132  | 0.72032337|
| Inc-C2CD4A-8:3               | -1.1589171     | Down       | 0.03249489  | 0.72031743|
| Inc-RAB9A-4:1                | -1.1570636     | Down       | 0.04423563  | 0.74774931|
| Inc-GRK4-2:1                 | -1.157003      | Down       | 0.01043825  | 0.62720663|
| AL356124.1–212               | -1.1529537     | Down       | 0.0059984   | 0.55690589|
| Inc-GRID1-10:2               | -1.1509303     | Down       | 0.00028173  | 0.33391458|
| Inc-DMRTA1-21:1              | -1.1494581     | Down       | 0.02080202  | 0.68520443|
| COPG2IT1                     | -1.1488501     | Down       | 0.03280207  | 0.7208865 |
| GUSBPI                       | -1.1442627     | Down       | 0.03300713  | 0.7208645 |
| Inc-AC016251.1–18:1          | -1.1426114     | Down       | 0.01124953  | 0.63705043|
| Inc-IGHMBP2-2:1              | -1.1410125     | Down       | 0.01522257  | 0.65476375|
| Inc-CLK1-5:1                 | -1.1408544     | Down       | 0.00456639  | 0.55690589|
| Inc-DDIT4L-1:1               | -1.139392      | Down       | 0.0033263   | 0.54489032|
| Inc-ATP8A2-4:1               | -1.1309851     | Down       | 0.01285546  | 0.63775317|
| AC002255.1–201               | -1.1258339     | Down       | 0.03121112  | 0.72031743|
| Inc-BX255923.1–4:1           | -1.1254471     | Down       | 0.02958836  | 0.71263333|
| LRRC37A6P                     | -1.1246433     | Down       | 0.01039373  | 0.62720663|
| Inc-THBD-3:1                 | -1.1181096     | Down       | 0.01823629  | 0.66321547|
| SMIM2-IT1                    | -1.1152686     | Down       | 0.04821159  | 0.75909133|
| Inc-EIF2AK3-10:1              | -1.1129693     | Down       | 0.00094609  | 0.41823037|
| AC072039.2–201               | -1.1023779     | Down       | 0.04427089  | 0.74774931|
| AC073655.1–201                | -1.1010143     | Down       | 0.00438297  | 0.55690589|
| Inc-HECA-8:3                 | -1.1007561     | Down       | 0.01730192  | 0.65667837|
| Inc-CAMK2N2-1:1               | -1.100534      | Down       | 0.02254575  | 0.69130412|

(Continued)
| IncRNAs                         | Log2FoldChange | Regulation | P-value  | P-adj   |
|--------------------------------|----------------|------------|----------|---------|
| Inc-RET-2:1                    | −1.0994363     | Down       | 0.02204275 | 0.6889443 |
| AC006482.1–201                 | −1.0943276     | Down       | 0.01606638 | 0.65476375 |
| NONHSAT0666757                 | −1.0893525     | Down       | 0.02619728 | 0.7025969 |
| Inc-PCIF1-1:1                  | −1.0831588     | Down       | 0.03331068 | 0.72302337 |
| Inc-RG59-1:9                   | −1.0808278     | Down       | 0.04328182 | 0.74348205 |
| Inc-TMEM63B-3:1                | −1.0806828     | Down       | 0.03297302 | 0.7208645 |
| AL354726.1–201                 | −1.0779947     | Down       | 0.03804582 | 0.7382395 |
| Inc-VPS45-5:1                  | −1.0767237     | Down       | 0.03551093 | 0.72695785 |
| MIR100HG-204                   | −1.0749286     | Down       | 0.00478367 | 0.5569089 |
| Inc-ERMN-3:1                   | −1.0724303     | Down       | 0.01323341 | 0.63919136 |
| Inc-PO1M121L112:9:1            | −1.0701442     | Down       | 0.01424926 | 0.64799971 |
| LINC02399-201                  | −1.0677909     | Down       | 0.00159699 | 0.47784335 |
| ZNF385D-AS2                    | −1.0675014     | Down       | 0.03541215 | 0.72695785 |
| Inc-CCNL3-3:1                  | −1.061945      | Down       | 0.03740759 | 0.73503181 |
| Inc-SLC4A3-7:4                 | −1.0657752     | Down       | 0.00420941 | 0.5569089 |
| AC096666.1–201                 | −1.0645687     | Down       | 0.0475234 | 0.75874445 |
| TRAPP12-AS1-201                | −1.0621034     | Down       | 0.00527019 | 0.5569089 |
| AC019073.1–201                 | −1.0620397     | Down       | 0.01113385 | 0.63705043 |
| Inc-PYGO1-3:1                  | −1.0617362     | Down       | 0.00735041 | 0.57770209 |
| NONHSAT016126                 | −1.0615194     | Down       | 0.00454088 | 0.5569089 |
| Inc-ZNF33A-7:1                 | −1.0611652     | Down       | 0.02394318 | 0.69169667 |
| AC021097.1–201                 | −1.0607721     | Down       | 0.00678068 | 0.56733936 |
| Inc-SNX11-9:1                  | −1.0565877     | Down       | 0.04932529 | 0.75985275 |
| LINC00092-202                  | −1.0542115     | Down       | 0.00493655 | 0.5569089 |
| LOC100130417                   | −1.0441384     | Down       | 0.02061929 | 0.68461156 |
| Inc-DACT1-2:1                  | −1.0422563     | Down       | 0.00276522 | 0.51224337 |
| Inc-CACNA1E-5:3                | −1.0418233     | Down       | 0.032085   | 0.72031743 |
| Inc-KCNJ2-2:1                  | −1.0409158     | Down       | 0.03770802 | 0.73763201 |
| ZNF451-AS1-202                 | −1.0407145     | Down       | 0.0199397  | 0.60003654 |
| AC022509.1–203                 | −1.0393619     | Down       | 0.04632896 | 0.75407344 |
| AL162253.1–201                 | −1.039287      | Down       | 0.04553105 | 0.75046363 |
| LINC01339                      | −1.0376761     | Down       | 0.01322858 | 0.63919136 |
| RNU4-30P-201                   | −1.03405       | Down       | 0.04484526 | 0.74859413 |
| Inc-ZNF527-3:1                 | −1.0331657     | Down       | 0.00495913 | 0.5569089 |
| Inc-VSTM4-1:3                  | −1.0311378     | Down       | 0.03884105 | 0.74199989 |
| Inc-ORMDL2-3:1                 | −1.0308522     | Down       | 0.03578571 | 0.7283161 |
| Inc-AKIP1-5:1                  | −1.0271559     | Down       | 0.02023333 | 0.68302181 |
| AL359091.4–201                 | −1.0270896     | Down       | 0.04632883 | 0.75407344 |
| Inc-PPIAL4G-24:1               | −1.0263086     | Down       | 0.02813286 | 0.70925942 |
| LOC100506679                   | −1.0230377     | Down       | 0.00087856 | 0.41820307 |
| Inc-TSSCI-1:12:1               | −1.0215854     | Down       | 0.00560415 | 0.5569089 |
| LOC100505984                   | −1.0208834     | Down       | 0.02557972 | 0.7025969 |
| Inc-FAM50B-12:1                | −1.0196309     | Down       | 0.02412553 | 0.69616967 |
| Inc-ALG9-1:1                   | −1.0176951     | Down       | 0.00552229 | 0.5569089 |
| AC096669.1–201                 | −1.0157852     | Down       | 0.03891397 | 0.74199989 |
| Inc-ZNF135-3:1                 | −1.0126176     | Down       | 0.02399892 | 0.69616967 |
| Inc-C2orf65-7:1                | −1.0125274     | Down       | 0.03958279 | 0.74199989 |
| NONHSAT093043                  | −1.0122218     | Down       | 0.0244619  | 0.69781796 |
| Inc-MARCKS-2:1                 | −1.0108829     | Down       | 0.01484675 | 0.65476375 |
Table 5 (Continued).

| IncRNAs          | Log2FoldChange | Regulation | P-value     | P-adj        |
|------------------|----------------|------------|-------------|--------------|
| lnc-ERI1-5:1     | -1.0096415     | Down       | 0.00105398  | 0.42609515   |
| lnc-AC011484.1–1:1 | -1.0085847    | Down       | 0.02523925  | 0.69822202   |
| lnc-C15orf41-16:1 | -1.0085698    | Down       | 0.00270442  | 0.51224337   |
| AC006116.7–201   | -1.0082255     | Down       | 0.0092013   | 0.6151086    |
| AL354760.1–201   | -1.007775      | Down       | 0.02302132  | 0.69368951   |
| lnc-H53ST3A1-6:1 | -1.005627      | Down       | 0.01277075  | 0.63775317   |
| LINC01007        | -1.0051638     | Down       | 0.04174436  | 0.74199989   |
| lnc-FSTL5-2:1    | -1.0044016     | Down       | 0.02732332  | 0.70738927   |
| lnc-OR10G2-7:1   | -1.0040498     | Down       | 0.02589504  | 0.7025969    |
| lnc-SCN11A-1:3   | -1.0003752     | Down       | 0.01675468  | 0.66667837   |
| KRT8P41          | 1.00323605     | Up         | 0.0157024   | 0.65476375   |
| lnc-TOMM70A-2:1  | 1.00437111     | Up         | 0.02094011  | 0.68579407   |
| ST20-AS1-201     | 1.00542536     | Up         | 0.00950719  | 0.6151086    |
| lnc-MCM3AP-2:1   | 1.00595783     | Up         | 0.04176048  | 0.74199989   |
| NONHSAT103382    | 1.00610895     | Up         | 0.01949203  | 0.67733348   |
| lnc-SCARF1-1:1   | 1.00878014     | Up         | 0.00141575  | 0.46126795   |
| lnc-ZNF613-1:5   | 1.00881485     | Up         | 0.00992771  | 0.61994889   |
| ZKSCAN7-AS1-201  | 1.01240919     | Up         | 0.01157844  | 0.63705043   |
| LINC00173        | 1.01400481     | Up         | 0.00981816  | 0.61762722   |
| lnc-SCARF1-1:1   | 1.0156664      | Up         | 0.03530082  | 0.72695785   |
| ST20-AS1-201     | 1.01593666     | Up         | 0.002276    | 0.32373463   |
| lnc-SSX1-3:1     | 1.01645757     | Up         | 0.01641438  | 0.65588218   |
| LINC01640-201    | 1.01953621     | Up         | 0.0409227   | 0.74199989   |
| lnc-FAM98A-4:1   | 1.02021781     | Up         | 7.97×10⁻⁵   | 0.23823842   |
| LINC02531-201    | 1.0290261      | Up         | 0.0217835   | 0.6875777    |
| lnc-MKKS-2:1     | 1.02955298     | Up         | 0.0127837   | 0.63775317   |
| lnc-ATP6AP2-5:1  | 1.03014956     | Up         | 0.02882574  | 0.71105768   |
| lnc-SSX1-3:1     | 1.03058486     | Up         | 0.01059718  | 0.62720663   |
| lnc-TMEM144-6:1  | 1.03101365     | Up         | 0.03545991  | 0.54892347   |
| lnc-TMEM144-6:1  | 1.03146297     | Up         | 0.00218147  | 0.49624236   |
| AC091906.1–201   | 1.03207632     | Up         | 0.0476632   | 0.65476375   |
| lnc-CD3B-5:1     | 1.03373123     | Up         | 0.02413739  | 0.69616967   |
| lnc-RDH10-3:1    | 1.0345704      | Up         | 0.00905218  | 0.6151086    |
| MIR527           | 1.03634444     | Up         | 0.04629443  | 0.75407344   |
| lnc-IL36B-3:1    | 1.04032276     | Up         | 0.03473281  | 0.72695785   |
| lnc-AP3S1-8:1    | 1.04706344     | Up         | 0.01681226  | 0.65667837   |
| lnc-AC004381.6:1–2:2 | 1.04706933 | Up         | 0.03502406  | 0.72695785   |
| lnc-ARL11-1:1    | 1.05123661     | Up         | 0.04263733  | 0.74199989   |
| lnc-DEFB116:8:1  | 1.05366198     | Up         | 0.02045757  | 0.68302181   |
| lnc-COBLL1-2:1   | 1.05373818     | Up         | 0.00428499  | 0.55695089   |
| lnc-TLX1-6:4     | 1.05385144     | Up         | 0.02973516  | 0.71383843   |
| lnc-FAM135A-3:1  | 1.0543549      | Up         | 0.00588203  | 0.55695089   |
| lnc-TFF3-2:1     | 1.0556941      | Up         | 0.00929413  | 0.6151086    |
| lnc-NBPF6-1:5    | 1.06191301     | Up         | 0.0039231   | 0.55546359   |
| LINC00470-208    | 1.06395777     | Up         | 0.02171233  | 0.6875777    |
| lnc-FREM3-4:1    | 1.06877234     | Up         | 0.03813847  | 0.73862272   |

(Continued)
| lncRNAs                      | Log2FoldChange | Regulation | P-value      | P-adj       |
|-----------------------------|----------------|------------|--------------|-------------|
| Inc-ZAP70-2:44              | 1.0688365      | Up         | 0.01504184   | 0.65476375  |
| Inc-ZSCANS-A-1:1            | 1.0698443      | Up         | 0.01950186   | 0.67753348  |
| Inc-DDHD1-7:1               | 1.07032663     | Up         | 0.00334132   | 0.54489032  |
| TMEM18-DT-201               | 1.07452939     | Up         | 0.004897     | 0.5569089   |
| ENST00000614227             | 1.07841408     | Up         | 0.00384573   | 0.55546359  |
| Inc-NADKD1-2:1              | 1.06985443     | Up         | 0.01950186   | 0.67753348  |
| Inc-WDR96-3:1               | 1.0816487      | Up         | 0.02824276   | 0.7092492   |
| AC106028.4–201              | 1.08328489     | Up         | 0.04826811   | 0.76054043  |
| Inc-LYSMD3-2:1              | 1.0840707      | Up         | 0.01190799   | 0.63705043  |
| TMEM18-DT-201               | 1.08830209     | Up         | 0.02084896   | 0.68520443  |
| Inc-CYDYL-9:1               | 1.08948305     | Up         | 0.00637373   | 0.5569089   |
| Inc-PDE1C-2:3               | 1.09008387     | Up         | 0.02298006   | 0.69368951  |
| Inc-RP1L1-4:1               | 1.09109086     | Up         | 0.01620667   | 0.65476375  |
| AC012363.1–201              | 1.09404463     | Up         | 0.04399763   | 0.75909133  |
| Inc-RP1L1-4:1               | 1.09404463     | Up         | 0.04399763   | 0.7634378   |
| AC011481.1–201              | 1.09608317     | Up         | 0.02649529   | 0.7025969   |
| ATN1L1                      | 1.1028884      | Up         | 0.02159311   | 0.6270663   |
| SNHGT1-221                  | 1.11243266     | Up         | 0.04766525   | 0.7584445   |
| Inc-ACAD11-2:1              | 1.1130875      | Up         | 0.02148542   | 0.6875777   |
| AC012363.1–201              | 1.1185844      | Up         | 0.00210834   | 0.49624326  |
| Inc-RP1L1-4:1               | 1.1199024      | Up         | 4.32×10⁻⁵    | 0.23823842  |
| AC011481.1–201              | 1.1228845      | Up         | 0.02649529   | 0.7025969   |
| Inc-RP1L1-4:1               | 1.1228845      | Up         | 0.02649529   | 0.7025969   |
| ATRNL1                      | 1.12368531     | Up         | 0.01534705   | 0.65476375  |
| SNHGT1-221                  | 1.12569191     | Up         | 0.04719373   | 0.75708084  |
| Inc-ACAD11-2:1              | 1.12954103     | Up         | 0.01867463   | 0.66684299  |
| AC127496.3–201              | 1.1336155      | Up         | 0.0210834    | 0.49624326  |
| Inc-RPM27B-9:1              | 1.13529595     | Up         | 0.01792398   | 0.65667837  |
| Inc-ANO6-2:1                | 1.1410763      | Up         | 0.00329799   | 0.6151086   |
| Inc-BA4A-4:1                | 1.1424342      | Up         | 0.02936139   | 0.71263333  |
| Inc-ABCA1-1:2               | 1.14734442     | Up         | 0.00747609   | 0.58535254  |
| Inc-GGSP1-7:1               | 1.1489917      | Up         | 0.01982258   | 0.68003654  |
| Inc-TPRIP1-7:1              | 1.1488135      | Up         | 0.02032843   | 0.68302181  |
| Inc-PCBPI-4:1               | 1.15063821     | Up         | 0.00625079   | 0.5569089   |
| Inc-PABPC3-3:2              | 1.1529063      | Up         | 0.0091832    | 0.41823037  |
| Inc-HERC4-1:1               | 1.1552135      | Up         | 0.03708868   | 0.73471054  |
| Inc-ICQCH-1:1               | 1.1603186      | Up         | 0.01001295   | 0.62174278  |
| Inc-C16orf78-5:3            | 1.16644237     | Up         | 8.81×10⁻⁵    | 0.23823842  |
| CIQTNF7-A5:201              | 1.17053152     | Up         | 0.00916598   | 0.6151086   |
| Inc-VASH2-1:1               | 1.17220568     | Up         | 0.04245329   | 0.7199989   |
| LINC01255-204               | 1.17230984     | Up         | 0.0053825    | 0.6151086   |
| Inc-ATG3-2:1                | 1.17235799     | Up         | 0.01125376   | 0.63705043  |
| Inc-GLT1D1-5:1              | 1.1747163      | Up         | 0.04455268   | 0.74859413  |
| Inc-CR3200.1–2:1            | 1.17483834     | Up         | 0.0400751    | 0.7419989   |
| Inc-HMGB2-5:1               | 1.17590206     | Up         | 0.02536006   | 0.69966978  |
| Inc-CYDYL-9:1               | 1.18188326     | Up         | 0.0148538    | 0.65476375  |

(Continued)
Table 5 (Continued).

| IncRNAs                        | Log2FoldChange | Regulation | P-value   | P-adj       |
|--------------------------------|----------------|------------|-----------|-------------|
| AC023355.1–202                 | 1.1849183      | Up         | 0.01732148| 0.65667837  |
| Inc-USP12-5:2                  | 1.18622738     | Up         | 0.04358103| 0.74483576  |
| LOC101929080                   | 1.19054239     | Up         | 0.01223231| 0.63775317  |
| Inc-KCNNC2-5:1                 | 1.19486915     | Up         | 0.009252  | 0.6151086   |
| Inc-KNTCI-4:1                  | 1.19535911     | Up         | 0.00297243| 0.53593679  |
| Inc-JAM3-8:1                   | 1.19852384     | Up         | 0.00257337| 0.51224337  |
| Inc-NKX6-1-10:1                | 1.19948691     | Up         | 0.01409262| 0.64546217  |
| Inc-KCNNC3-5:1                 | 1.20120674     | Up         | 0.00126408| 0.43152476  |
| Inc-URB2-1:3                   | 1.20260566     | Up         | 0.00664972| 0.56471029  |
| Inc-HS3ST3A1-5:2               | 1.20515033     | Up         | 0.02185892| 0.68799902  |
| Z98885.3–201                   | 1.21290644     | Up         | 0.04894508| 0.75985275  |
| Inc-WDR64-2:2                  | 1.21682833     | Up         | 0.00010236| 0.23823842  |
| LOC101929452                   | 1.2233498      | Up         | 0.0006972 | 0.39679443  |
| Inc-PAICS-4:1                  | 1.22411726     | Up         | 0.00037776| 0.33998788  |
| AL020994.1–201                 | 1.2316038      | Up         | 0.00123669| 0.43152476  |
| Inc-CNIH3-1-1                  | 1.23515033     | Up         | 0.00226292| 0.32373463  |
| PRNCR1                         | 1.23856565     | Up         | 0.01741856| 0.66678373  |
| AC024475.1–201                 | 1.24543291     | Up         | 0.02421639| 0.69619667  |
| Inc-DDX52-2:1                  | 1.24950582     | Up         | 0.00022629| 0.32373463  |
| Inc-SLFN12-6:1                 | 1.24993787     | Up         | 0.03632989| 0.73000405  |
| AC093297.1–201                 | 1.26032356     | Up         | 0.03683869| 0.73355985  |
| U1.18–201                      | 1.26323973     | Up         | 0.00602542| 0.55695089  |
| Inc-GTPBP5-3:1                 | 1.26463283     | Up         | 0.00102369| 0.23823842  |
| LINC02773-201                  | 1.27552196     | Up         | 0.00884705| 0.6151086   |
| Inc-FAM104A-4:2                | 1.2756097      | Up         | 0.00387626| 0.55546359  |
| Inc-SYCP2-3:1                  | 1.27585656     | Up         | 0.01471856| 0.66678373  |
| NONHSAT106296                  | 1.28232348     | Up         | 0.02753193| 0.70738927  |
| Inc-TEMEM123-3:2               | 1.28431214     | Up         | 0.00636859| 0.55695089  |
| LOC10273833                    | 1.28894382     | Up         | 0.00191368| 0.49624236  |
| Inc-GPR149-4:1                 | 1.29256774     | Up         | 0.00893933| 0.6151086   |
| Inc-SLOC4C1-4:1                | 1.29343344     | Up         | 0.02627738| 0.7029569   |
| AL359541.1–201                 | 1.2959487      | Up         | 0.0009658 | 0.6151086   |
| Inc-ITGB1-4:2                  | 1.30515033     | Up         | 0.01303033| 0.63911018  |
| Inc-RP11-257K9.7.1–3:1         | 1.30753746     | Up         | 0.00014704| 0.27188326  |
| LOC102546298                   | 1.30773357     | Up         | 0.01041044| 0.62720663  |
| Inc-ZCCH9C9-2:5                | 1.30773357     | Up         | 0.00767846| 0.59393265  |
| Inc-RP11-257K9.7.1–3:1         | 1.31035839     | Up         | 0.01635308| 0.65888218  |
| LINC02864-202                  | 1.31194048     | Up         | 0.01303027| 0.63911018  |
| LINC01855-201                  | 1.32675457     | Up         | 0.00587822| 0.55695089  |
| Inc-C8orf4-1:2                 | 1.33018827     | Up         | 0.02627738| 0.7029569   |
| Inc-RP11-150O12.3.1–1:4        | 1.34017651     | Up         | 0.01509456| 0.65476375  |
| Inc-ZNF503-AS2-9:1             | 1.34488751     | Up         | 0.0296829 | 0.7206845   |
| AC120498.2–201                 | 1.34576622     | Up         | 0.00320335| 0.53930742  |
| Inc-HEATR4-5:1                 | 1.34613233     | Up         | 0.03623736| 0.73000405  |
| Inc-CNR1-1-2                    | 1.35206876     | Up         | 0.00627778| 0.55695089  |

(Continued)
Table 5 (Continued).

| lncRNAs                        | Log2FoldChange | Regulation | P-value    | P-adj       |
|--------------------------------|----------------|------------|------------|-------------|
| Inc-SMYD5-1:4                  | 1.35280066     | Up         | 0.00601195 | 0.55695089  |
| Inc-NUPL1-1:1                  | 1.35697674     | Up         | 0.02392115 | 0.69616967  |
| Inc-AKR1E2-5:1                 | 1.35847468     | Up         | 0.01769903 | 0.6567837   |
| AC012314.2-2-201               | 1.35985353     | Up         | 0.03496286 | 0.7269785   |
| Inc-CNDP2-1:1                  | 1.36188928     | Up         | 0.00584868 | 0.55695089  |
| Inc-CHGA-2:1                   | 1.3642467      | Up         | 0.02269448 | 0.6928576   |
| MIR1307                        | 1.36484241     | Up         | 0.03613377 | 0.73000405  |
| AC012314.2–201                 | 1.36985353     | Up         | 0.03496286 | 0.7269785   |
| Inc-SRGN-3:1                   | 1.37117291     | Up         | 0.00300049 | 0.53721319  |
| Inc-XRCC2-3:1                  | 1.3735139      | Up         | 0.00206033 | 0.49624236  |
| LRRK2-DT-202                   | 1.39577039     | Up         | 0.01136359 | 0.63705043  |
| AC113133.1–203                 | 1.43171942     | Up         | 0.00455193 | 0.55695089  |
| Inc-CCL3-1:2                   | 1.43199469     | Up         | 0.02679513 | 0.70508418  |
| Inc-RTKN2-5:1                  | 1.43324395     | Up         | 0.00204034 | 0.49624236  |
| BX005019.1–201                 | 1.4392263      | Up         | 0.03382324 | 0.7243778   |
| Inc-C14orf1182-4:1             | 1.44544826     | Up         | 0.01695345 | 0.6567837   |
| AC034199.1–201                 | 1.4544017      | Up         | 0.0213565  | 0.7269785   |
| Inc-LYZL1-10:1                 | 1.4578941      | Up         | 0.00124885 | 0.43152476  |
| Inc-LRIG1-3:1                  | 1.4642183      | Up         | 0.00455193 | 0.55695089  |
| MIR425                         | 1.47353585     | Up         | 0.0213565  | 0.7269785   |
| Inc-SIM2-2:1                   | 1.47895899     | Up         | 0.00014303 | 0.27188326  |
| MIR245                         | 1.49568926     | Up         | 0.0042996  | 0.55695089  |
| Inc-SIM2-2:1                   | 1.50294782     | Up         | 0.04100787 | 0.74199989  |
| PRMT5-AS1-206                  | 1.5303618      | Up         | 0.00853801 | 0.615086    |
| AC027018.1–202                 | 1.53360857     | Up         | 0.01496409 | 0.65476375  |
| Inc-ARF6-5:1                   | 1.5402516      | Up         | 0.0042996  | 0.55695089  |
| Inc-KCNI9-3:1                  | 1.5537316      | Up         | 0.835×10−5 | 0.2382342   |
| LOC102724484                   | 1.55813648     | Up         | 0.00484276 | 0.55695089  |
| Inc-VAMP3-3:1                  | 1.55906935     | Up         | 0.01857284 | 0.66521456  |
| Inc-MRPS18A-2:6                | 1.5595027      | Up         | 0.00187188 | 0.49624236  |
| Inc-TACR2-5:1                  | 1.5601837      | Up         | 0.03954105 | 0.74199989  |
| Inc-APCDDL1-1:1                | 1.56781969     | Up         | 0.00071636 | 0.3987193   |
| Inc-RILP-1:5                   | 1.57733865     | Up         | 0.01232391 | 0.63775317  |
| NONHAT0106835                  | 1.58291652     | Up         | 0.04103104 | 0.74199989  |
| AC066595.1–201                 | 1.59152878     | Up         | 0.00607687 | 0.55695089  |
| AP002505.2–201                 | 1.61111587     | Up         | 0.00528326 | 0.55695089  |
| Inc-RPN1B-8:1                  | 1.6647053      | Up         | 0.0033198  | 0.5449038   |
| Inc-NLK-1:2                    | 1.6679315      | Up         | 0.01702869 | 0.6567837   |
| Inc-SH3BGRL2-8:1               | 1.68256761     | Up         | 0.01627335 | 0.6558218   |
| LINC00862                      | 1.69076057     | Up         | 0.04360851 | 0.74483576  |
| Inc-KK-2:1                     | 1.69608599     | Up         | 0.02384559 | 0.69616967  |
| AL0664681.1–201                | 1.72966979     | Up         | 0.00784283 | 0.59809568  |
| Inc-DRD3-2:1                   | 1.73507434     | Up         | 0.00020353 | 0.32374363  |
| Inc-ASMT-7:1                   | 1.77985488     | Up         | 0.00354204 | 0.55695089  |
| AC022001.3–201                 | 1.7853082      | Up         | 0.01479698 | 0.65476375  |
| AC090643.2–201                 | 1.83684053     | Up         | 0.00079596 | 0.41823037  |
| NONHAT0106837                  | 1.84066898     | Up         | 0.02058467 | 0.68443575  |
| AC103993.1–202                 | 1.85414231     | Up         | 0.00017245 | 0.29435292  |

(Continued)
the cellular localization of hsa_circ_0002202 in THP-1-derived macrophages. The results showed that hsa_circ_0002202 was mainly localized in the cytoplasm of THP-1-derived macrophage. Furthermore, we found that knockdown of hsa_circ_0002202 suppressed the IFN-I-induced inflammation, which was in line with the previous study. These findings suggested that hsa_circ_0002202 play an important role in T1DM, which will be verified by tissue sample experiments, cell lines experiments, and even animal model construction in future studies.

The miRNAs in the T1DM-related ceRNA regulatory network are also important regulators in T1DM. In this study, we found that hsa_circ_0002202 could sponge miR-487a-3p, miR-576-5p, miR-326, miR-186-5p, and many other miRNAs. Among the miRNAs, miR-487a-3p is reported to be up-regulated in the PBMCs of T1DM patients. Increased expression of miR-326 was identified in PBMSCs and peripheral blood lymphocytes of patients with T1DM. Another study showed a decreased expression level of miR-326 in PBMCs of patients with T1DM. These same or opposite results may be related to the genetic or environmental factors of T1DM patients. Besides, some other miRNAs in the ceRNA network may be related to other autoimmune disorders, which have strong complications with T1DM. The pro-inflammatory cytokines promote the miR-455-3p expression and then cause the inflammatory β-cell failure. miR-31-5p, miR-665, miR-326, miR-224 are associated with inflammatory bowel disease. We will also conduct verification and analysis in future experimental studies to obtain more in-depth and comprehensive scientific conclusions.

In the present study, the biological function and potential pathways of the DEcircRNAs and DElncRNAs were also analyzed. The enriched GO terms were mainly related to extracellular matrix.

Table 5 (Continued).

| lncRNAs         | Log2FoldChange | Regulation | P-value | P-adj     |
|-----------------|---------------|------------|---------|-----------|
| Inc-CFPM2-2:2   | 1.86775188    | Up         | 0.01688355 | 0.65667837 |
| SNHG21          | 1.90852825    | Up         | 0.00532982 | 0.55695089 |
| AC116021.1–201  | 1.93990875    | Up         | 0.02097564 | 0.68579407 |
| LOC102467217    | 1.9623212     | Up         | 0.00440907 | 0.55695089 |
| Inc-C2orf62-1:1 | 1.96238874    | Up         | 0.01728119 | 0.65667837 |
| PELATON-201     | 2.00463147    | Up         | 0.03488425 | 0.72695785 |
| Inc-CS-1:1      | 2.0585191     | Up         | 0.01120735 | 0.63705043 |
| Inc-PON2-3:1    | 2.0677784     | Up         | 0.02628724 | 0.7025969 |
| Inc-IFNA2-2:1   | 2.17522445    | Up         | 0.0119433 | 0.63705043 |
| AL359258.1–201  | 2.17725336    | Up         | 0.01246482 | 0.63775317 |
| Inc-CEACAM6-1:1 | 2.22056145    | Up         | 0.02321939 | 0.6949317 |
| Inc-EVI2A-1:1   | 2.2533756     | Up         | 0.00361964 | 0.54892347 |
| Inc-CXCL3-1:1   | 2.28502109    | Up         | 0.03936439 | 0.74199989 |
| Inc-SRGN-4:1    | 2.3926122     | Up         | 0.00530242 | 0.55695089 |

Table 6 Results of Gene Ontology (GO) Enrichment Analysis of Differentially Expressed lncRNAs

| Ontology | Term          | Description          | Gene Number | P-adj     |
|----------|---------------|----------------------|-------------|-----------|
| BP       | GO:0042116    | Macrophage activation| 5           | 0.01572240 |
| BP       | GO:0043030    | Regulation of macrophage activation | 4 | 0.01885761 |
| CC       | GO:00005902   | Microvillus          | 4           | 0.02267082 |

Abbreviations: BP, biological process; CC, cellular component.
components (ECM) and macrophage activation. The ECM contributes to islet inflammation and creates a permissive environment for immune cells to infiltrate the pancreatic islets and impair β-cell survival. Macrophages participate in interacting, directing, or restricting trafficking of the autoreactive-specific T cells into the islets via the IFN-I signaling during the development of T1DM. Thus, our in vitro experiments focused on macrophage inflammation, and the results indicated the anti-inflammatory effect of hsa_circ_0002202 inhibition. In terms of the KEGG pathway, the protein digestion and absorption were enriched, indicating that the activation of these genes was closely related to the T1DM progression.
| mRNAs    | Log2FoldChange | Regulation | P-value     | P-adj       |
|----------|----------------|------------|-------------|-------------|
| RBFOX1   | -2.3079121     | Down       | 0.00020929  | 0.48868466  |
| FAM132B  | -1.9940805     | Down       | 0.00498156  | 0.79896357  |
| SLFN1L   | -1.923862      | Down       | 0.00176092  | 0.71338425  |
| CLDN22   | -1.7963769     | Down       | 0.00866828  | 0.8200064   |
| GNAL     | -1.7753788     | Down       | 0.01707197  | 0.82671544  |
| MUC15    | -1.5965074     | Down       | 0.00413517  | 0.71338425  |
| CA8      | -1.5357652     | Down       | 0.01131812  | 0.82671544  |
| PTGDR    | -1.5165361     | Down       | 0.01513717  | 0.82671544  |
| TEX13A   | -1.495935      | Down       | 0.00606045  | 0.79896357  |
| TAAR2    | -1.4635903     | Down       | 0.02574051  | 0.82671544  |
| KIR3DL1  | -1.4479695     | Down       | 0.02572008  | 0.82671544  |
| COL6A3   | -1.4263206     | Down       | 0.00181007  | 0.71338425  |
| B4GALNT2 | -1.3947065     | Down       | 0.01298325  | 0.82671544  |
| PARD3    | -1.3582746     | Down       | 0.01926125  | 0.82671544  |
| SORBS1   | -1.3306212     | Down       | 0.0041603   | 0.78986357  |
| DUOX2    | -1.3208459     | Down       | 0.01957626  | 0.82671544  |
| HPGD     | -1.3088539     | Down       | 0.01853011  | 0.82671544  |
| NNMT     | -1.2274537     | Down       | 0.04763409  | 0.82671544  |
| TMEM74   | -1.2255201     | Down       | 0.04330755  | 0.82671544  |
| COL6A2   | -1.2224407     | Down       | 0.02822533  | 0.82671544  |
| HSPB8    | -1.2153355     | Down       | 0.01531611  | 0.82671544  |
| BFSP1    | -1.1921939     | Down       | 0.0392896   | 0.82671544  |
| GNG11    | -1.179029      | Down       | 0.00163335  | 0.71338425  |
| GPR1     | -1.1631327     | Down       | 0.02166454  | 0.82671544  |
| B3GALT5  | -1.1584697     | Down       | 0.01946241  | 0.82671544  |
| C20orf173| -1.1568903     | Down       | 0.01892708  | 0.82671544  |
| CYP11B1  | -1.152487      | Down       | 0.00018277  | 0.48684666  |
| DHH      | -1.1517769     | Down       | 0.00194518  | 0.71338425  |
| CRYM     | -1.1448803     | Down       | 0.00232428  | 0.71338425  |
| SMKR1    | -1.1381526     | Down       | 0.04519693  | 0.82671544  |
| BPIFB3   | -1.1194083     | Down       | 0.03620019  | 0.82671544  |
| FAM150B  | -1.1105272     | Down       | 0.04200652  | 0.82671544  |
| TEX11    | -1.0986657     | Down       | 0.00098015  | 0.71338425  |
| NPR3     | -1.0702284     | Down       | 0.03640359  | 0.82671544  |
| ATP13A4  | -1.0357916     | Down       | 0.03639288  | 0.82671544  |
| CAMK2N2  | -1.0343627     | Down       | 0.00591547  | 0.79896357  |
| KIR2DL3  | -1.0313509     | Down       | 0.03836931  | 0.82671544  |
| CACNA2D2 | -1.0155401     | Down       | 0.02373916  | 0.82671544  |
| WDR76    | -1.0120059     | Down       | 0.00116238  | 0.71338425  |
| GPR18    | -1.0109237     | Down       | 0.00320393  | 0.79896357  |
| AMHR2    | -1.0089921     | Down       | 0.03106529  | 0.82671544  |
| PCDHBI5  | 1.00754421     | Up         | 0.01257116  | 0.82671544  |
| MARCH5   | 1.02701386     | Up         | 0.03176063  | 0.82671544  |
| DEFB123  | 1.0296089      | Up         | 0.04036705  | 0.82671544  |
| DNAJB7   | 1.05742045     | Up         | 0.04277946  | 0.82671544  |
| C2CD4B   | 1.0577298      | Up         | 0.02772476  | 0.82671544  |
| IL6      | 1.05994453     | Up         | 0.04788638  | 0.82671544  |
| OR2LI3   | 1.07004067     | Up         | 0.04427013  | 0.82671544  |

(Continued)
We also identified some genes associated with T1DM, including GREM2, RAPGEF5, C9orf152, SMKR1, SORBS1, HSPB8, CACNA2D2, SKOR1, and SLFNL1. Among these, SORBS1 and CACNA2D2 are previously reported to be related to diabetes. SORBS1, a human homologue for c-Cbl-associated protein (CAP), is an important adaptor protein in the insulin-signaling pathway, and its genetic polymorphism is related to insulin resistance. Meanwhile, another study showed that SORBS1 might be a new susceptibility gene for diabetic nephropathy. CACNA2D2 is the voltage-gated calcium channel auxiliary subunit alpha2delta2 gene that encodes a calcium channel protein, and Huang et al identified CACNA2D2 as a diabetes-related atherogenesis gene. Besides, GREM2 and HSPB8 are closely related to inflammatory response, suggesting a regulatory role in the T1DM macrophages inflammation.

| mRNAs      | Log2FoldChange | Regulation | P-value   | P-adj   |
|------------|----------------|------------|-----------|---------|
| C17orf64   | 1.07345437     | Up         | 0.01738992| 0.82671544|
| SGK1       | 1.10667874     | Up         | 0.00379544| 0.82671544|
| COMP       | 1.11621286     | Up         | 0.00132896| 0.82671544|
| RASSF8     | 1.1211237      | Up         | 0.00268822| 0.82671544|
| SLC6A14    | 1.12250998     | Up         | 0.00605879| 0.7896357|
| RAPGEF5    | 1.13847388     | Up         | 0.02042072| 0.82671544|
| GREM2      | 1.18378203     | Up         | 0.00260099| 0.71338425|
| ARRDC3     | 1.18900995     | Up         | 0.00721663| 0.7896357|
| FILIP1L    | 1.20891948     | Up         | 0.00719201| 0.7896357|
| ADGRG4     | 1.20976755     | Up         | 0.01358302| 0.82671544|
| ASIC2      | 1.21384452     | Up         | 0.01333649| 0.82671544|
| MARCH1     | 1.2672335      | Up         | 0.02731178| 0.82671544|
| AGXT       | 1.28961174     | Up         | 0.00580496| 0.7896357|
| HSPA12A    | 1.29400344     | Up         | 0.04457166| 0.82671544|
| C9orf152   | 1.34773511     | Up         | 0.00068838| 0.71338425|
| MAPT       | 1.38818206     | Up         | 0.00264472| 0.71338425|
| DOCK4      | 1.43931041     | Up         | 0.01074391| 0.82671544|
| SKOR1      | 1.46453595     | Up         | 0.01818479| 0.82671544|
| CXCL13     | 1.52896795     | Up         | 0.01173074| 0.82671544|
| SLC5A7     | 1.57904371     | Up         | 0.04645311| 0.82671544|
| LOC388780  | 1.58723305     | Up         | 0.01831587| 0.82671544|
| CCL8       | 1.64314463     | Up         | 0.02259273| 0.82671544|
| PDK4       | 1.68428709     | Up         | 0.02094083| 0.82671544|
| MYO7B      | 1.80214766     | Up         | 0.01684902| 0.82671544|

| Table 8 Results of Gene Ontology (GO) Enrichment Analysis of Differentially Expressed mRNAs |
|-----------------------------------------------|---------------------------------|----------------------------------|
| **Ontology**                                  | **Term**                        | Description                      |
| **MF**                                        | GO:0004955                      | Prostaglandin receptor activity   |
| **MF**                                        | GO:0004954                      | Prostanoid receptor activity      |
| **MF**                                        | GO:0036122                      | BMP binding                      |
| **MF**                                        | **Gene Number**                 | **P-adj**                        |
|                                               | 2                               | 0.043054                         |
|                                               | 2                               | 0.043054                         |
|                                               | 2                               | 0.04305384                       |

Abbreviation: MF, molecular function.
genes with special functions may be the latest molecular markers of T1DM and need further experimental verification.

Despite the above results, there are still some limitations in the current study. First, the small sample size may affect the number of altered RNAs. Further studies based on a larger sample size should be performed to confirm our conclusions. Second, besides acting as miRNA sponges, circRNAs or IncRNAs can also regulate gene expression by affecting transcription. At the same time, most of the results are obtained using bioinformatics analysis. Thus, experimental studies are needed to validate our results and further investigate the deeper mechanism. Third, the progress of T1DM is not

Figure 5 The circRNA-IncRNA-mRNA network. The round nodes represent DEcircRNAs, the rhombic nodes represent DEincRNAs, the v-type nodes represent DEMRNAs. The up or down-regulated genes are represented in red and green, respectively.
### Table 9 The Fold Change of All miRNAs Between the Control Group and T1DM Group

| miRNAs          | Log2FoldChange | Regulation | P-value  | P-adj   |
|-----------------|----------------|------------|----------|---------|
| miR-1-3p        | −1.5165809     | Down       | 0.00670577 | 0.40231598 |
| miR-133b        | −1.2850481     | Down       | 0.00702946 | 0.40231598 |
| miR-99b-5p      | −0.8676123     | Down       | 0.03302164 | 0.59871978 |
| let-7e-5p       | −0.7792672     | Down       | 0.03530638 | 0.59871978 |
| miR-125a-5p     | −0.7761986     | Down       | 0.05533304 | 0.64056718 |
| miR-6885-5p     | −0.637504      | Down       | 1.38 × 10^{-6} | 0.00354783 |
| miR-551b-3p     | −0.5977145     | Down       | 0.01706182 | 0.53220869 |
| miR-10a-5p      | −0.5042807     | Down       | 0.04874767 | 0.61412501 |
| miR-181a-2-3p   | −0.4754952     | Down       | 0.00897879 | 0.40696367 |
| miR-27b-3p      | −0.4519303     | Down       | 0.07953434 | 0.68910078 |
| miR-151a-3p     | −0.4402091     | Down       | 0.02080807 | 0.53734625 |
| miR-139-5p      | −0.4381705     | Down       | 0.04665277 | 0.61412501 |
| miR-151b        | −0.4337404     | Down       | 0.00166047 | 0.32405862 |
| miR-584-5p      | −0.4115123     | Down       | 0.24226951 | 0.80715125 |
| miR-151a-5p     | −0.4054726     | Down       | 0.00857359 | 0.40696367 |
| miR-5787        | −0.4016736     | Down       | 0.00690767 | 0.40231598 |
| miR-130a-3p     | −0.3983994     | Down       | 0.06518421 | 0.65958378 |
| miR-133a-3p     | −0.3786417     | Down       | 0.01526582 | 0.49284222 |
| miR-431-5p      | −0.376715      | Down       | 0.2669136  | 0.82438552 |
| miR-30a-5p      | −0.3686175     | Down       | 0.04189063 | 0.60118096 |
| miR-23b-3p      | −0.3650878     | Down       | 0.06512818 | 0.65958378 |
| miR-598-3p      | −0.3548441     | Down       | 0.00450404 | 0.34045223 |
| miR-98-5p       | −0.3512228     | Down       | 0.02419159 | 0.55019809 |
| miR-126-5p      | −0.3460713     | Down       | 0.10065779 | 0.73085631 |
| miR-3120-3p     | −0.3425895     | Down       | 0.00372022 | 0.36452232 |
| miR-330-3p      | −0.3418255     | Down       | 0.04863712 | 0.61412501 |
| miR-6085        | −0.3367        | Down       | 0.01118897 | 0.4937422 |
| miR-196b-5p     | −0.3352881     | Down       | 0.05202185 | 0.6253999 |
| miR-324-5p      | −0.3283337     | Down       | 0.05990781 | 0.6483233 |
| miR-210-3p      | −0.3265283     | Down       | 0.30730975 | 0.84469096 |
| miR-326         | −0.3226899     | Down       | 0.04104522 | 0.60118096 |
| miR-181d-5p     | −0.3203042     | Down       | 0.04674485 | 0.61412501 |
| miR-335-5p      | −0.2992288     | Down       | 0.28050619 | 0.83108541 |
| miR-5739        | −0.2981961     | Down       | 0.00422458 | 0.34045223 |
| miR-126-3p      | −0.293697      | Down       | 0.05433041 | 0.64056718 |
| miR-590-5p      | −0.2899434     | Down       | 0.04821654 | 0.61412501 |
| miR-146a-5p     | −0.2839604     | Down       | 0.1538926  | 0.75393664 |
| miR-148a-3p     | −0.28039       | Down       | 0.23451265 | 0.80105138 |
| miR-6756-5p     | −0.2760184     | Down       | 0.00400347 | 0.36045223 |
| miR-199a-3p     | −0.2669967     | Down       | 0.18245092 | 0.77350881 |
| miR-28-5p       | −0.2650704     | Down       | 0.00020694 | 0.11527438 |
| miR-128-3p      | −0.2599197     | Down       | 0.04105635 | 0.60118096 |
| miR-301a-3p     | −0.2587877     | Down       | 0.1947074  | 0.79974919 |
| miR-652-3p      | −0.2571135     | Down       | 0.014974   | 0.49248222 |
| miR-1301-3p     | −0.2557511     | Down       | 0.01179643 | 0.4937422 |
| miR-379-5p      | −0.2531956     | Down       | 0.353501   | 0.8588192 |
| miR-181c-5p     | −0.2521543     | Down       | 0.13770206 | 0.75376261 |
| miR-432-5p      | −0.2503287     | Down       | 0.48408203 | 0.90449982 |
| miR-18b-5p      | −0.2457859     | Down       | 0.00032042 | 0.11763941 |
| miR-194-5p      | −0.2451756     | Down       | 0.22699131 | 0.79102241 |

(Continued)
| miRNAs     | Log2FoldChange | Regulation | P-value       | P-adj       |
|------------|----------------|------------|---------------|-------------|
| miR-127-3p | -0.2446309     | Down       | 0.33136688    | 0.85489649  |
| miR-223-3p | -0.240992      | Down       | 0.01055265    | 0.43917422  |
| miR-32-5p  | -0.2428206     | Down       | 0.0475609     | 0.61412501  |
| miR-328-3p | -0.2426408     | Down       | 0.04244989    | 0.60118096  |
| miR-132-3p | -0.2426316     | Down       | 0.07861796    | 0.68910078  |
| let-7i-5p  | -0.2425701     | Down       | 0.01112698    | 0.43937422  |
| miR-493-5p | -0.2404954     | Down       | 0.29956191    | 0.83872374  |
| miR-27a-3p | -0.2375163     | Down       | 0.07375852    | 0.68406327  |
| miR-1307-5p| -0.2345506     | Down       | 0.04837714    | 0.61412501  |
| miR-495-3p | -0.2335808     | Down       | 0.44444021    | 0.88952595  |
| miR-6165   | -0.2328824     | Down       | 0.04757592    | 0.61412501  |
| miR-221-3p | -0.2320004     | Down       | 0.19653159    | 0.77997491  |
| miR-4317   | -0.2301339     | Down       | 9.82×10⁻⁵     | 0.08040842  |
| miR-374c-5p| -0.2292803     | Down       | 0.02373626    | 0.58146271  |
| miR-152-3p | -0.2286181     | Down       | 0.06717209    | 0.65890175  |
| miR-497-5p | -0.2266935     | Down       | 0.11867951    | 0.7426488   |
| miR-744-5p | -0.2244425     | Down       | 0.13054129    | 0.74892227  |
| miR-195-5p | -0.2242765     | Down       | 0.00184957    | 0.32405862  |
| miR-543    | -0.2217568     | Down       | 0.07709504    | 0.68910078  |
| miR-7-1-3p | -0.2212061     | Down       | 0.00065497    | 0.15302397  |
| miR-17-3p  | -0.2202809     | Down       | 0.47456765    | 0.8954764   |
| miR-26a-5p | -0.2097921     | Down       | 0.03685477    | 0.59871978  |
| miR-148b-3p| -0.2014556     | Down       | 0.27332485    | 0.83107769  |
| miR-22-3p  | -0.2014406     | Down       | 0.00809954    | 0.40696367  |
| miR-340-5p | -0.1994898     | Down       | 0.35912007    | 0.8588192   |
| miR-769-5p | -0.199198      | Down       | 0.28288034    | 0.83193599  |
| miR-1271-5p| -0.1944416     | Down       | 0.19561173    | 0.77997491  |
| miR-224-5p | -0.1934675     | Down       | 0.68365226    | 0.95853044  |
| miR-6852-5p| -0.191647      | Down       | 0.00589685    | 0.38858751  |
| miR-337-5p | -0.1901206     | Down       | 0.36210628    | 0.8588192   |
| miR-625-5p | -0.1893543     | Down       | 0.54798536    | 0.92261663  |
| miR-376a-3p| -0.1877679     | Down       | 0.65014785    | 0.95321673  |
| miR-101-3p | -0.1832045     | Down       | 0.36292288    | 0.8588192   |
| miR-487a-3p| -0.182157      | Down       | 0.16729778    | 0.76915081  |
| miR-411-5p | -0.1802523     | Down       | 0.11624338    | 0.7426488   |
| miR-33a-5p | -0.1803366     | Down       | 0.1091139     | 0.7426488   |
| miR-2355-5p| -0.1784709     | Down       | 0.01806897    | 0.53734625  |
| miR-182-5p | -0.1775695     | Down       | 0.00022427    | 0.11527458  |
| miR-421    | -0.1717140     | Down       | 0.03728568    | 0.59871978  |
| miR-339-5p | -0.1761355     | Down       | 0.1359837     | 0.75376261  |
| miR-186-5p | -0.1734146     | Down       | 0.14060276    | 0.75376261  |
| miR-10b-5p | -0.1714752     | Down       | 0.00027399    | 0.11735825  |
| miR-5584-3p| -0.1686341     | Down       | 0.01165649    | 0.43937422  |
| miR-215-5p | -0.1682987     | Down       | 0.30023651    | 0.83872374  |

(Continued)
| miRNAs      | Log2FoldChange | Regulation | P-value  | P-adj     |
|------------|----------------|------------|----------|-----------|
| miR-320c   | -0.1660735     | Down       | 0.14388218 | 0.75376261 |
| miR-154-3p | -0.1638598     | Down       | 0.20356636 | 0.77997491 |
| miR-30b-5p | -0.1626831     | Down       | 0.00529837 | 0.36856555 |
| miR-18a-5p | -0.1601252     | Down       | 0.30503491 | 0.83933888 |
| miR-505-5p | -0.159129      | Down       | 0.03015598 | 0.59610588 |
| miR-146b-5p| -0.1575493     | Down       | 0.29357044 | 0.83723744 |
| miR-339-3p | -0.1562831     | Down       | 0.00529837 | 0.36856555 |
| miR-18a-5p | -0.1546221     | Down       | 0.67560231 | 0.95648223 |
| miR-505-5p | -0.1532056     | Down       | 0.27357655 | 0.83107778 |
| miR-143-3p | -0.1517947     | Down       | 0.57248969 | 0.93390911 |
| let-7a-5p  | -0.1495243     | Down       | 0.03567474 | 0.59871978 |
| miR-185-5p | -0.1490736     | Down       | 0.02508744 | 0.55568816 |
| miR-320e   | -0.1469298     | Down       | 0.28061814 | 0.83105841 |
| miR-1202   | -0.1447347     | Down       | 0.21813416 | 0.78840757 |
| miR-340-3p | -0.143247      | Down       | 0.33859524 | 0.85486949 |
| miR-331-3p | -0.1428154     | Down       | 0.1490403  | 0.75988515 |
| miR-5196-5p| -0.1427908     | Down       | 0.00386774 | 0.34045223 |
| miR-20a-3p | -0.142275      | Down       | 0.05772224 | 0.6832335  |
| miR-628-5p | -0.1421981     | Down       | 0.13722984 | 0.75376261 |
| miR-4443   | -0.1404353     | Down       | 0.37497999 | 0.86499071 |
| miR-381-3p | -0.1401495     | Down       | 0.62104792 | 0.94829596 |
| miR-628-5p | -0.1400851     | Down       | 0.16633836 | 0.76915081 |
| miR-221-5p | -0.1390408     | Down       | 0.13217561 | 0.74892227 |
| miR-4291   | -0.1371731     | Down       | 0.22098446 | 0.79098893 |
| miR-4323   | -0.1368585     | Down       | 0.31730879 | 0.84917098 |
| miR-30e-3p | -0.136426      | Down       | 0.09753727 | 0.73085631 |
| miR-29c-5p | -0.1359778     | Down       | 0.16497145 | 0.76915081 |
| miR-409-5p | -0.1346939     | Down       | 0.30048022 | 0.83872374 |
| miR-200b-3p| -0.1335934     | Down       | 0.19960532 | 0.77997491 |
| miR-15b-5p | -0.133299      | Down       | 0.14604411 | 0.75376261 |
| miR-6763-5p| -0.1325476     | Down       | 0.0551816  | 0.64056718 |
| miR-200c-3p| -0.1319846     | Down       | 0.114788   | 0.74226488 |
| miR-652-5p | -0.131862      | Down       | 0.03226253 | 0.59871978 |
| miR-103a-3p| -0.130681      | Down       | 0.15260836 | 0.75396664 |
| miR-548a-5p| -0.1286466     | Down       | 0.14518387 | 0.75376261 |
| miR-192-5p | -0.1269885     | Down       | 0.43987942 | 0.88952595 |
| miR-107    | -0.1264259     | Down       | 0.17675208 | 0.77062416 |
| miR-29b-3p | -0.1262268     | Down       | 0.44560284 | 0.88952595 |
| miR-548u   | -0.1254266     | Down       | 0.00389978 | 0.34045223 |
| miR-181c-3p| -0.1246399     | Down       | 0.38653847 | 0.86961208 |
| miR-130b-3p| -0.1231865     | Down       | 0.2852138  | 0.83298761 |
| miR-320d   | -0.123168      | Down       | 0.24893553 | 0.80715126 |
| miR-4788   | -0.1222474     | Down       | 0.0729118  | 0.68406327 |
| miR-484    | -0.1219113     | Down       | 0.12894549 | 0.74892227 |

(Continued)

Table 9 (Continued).
Table 9 (Continued).

| miRNAs          | Log2FoldChange | Regulation | P-value | P-adj  |
|-----------------|----------------|------------|---------|--------|
| miR-323a-3p     | -0.1208658     | Down       | 0.26817005 | 0.82860446 |
| miR-505-3p      | -0.1202214     | Down       | 0.3035112  | 0.83872374 |
| miR-4749-3p     | -0.1195975     | Down       | 0.15869565 | 0.75988515 |
| miR-15a-3p      | -0.1183105     | Down       | 0.03708407 | 0.59871978 |
| miR-320a        | -0.1182161     | Down       | 0.30403967 | 0.83872374 |
| miR-642b-5p     | -0.1180559     | Down       | 0.1856993  | 0.77677007 |
| miR-6071        | -0.1133686     | Down       | 0.00487931 | 0.3582046 |
| miR-17-5p       | -0.1130513     | Down       | 0.37019062 | 0.8625475 |
| miR-1307-3p     | -0.1127969     | Down       | 0.05488986 | 0.64056718 |
| miR-181a-3p     | -0.1127909     | Down       | 0.56807995 | 0.9303065 |
| miR-363-3p      | -0.1111045     | Down       | 0.60447515 | 0.94188142 |
| miR-6778-5p     | -0.1085699     | Down       | 0.1468648 | 0.75376261 |
| miR-6766-3p     | -0.1081158     | Down       | 0.11137142 | 0.74226488 |
| miR-370-3p      | -0.1079054     | Down       | 0.24840514 | 0.80715125 |
| miR-3912-5p     | -0.1077988     | Down       | 0.11473463 | 0.74226488 |
| miR-374a-5p     | -0.107496      | Down       | 0.38675744 | 0.86961208 |
| miR-548as-3p    | -0.1065386     | Down       | 0.00778767 | 0.40696367 |
| miR-627-5p      | -0.1061354     | Down       | 0.02263304 | 0.53734625 |
| miR-625-3p      | -0.1049602     | Down       | 0.16136836 | 0.76802692 |
| miR-766-3p      | -0.1048801     | Down       | 0.39499968 | 0.87310741 |
| miR-362-3p      | -0.1026706     | Down       | 0.45364747 | 0.89093879 |
| miR-487b-3p     | -0.1012303     | Down       | 0.74956338 | 0.97742837 |
| miR-95-3p       | -0.1007765     | Down       | 0.35316418 | 0.8588192 |
| miR-545-3p      | -0.1005441     | Down       | 0.06176618 | 0.65102084 |
| miR-423-3p      | -0.0987889     | Down       | 0.38194551 | 0.86612247 |
| miR-19b-3p      | -0.0986038     | Down       | 0.37474451 | 0.86499071 |
| miR-548aj-3p    | -0.098453      | Down       | 0.02308954 | 0.53734625 |
| miR-6724-5p     | -0.0973248     | Down       | 0.05694408 | 0.64812335 |
| miR-1299        | -0.097018      | Down       | 0.09632474 | 0.73085631 |
| miR-1306-5p     | -0.0968363     | Down       | 0.10062764 | 0.73085631 |
| miR-302a-3p     | -0.0965015     | Down       | 0.02612879 | 0.5595148 |
| miR-376b-3p     | -0.096174      | Down       | 0.33797387 | 0.85489649 |
| miR-3916        | -0.0958997     | Down       | 0.01268218 | 0.45268334 |
| miR-1287-5p     | -0.0954145     | Down       | 0.06349926 | 0.65539395 |
| miR-374b-5p     | -0.0947825     | Down       | 0.09792616 | 0.73085631 |
| miR-31-5p       | -0.0934179     | Down       | 0.81129553 | 0.99064883 |
| miR-4422        | -0.0933521     | Down       | 0.07548529 | 0.68726073 |
| miR-4682        | -0.0928982     | Down       | 0.12060406 | 0.74226488 |
| miR-3680-3p     | -0.0922184     | Down       | 0.00244716 | 0.34045223 |
| miR-191-5p      | -0.0910243     | Down       | 0.12444248 | 0.74454632 |
| miR-361-3p      | -0.090964      | Down       | 0.52487295 | 0.91825968 |
| miR-26b-5p      | -0.0908946     | Down       | 0.21108356 | 0.78263372 |
| miR-6727-5p     | -0.0908214     | Down       | 0.0219247  | 0.53734625 |
| miR-6888-3p     | -0.0908122     | Down       | 0.02132992 | 0.53734625 |
| miR-320b        | -0.0903495     | Down       | 0.4217382  | 0.8823614 |
| miR-106a-3p     | -0.0896953     | Down       | 0.0139619  | 0.46600109 |
| miR-4639-3p     | -0.0890044     | Down       | 0.02945662 | 0.5961058 |
| miR-548L        | -0.0889439     | Down       | 0.01327019 | 0.46067162 |
| miR-6856-3p     | -0.088886      | Down       | 0.01234784 | 0.44695703 |

(Continued)
| miRNAs       | Log2FoldChange | Regulation | P-value   | P-adj    |
|-------------|---------------|------------|-----------|----------|
| miR-3192-3p | -0.0887498    | Down       | 0.01718806 | 0.53220869 |
| miR-550a-3p | -0.088041     | Down       | 0.36796855 | 0.86195734 |
| miR-125b-1-3p | -0.0877112 | Down       | 0.24414246 | 0.80715125 |
| miR-4668-3p | -0.0875502    | Down       | 0.02816443 | 0.59258245 |
| miR-6082    | -0.0865329    | Down       | 0.15071067 | 0.75393664 |
| miR-574-3p  | -0.0854029    | Down       | 0.47265855 | 0.89396011 |
| miR-3606-5p | -0.0844866    | Down       | 0.02275562 | 0.53736252 |
| miR-148a-5p | -0.0830321    | Down       | 0.01814262 | 0.53736252 |
| miR-664a-3p | -0.0828903    | Down       | 0.55610772 | 0.9268462 |
| miR-6826-5p | -0.0828478    | Down       | 0.28421782 | 0.83193599 |
| miR-541-5p  | -0.0823983    | Down       | 0.03891282 | 0.59871978 |
| miR-6884-3p | -0.0821635    | Down       | 0.15347294 | 0.75393664 |
| miR-3124-5p | -0.082068     | Down       | 0.11585557 | 0.74226488 |
| miR-3616-3p | -0.0817705    | Down       | 0.09990518 | 0.73085631 |
| miR-618     | -0.0814829    | Down       | 0.01137468 | 0.43937422 |
| miR-629-5p  | -0.0814154    | Down       | 0.32853493 | 0.85486949 |
| miR-6784-5p | -0.0814167    | Down       | 0.03529383 | 0.59871978 |
| miR-425-5p  | -0.0813279    | Down       | 0.23355464 | 0.80019585 |
| miR-4261    | -0.0811265    | Down       | 0.16684807 | 0.76915081 |
| miR-4482-3p | -0.0811175    | Down       | 0.04757793 | 0.61412501 |
| miR-1291    | -0.0810705    | Down       | 0.14627622 | 0.75376261 |
| miR-3158-3p | -0.0800994    | Down       | 0.07766898 | 0.68910078 |
| miR-590-3p  | -0.0792172    | Down       | 0.03519026 | 0.59871978 |
| miR-26a-1-3p | -0.0791541 | Down       | 0.17249915 | 0.77062416 |
| miR-6813-5p | -0.0783623    | Down       | 0.02180293 | 0.53736252 |
| lex-7c-3p   | -0.0778908    | Down       | 0.11832515 | 0.74226488 |
| miR-150-5p  | -0.07768      | Down       | 0.49872051 | 0.91032268 |
| miR-5190    | -0.0774762    | Down       | 0.15597493 | 0.75633126 |
| miR-20b-5p  | -0.0772418    | Down       | 0.1460428  | 0.75376261 |
| miR-4270    | -0.0770622    | Down       | 0.38633037 | 0.86961208 |
| miR-31-3p   | -0.076925     | Down       | 0.2362799  | 0.80380192 |
| miR-5088-3p | -0.0768011    | Down       | 0.09382537 | 0.72555728 |
| miR-6511b-3p | -0.076708 | Down       | 0.02162468 | 0.53736252 |
| miR-196a-5p | -0.0765723    | Down       | 0.27610779 | 0.83108541 |
| miR-1249-3p | -0.0757546    | Down       | 0.2545288  | 0.81031406 |
| miR-9-5p    | -0.0751537    | Down       | 0.12932434 | 0.74892227 |
| miR-6516-5p | -0.0745078    | Down       | 0.06014748 | 0.64823335 |
| miR-4687-5p | -0.0740003    | Down       | 0.30258663 | 0.83873734 |
| miR-6731-5p | -0.0739289    | Down       | 0.03193883 | 0.59871978 |
| miR-141-5p  | -0.0733955    | Down       | 0.07957451 | 0.68910078 |
| miR-4780    | -0.073278     | Down       | 0.1286269  | 0.74892227 |
| miR-374b-3p | -0.0731784    | Down       | 0.06692731 | 0.65890175 |
| miR-369-5p  | -0.0731604    | Down       | 0.57647798 | 0.93390911 |
| lex-7d-3p   | -0.0728777    | Down       | 0.17184823 | 0.77062416 |
| miR-661     | -0.0728391    | Down       | 0.03624906 | 0.59871978 |
| miR-649     | -0.0727858    | Down       | 0.04419742 | 0.61412501 |
| miR-4298    | -0.0724915    | Down       | 0.47222756 | 0.89396011 |
| miR-4683    | -0.0724638    | Down       | 0.05467774 | 0.64056718 |
| miR-5692c   | -0.0723209    | Down       | 0.08824084 | 0.71090581 |

(Continued)
Table 9 (Continued).

| miRNAs      | Log2FoldChange | Regulation | P-value       | P-adj         |
|-------------|----------------|------------|---------------|---------------|
| miR-468     | -0.0717924     | Down       | 0.1290666     | 0.74892227    |
| miR-874-5p  | -0.0713546     | Down       | 0.03569465    | 0.59871978    |
| miR-654-3p  | -0.0712607     | Down       | 0.77258369    | 0.98440262    |
| miR-6772-5p | -0.0708382     | Down       | 0.14810668    | 0.75376261    |
| miR-361-5p  | -0.0707358     | Down       | 0.46871632    | 0.89396011    |
| miR-526b-3p | -0.0697051     | Down       | 0.03156651    | 0.59871978    |
| miR-7156-5p | -0.0690574     | Down       | 0.1545765     | 0.75376261    |
| miR-6886-3p | -0.0685914     | Down       | 0.30047948    | 0.83872374    |
| miR-361-5p  | -0.0681986     | Down       | 0.12854264    | 0.74892227    |
| miR-16-2-3p | -0.0677311     | Down       | 0.14111828    | 0.75376261    |
| miR-4680-3p | -0.0675655     | Down       | 0.21604469    | 0.75376261    |
| miR-6749-5p | -0.0673259     | Down       | 0.33082272    | 0.85489649    |
| miR-337-3p  | -0.06711       | Down       | 0.55060733    | 0.92349191    |
| miR-504-3p  | -0.0669662     | Down       | 0.05630095    | 0.64832335    |
| miR-758-3p  | -0.0665848     | Down       | 0.05297921    | 0.63842356    |
| miR-937-3p  | -0.0665441     | Down       | 0.08677757    | 0.70907074    |
| miR-548av-3p| -0.066494      | Down       | 0.45251254    | 0.89093879    |
| miR-5572    | -0.0661791     | Down       | 0.05630095    | 0.64823235    |
| miR-140-5p  | -0.0660041     | Down       | 0.43755338    | 0.89093879    |
| miR-1227-5p | -0.0658486     | Down       | 0.03691231    | 0.59871978    |
| miR-4776-5p | -0.0657861     | Down       | 0.03971689    | 0.59871978    |
| miR-15b-3p  | -0.0655982     | Down       | 0.10853319    | 0.74226488    |
| miR-6796-3p | -0.0655518     | Down       | 0.0747368     | 0.68910078    |
| miR-1233-5p | -0.0654842     | Down       | 0.15416195    | 0.75393664    |
| miR-922     | -0.0653003     | Down       | 0.08895039    | 0.7141286     |
| miR-5189-3p | -0.0649979     | Down       | 0.15558891    | 0.75588563    |
| miR-4267    | -0.0648969     | Down       | 0.03895436    | 0.59871978    |
| miR-7162-5p | -0.0647263     | Down       | 0.1095319     | 0.74226488    |
| miR-33a-3p  | -0.0642384     | Down       | 0.11657237    | 0.74226488    |
| miR-942-5p  | -0.0637306     | Down       | 0.06524443    | 0.65598378    |
| miR-134-5p  | -0.0637176     | Down       | 0.44938568    | 0.88964976    |
| miR-539-5p  | -0.0636818     | Down       | 0.46151992    | 0.89396011    |
| miR-28-3p   | -0.063576      | Down       | 0.19253465    | 0.77997491    |
| miR-6081    | -0.0634098     | Down       | 0.2394534     | 0.80380192    |
| miR-7854-3p | -0.0633369     | Down       | 0.08213352    | 0.69839839    |
| miR-624-5p  | -0.0632708     | Down       | 0.26163925    | 0.81989814    |
| miR-2115-3p | -0.0630218     | Down       | 0.07815829    | 0.68910078    |
| miR-4652-3p | -0.063004      | Down       | 0.24882332    | 0.80715125    |
| miR-489-5p  | -0.0629817     | Down       | 0.05217839    | 0.63253996    |
| miR-212-5p  | -0.062839      | Down       | 0.19944415    | 0.77997491    |
| miR-1273e   | -0.0621333     | Down       | 0.1009184     | 0.73085631    |
| miR-134-3p  | -0.0622349     | Down       | 0.17724741    | 0.77062416    |
| miR-6875-3p | -0.0617556     | Down       | 0.1375524     | 0.75376261    |

(Continued)
Table 9 (Continued).

| miRNAs          | Log2FoldChange | Regulation | P-value   | P-adj   |
|-----------------|---------------|------------|-----------|---------|
| miR-219a-5p     | -0.0616904    | Down       | 0.2533948 | 0.80998089 |
| miR-493-3p      | -0.0611597    | Down       | 0.09806579 | 0.73085631 |
| miR-6881-5p     | -0.0609269    | Down       | 0.09484994 | 0.72765477 |
| miR-125a-3p     | -0.0608378    | Down       | 0.21286419 | 0.78263372 |
| miR-4439        | -0.0605871    | Down       | 0.1233437  | 0.74454632 |
| miR-4730        | -0.0605398    | Down       | 0.06998566 | 0.67187824 |
| miR-383-3p      | -0.0604946    | Down       | 0.09662856 | 0.73085631 |
| miR-548ay-3p    | -0.060446     | Down       | 0.03093749 | 0.59781471 |
| miR-3180-3p     | -0.0601756    | Down       | 0.07181798 | 0.68344128 |
| miR-10b-3p      | -0.0598146    | Down       | 0.11849442 | 0.74226488 |
| miR-539-3p      | -0.05978      | Down       | 0.12258423 | 0.74454632 |
| let-7d-5p       | -0.0595976    | Down       | 0.2632232  | 0.82197281 |
| miR-181b-2-3p   | -0.0595467    | Down       | 0.05810103 | 0.64832335 |
| miR-5683        | -0.0595096    | Down       | 0.29822618 | 0.83872374 |
| miR-517c-3p     | -0.0591456    | Down       | 0.111974   | 0.74226488 |
| miR-1185-1-3p   | -0.0591174    | Down       | 0.73750148 | 0.97354829 |
| miR-432-3p      | -0.0589101    | Down       | 0.15090885 | 0.75391664 |
| miR-192-3p      | -0.0588899    | Down       | 0.20081511 | 0.77997491 |
| miR-301b-3p     | -0.0588816    | Down       | 0.41071015 | 0.8793356 |
| miR-550a-3-5p   | -0.0588116    | Down       | 0.30975262 | 0.84687685 |
| miR-590         | -0.0587267    | Down       | 0.09431345 | 0.72570526 |
| miR-4700-3p     | -0.0586154    | Down       | 0.16039599 | 0.76082142 |
| miR-26b-3p      | -0.058326     | Down       | 0.13777214 | 0.75376261 |
| miR-8087        | -0.0582875    | Down       | 0.11944341 | 0.74226488 |
| miR-138-2-3p    | -0.0580683    | Down       | 0.04430432 | 0.61412501 |
| miR-3163        | -0.05801      | Down       | 0.06534313 | 0.65598378 |
| miR-877-5p      | -0.0578883    | Down       | 0.02966172 | 0.59616058 |
| miR-3187-3p     | -0.0574442    | Down       | 0.06122058 | 0.6501524 |
| miR-6752-5p     | -0.0571494    | Down       | 0.23470494 | 0.80105138 |
| miR-6841-3p     | -0.0569437    | Down       | 0.25203953 | 0.80715125 |
| miR-1322        | -0.056926     | Down       | 0.2324719  | 0.79873366 |
| miR-668-3p      | -0.0565419    | Down       | 0.29465392 | 0.83872374 |
| miR-4668-5p     | -0.0563801    | Down       | 0.07717657 | 0.68910078 |
| miR-3615        | -0.0563464    | Down       | 0.17425676 | 0.77062416 |
| miR-409-3p      | -0.0559845    | Down       | 0.87164183 | 0.99898712 |
| miR-154-5p      | -0.0555697    | Down       | 0.75862106 | 0.98140055 |
| miR-5699-3p     | -0.0554852    | Down       | 0.17600494 | 0.77062416 |
| miR-632         | -0.0552967    | Down       | 0.07228476 | 0.68344128 |
| miR-7157-5p     | -0.0549047    | Down       | 0.07072583 | 0.67507774 |
| miR-4464        | -0.0548509    | Down       | 0.22364029 | 0.79102241 |
| miR-4446-3p     | -0.0545982    | Down       | 0.41195333 | 0.8793356 |
| miR-8083        | -0.0545119    | Down       | 0.20041269 | 0.77997491 |
| miR-30e-5p      | -0.0545001    | Down       | 0.60176327 | 0.93952361 |
| miR-595         | -0.0542951    | Down       | 0.07233309 | 0.68344128 |
| miR-6505-5p     | -0.0539884    | Down       | 0.09749892 | 0.73085631 |
| miR-4686        | -0.0539254    | Down       | 0.04492707 | 0.61412501 |
| miR-449b-5p     | -0.0538689    | Down       | 0.09933491 | 0.73085631 |
| miR-4693-5p     | -0.0538069    | Down       | 0.09863654 | 0.73085631 |
| miR-4297        | -0.0537088    | Down       | 0.14814504 | 0.75376261 |

(Continued)
| miRNAs      | Log2FoldChange | Regulation | P-value   | P-adj     |
|-------------|----------------|------------|-----------|-----------|
| miR-1237-3p | 0.053556       | Down       | 0.199575  | 0.0501719 |
| miR-6739-3p | -0.0534981     | Down       | 0.07988723| 0.050155  |
| miR-513a-3p | -0.0534758     | Down       | 0.37180756| 0.050099  |
| miR-3691-3p | -0.0526913     | Down       | 0.16679352| 0.0503661 |
| miR-6764-5p | -0.0526382     | Down       | 0.22074979| 0.0503648 |
| miR-1245b-5p| -0.052259      | Down       | 0.31143873| 0.0519039 |
| miR-5194    | -0.0519302     | Down       | 0.0527582 | 0.0512733 |
| miR-4520-2-3p| -0.0518119 | Down       | 0.27873305| 0.0517576 |
| miR-152-5p  | -0.0512067     | Down       | 0.20749798| 0.0511185 |
| miR-4446-5p | -0.051185      | Down       | 0.3283045 | 0.0511152 |
| miR-449c-5p | -0.0517126     | Down       | 0.08718535| 0.051703  |
| miR-4708-3p | -0.051703      | Down       | 0.18474022| 0.051404  |
| miR-4659b-3p| -0.0506055     | Down       | 0.1481356 | 0.0505099 |
| miR-7706    | -0.0513624     | Down       | 0.03554956| 0.0503778 |
| miR-6837-3p | -0.051295      | Down       | 0.07988723| 0.0503661 |
| miR-6757-5p | -0.0512733     | Down       | 0.37180756| 0.0503648 |
| miR-4798-5p | -0.0512673     | Down       | 0.16679352| 0.0503648 |
| miR-6832-3p | -0.051185      | Down       | 0.20749798| 0.0503648 |
| miR-30c-5p  | -0.0511152     | Down       | 0.15251966| 0.051155  |
| miR-1266-3p | -0.0506055     | Down       | 0.1481356 | 0.0505099 |
| miR-1262    | -0.0505009     | Down       | 0.23316458| 0.0503778 |
| miR-885-5p  | -0.0503661     | Down       | 0.29076307| 0.0503778 |
| miR-3529-3p | -0.0503661     | Down       | 0.24372971| 0.0503661 |
| miR-2052    | -0.0503661     | Down       | 0.24372971| 0.0503661 |
| miR-4743-5p | -0.0503648     | Down       | 0.35389778| 0.0503778 |
| miR-125b-2-3p| -0.0502628 | Down       | 0.1992263 | 0.0503661 |
| miR-4275    | -0.0501719     | Down       | 0.23383155| 0.0503661 |
| miR-3166    | -0.050155      | Down       | 0.11485278| 0.0503661 |
| miR-4492    | -0.0499947     | Down       | 0.23805179| 0.0503661 |
| miR-6864-5p | -0.0499078     | Down       | 0.12101513| 0.0503661 |
| miR-384     | -0.049905      | Down       | 0.19524287| 0.0503661 |
| miR-6885-3p | -0.0495386     | Down       | 0.2725345 | 0.0503661 |
| miR-4665-5p | -0.0494764     | Down       | 0.1985748 | 0.0503661 |
| miR-6865-5p | -0.0494428     | Down       | 0.20017313| 0.0503661 |
| miR-3977    | -0.0491608     | Down       | 0.217245 | 0.0503661 |
| miR-6873-3p | -0.0490828     | Down       | 0.4649756 | 0.0503661 |
| miR-3136-5p | -0.0490032     | Down       | 0.1782882 | 0.0503661 |
| miR-550b-3p | -0.0489291     | Down       | 0.21365444| 0.0503661 |
| miR-1197    | -0.0487257     | Down       | 0.25155855| 0.0503661 |
| miR-4487    | -0.048424      | Down       | 0.16645497| 0.0503661 |
| miR-769-3p  | -0.0484013     | Down       | 0.31433383| 0.0503661 |
| miR-4519    | -0.0483057     | Down       | 0.07649724| 0.0503661 |
| miR-647     | -0.0482847     | Down       | 0.35163792| 0.0503661 |
| miR-6728-5p | -0.0481616     | Down       | 0.39964052| 0.0503661 |
| miR-2114-5p | -0.0480611     | Down       | 0.10413781| 0.0503661 |
| miR-488-3p  | -0.0479121     | Down       | 0.22846615| 0.0503661 |
| miR-4633-5p | -0.0477808     | Down       | 0.14610901| 0.0503661 |
| miR-6794-3p | -0.0476669     | Down       | 0.28649085| 0.0503661 |
| miR-4522    | -0.0476432     | Down       | 0.23913101| 0.0503661 |

(Continued)
Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value | P-adj   |
|------------|----------------|------------|---------|---------|
| miR-95-5p  | -0.0471746     | Down       | 0.28640069 | 0.83289761 |
| miR-6510-5p| -0.0471527     | Down       | 0.22252947 | 0.79102241 |
| miR-6738-5p| -0.0466691     | Down       | 0.292255   | 0.83872374 |
| miR-887-5p | -0.0465034     | Down       | 0.20770552 | 0.78263372 |
| miR-521    | -0.046491      | Down       | 0.14795142 | 0.75376261 |
| miR-3161   | -0.0464806     | Down       | 0.22632853 | 0.79102241 |
| miR-4754   | -0.0463985     | Down       | 0.19022343 | 0.77997491 |
| miR-3680-5p| -0.0463564     | Down       | 0.08453247 | 0.70096725 |
| miR-503-3p | -0.0463332     | Down       | 0.18006004 | 0.77062416 |
| miR-3074-5p| -0.0463157     | Down       | 0.05369175 | 0.63883244 |
| miR-1254   | -0.046131      | Down       | 0.09134723 | 0.72012996 |
| miR-578    | -0.0461182     | Down       | 0.23681458 | 0.80380192 |
| miR-3667-3p| -0.0459469     | Down       | 0.20349294 | 0.77997491 |
| miR-1273h-5p| -0.0459311   | Down       | 0.17028256 | 0.77062416 |
| miR-1224-3p| -0.0457998     | Down       | 0.14643085 | 0.75376261 |
| miR-6793-5p| -0.0457419     | Down       | 0.25446121 | 0.81034106 |
| miR-6770-5p| -0.045575      | Down       | 0.11368816 | 0.74226488 |
| miR-423-5p | -0.0455524     | Down       | 0.63293665 | 0.95096807 |
| miR-99a-3p | -0.0455344     | Down       | 0.17224632 | 0.77062416 |
| miR-205-3p | -0.0453114     | Down       | 0.10376792 | 0.74226488 |
| miR-581    | -0.0451704     | Down       | 0.20455373 | 0.77997491 |
| miR-1269a  | -0.0451647     | Down       | 0.16385234 | 0.76892691 |
| miR-5690   | -0.0451396     | Down       | 0.45378945 | 0.89093879 |
| miR-6830-5p| -0.0450438     | Down       | 0.16855393 | 0.77062416 |
| miR-6758-3p| -0.044947      | Down       | 0.30113939 | 0.83872374 |
| miR-3133   | -0.044896      | Down       | 0.24881996 | 0.80715125 |
| miR-1468-5p| -0.0447274     | Down       | 0.35320208 | 0.8588192 |
| miR-675-5p | -0.0446309     | Down       | 0.07567891 | 0.68726073 |
| miR-6808-3p| -0.0446026     | Down       | 0.17878595 | 0.77062416 |
| miR-558    | -0.0445564     | Down       | 0.20364686 | 0.77997491 |
| miR-4282   | -0.0445282     | Down       | 0.30245771 | 0.83872374 |
| miR-584-3p | -0.0444941     | Down       | 0.1360289 | 0.75376261 |
| miR-577    | -0.0442789     | Down       | 0.22696156 | 0.79102241 |
| miR-802    | -0.044274      | Down       | 0.32802998 | 0.85489649 |
| miR-1303   | -0.0440308     | Down       | 0.06970506 | 0.67187824 |
| miR-891b   | -0.0439852     | Down       | 0.14633769 | 0.75376261 |
| miR-4483   | -0.0438818     | Down       | 0.17627144 | 0.77062416 |
| miR-302b-5p| -0.0438292     | Down       | 0.19508308 | 0.77997491 |
| miR-1343-5p| -0.0436694     | Down       | 0.20551786 | 0.78047751 |
| miR-4742-5p| -0.0432328     | Down       | 0.28713222 | 0.83813898 |
| miR-6785-3p| -0.043203      | Down       | 0.3395073  | 0.9213181 |
| miR-5000-5p| -0.0430893     | Down       | 0.16801664 | 0.77062416 |
| miR-222-5p | -0.0429509     | Down       | 0.18788251 | 0.77997491 |
| miR-1178-5p| -0.0428242     | Down       | 0.29950566 | 0.83872374 |
| miR-548k   | -0.042777      | Down       | 0.11181738 | 0.74226488 |
| miR-486-3p | -0.042765      | Down       | 0.35734147 | 0.8588192 |
| miR-516a-5p| -0.0425529     | Down       | 0.42420656 | 0.8823614 |
| miR-487b-5p| -0.0424956     | Down       | 0.27527601 | 0.83108541 |
| miR-4470   | -0.0424497     | Down       | 0.18738773 | 0.77997491 |
Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value       | P-adj        |
|------------|----------------|------------|---------------|--------------|
| miR-3197   | -0.0424123     | Down       | 0.40575495    | 0.87475982   |
| miR-223-5p | -0.0423677     | Down       | 0.77529043    | 0.985258     |
| miR-593-3p | -0.0432111     | Down       | 0.18015658    | 0.77062416   |
| miR-651-5p | -0.0422148     | Down       | 0.33409291    | 0.85489649   |
| miR-6854-3p| -0.0421954     | Down       | 0.37715408    | 0.86499071   |
| miR-4419b  | -0.04196       | Down       | 0.22498221    | 0.79102241   |
| miR-4728-3p| -0.0419086     | Down       | 0.11897989    | 0.74226488   |
| miR-4268   | -0.0419035     | Down       | 0.13293728    | 0.74892227   |
| miR-518c-3p| -0.0418151     | Down       | 0.29336201    | 0.83872374   |
| miR-4712-3p| -0.0416429     | Down       | 0.22564071    | 0.79102241   |
| miR-4711-5p| -0.0416366     | Down       | 0.19518099    | 0.77997491   |
| miR-3692-3p| -0.0416267     | Down       | 0.1156964     | 0.74226488   |
| miR-4280   | -0.0416189     | Down       | 0.25672311    | 0.81105473   |
| miR-4314   | -0.0414178     | Down       | 0.15047172    | 0.75393664   |
| miR-6732-5p| -0.0413921     | Down       | 0.32329392    | 0.85489649   |
| miR-7106-3p| -0.0413412     | Down       | 0.25137777    | 0.80715125   |
| miR-5591-3p| -0.04123      | Down       | 0.29949998    | 0.83872374   |
| miR-7705   | -0.041217      | Down       | 0.0634476     | 0.65533995   |
| miR-6855-3p| -0.0410619     | Down       | 0.45728436    | 0.89244441   |
| miR-568    | -0.0408745     | Down       | 0.33324655    | 0.85489649   |
| miR-1343-3p| -0.0408367     | Down       | 0.24415703    | 0.80715125   |
| miR-4781-5p| -0.0407069     | Down       | 0.13214069    | 0.74892227   |
| miR-491-3p | -0.0406668     | Down       | 0.22868858    | 0.79102241   |
| miR-4707-5p| -0.0405516     | Down       | 0.22322314    | 0.79102241   |
| miR-3129-5p| -0.0401239     | Down       | 0.25161482    | 0.80715125   |
| miR-6086   | -0.0401014     | Down       | 0.4948927     | 0.90848159   |
| miR-203a-3p| -0.0400958     | Down       | 0.34293226    | 0.8578521    |
| NC2_00122731| -0.0399138    | Down       | 0.19213775    | 0.77997491   |
| miR-3065-3p| -0.0399098     | Down       | 0.22485811    | 0.79102241   |
| miR-5585-5p| -0.0399008     | Down       | 0.3792633     | 0.86499071   |
| miR-576-5p | -0.0397585     | Down       | 0.35921288    | 0.8588192    |
| miR-374c-3p| -0.0395254     | Down       | 0.35134596    | 0.8588192    |
| miR-5009-3p| -0.0391632     | Down       | 0.31867916    | 0.84959071   |
| miR-4303   | -0.0390723     | Down       | 0.0998174     | 0.73085631   |
| miR-4662a-5p| -0.0390549   | Down       | 0.48355794    | 0.90449982   |
| miR-6868-3p| -0.0390428     | Down       | 0.11010451    | 0.74226488   |
| miR-4525   | -0.0389599     | Down       | 0.21635149    | 0.7853205    |
| miR-1269b  | -0.0389451     | Down       | 0.31640306    | 0.84917098   |
| miR-329-3p | -0.038917      | Down       | 0.71268513    | 0.96505269   |
| miR-6500-3p| -0.0388368     | Down       | 0.21551632    | 0.7853205    |
| miR-3177-3p| -0.0387482     | Down       | 0.23821507    | 0.80380192   |
| miR-142-3p | -0.0387095     | Down       | 0.80992531    | 0.99064883   |
| miR-212-3p | -0.0386542     | Down       | 0.4975312     | 0.91032268   |
| miR-623    | -0.0385079     | Down       | 0.19978928    | 0.77997491   |
| miR-518e-3p| -0.038422      | Down       | 0.3563435     | 0.8588192    |
| miR-3658   | -0.0384105     | Down       | 0.27866195    | 0.83108541   |
| miR-6744-3p| -0.0384055     | Down       | 0.20071422    | 0.77997491   |
| miR-6755-3p| -0.0382967     | Down       | 0.19995738    | 0.77997491   |
| miR-4423-3p| -0.03821       | Down       | 0.3154744     | 0.84917098   |

(Continued)
### Table 9 (Continued)

| miRNAs          | Log2FoldChange | Regulation | P-value    | P-adj     |
|-----------------|----------------|------------|------------|-----------|
| miR-4445-3p     | -0.0381457     | Down       | 0.38961402 | 0.87281803|
| miR-5582-5p     | -0.0380637     | Down       | 0.12812294 | 0.74892227|
| miR-3917        | -0.037903      | Down       | 0.26173436 | 0.81989814|
| miR-873-5p      | -0.0377577     | Down       | 0.41493701 | 0.8804535 |
| miR-4801        | -0.0377502     | Down       | 0.34630214 | 0.8588192 |
| miR-548e-3p     | -0.0376306     | Down       | 0.33820611 | 0.85489649|
| miR-1285-3p     | -0.0374564     | Down       | 0.19647604 | 0.77997491|
| miR-4790-3p     | -0.03735       | Down       | 0.20157842 | 0.77997491|
| miR-6831-3p     | -0.0372781     | Down       | 0.58185088 | 0.93436563|
| miR-508-3p      | -0.037225      | Down       | 0.23101382 | 0.79502561|
| miR-204-3p      | -0.0371964     | Down       | 0.45469283 | 0.891297  |
| miR-8079        | -0.037174      | Down       | 0.21082788 | 0.78263372|
| miR-6726-3p     | -0.0370802     | Down       | 0.27602556 | 0.83108541|
| miR-3938        | -0.0369838     | Down       | 0.15952768 | 0.76064219|
| miR-3152-3p     | -0.0368768     | Down       | 0.21985777 | 0.78841048|
| miR-541-3p      | -0.0368742     | Down       | 0.25219531 | 0.80715125|
| miR-21-5p       | -0.0368457     | Down       | 0.89595162 | 0.96987912|
| miR-4257        | -0.0367867     | Down       | 0.53676574 | 0.9213181 |
| miR-3173-5p     | -0.036755      | Down       | 0.43432459 | 0.88898739|
| miR-6866-3p     | -0.0365902     | Down       | 0.260655   | 0.818928  |
| miR-1301-5p     | -0.0365849     | Down       | 0.39157163 | 0.87281803|
| miR-608         | -0.0364538     | Down       | 0.20435884 | 0.77997491|
| miR-3923        | -0.0363088     | Down       | 0.43136219 | 0.88759074|
| miR-5193        | -0.0362094     | Down       | 0.33412701 | 0.85489649|
| miR-509-5p      | -0.0361572     | Down       | 0.31399227 | 0.84972893|
| miR-4509        | -0.0360699     | Down       | 0.22833098 | 0.79102241|
| miR-1289        | -0.0360075     | Down       | 0.30327032 | 0.83872374|
| miR-6503-5p     | -0.0359935     | Down       | 0.50191361 | 0.9147569 |
| miR-1066-5p     | -0.0359461     | Down       | 0.61507233 | 0.94689808|
| let-7a-3p       | -0.0357979     | Down       | 0.56296401 | 0.92970327|
| miR-5181-5p     | -0.0357722     | Down       | 0.33145655 | 0.85489649|
| miR-4718        | -0.0357336     | Down       | 0.43521457 | 0.88945554|
| miR-2682-5p     | -0.0357322     | Down       | 0.15095123 | 0.75399664|
| miR-766-5p      | -0.0357183     | Down       | 0.31585755 | 0.84917098|
| NegativeControl | -0.035584      | Down       | 0.13903884 | 0.75376261|
| miR-5587-3p     | -0.0355696     | Down       | 0.1775629  | 0.77062416|
| miR-27b-5p      | -0.0355676     | Down       | 0.39363988 | 0.87310741|
| miR-500b-3p     | -0.0355306     | Down       | 0.36318667 | 0.8588192 |
| miR-4735-5p     | -0.0355125     | Down       | 0.4156067  | 0.8804535 |
| miR-6716-5p     | -0.0354956     | Down       | 0.19348116 | 0.77997491|
| miR-676-5p      | -0.0354686     | Down       | 0.44701629 | 0.88952595|
| miR-7111-3p     | -0.0353822     | Down       | 0.52941856 | 0.92119547|
| miR-422a        | -0.0352602     | Down       | 0.43842522 | 0.88952595|
| miR-4722-3p     | -0.0349901     | Down       | 0.36975335 | 0.86231045|
| miR-7106-5p     | -0.0349495     | Down       | 0.48820261 | 0.90656383|
| miR-299-5p      | -0.0348796     | Down       | 0.79516654 | 0.98759926|
| miR-6733-3p     | -0.0348434     | Down       | 0.43778503 | 0.88952595|
| miR-4322        | -0.0347927     | Down       | 0.19871571 | 0.77997491|
| miR-8062        | -0.0346104     | Down       | 0.24081785 | 0.80586181|

(Continued)
### Table 9 (Continued).

| miRNAs         | Log2FoldChange | Regulation | P-value    | P-adj     |
|----------------|----------------|------------|------------|-----------|
| miR-6853-3p    | -0.0346078     | Down       | 0.25116815 | 0.80715125|
| miR-4757-5p    | -0.035925      | Down       | 0.20637386 | 0.78227259|
| miR-3144-3p    | -0.035136      | Down       | 0.37885574 | 0.86499071|
| miR-4799-3p    | -0.0343495     | Down       | 0.32812539 | 0.85489649|
| miR-412-3p     | -0.0343588     | Down       | 0.31780759 | 0.84917098|
| miR-4703-5p    | -0.0341043     | Down       | 0.42700851 | 0.88287358|
| miR-4632-5p    | -0.0340734     | Down       | 0.2568866  | 0.81105473|
| miR-5689       | -0.0336971     | Down       | 0.33937179 | 0.85489649|
| miR-4708-5p    | -0.0334763     | Down       | 0.19560352 | 0.77997491|
| miR-6741-5p    | -0.0334723     | Down       | 0.38032665 | 0.86499071|
| miR-4278       | -0.0334465     | Down       | 0.24981153 | 0.80711525|
| miR-4636       | -0.0333881     | Down       | 0.20375987 | 0.77997491|
| miR-200a-5p    | -0.0332625     | Down       | 0.3457056  | 0.8586192 |
| miR-513c-3p    | -0.0332121     | Down       | 0.44118445 | 0.88952595|
| miR-5008-3p    | -0.0331369     | Down       | 0.29943133 | 0.83723734|
| miR-4666a-5p   | -0.0331367     | Down       | 0.41658812 | 0.8804535 |
| miR-20a-5p     | -0.033089      | Down       | 0.47247238 | 0.89396011|
| miR-3175       | -0.033046      | Down       | 0.37087896 | 0.86336859|
| miR-1324       | -0.0329818     | Down       | 0.3102379  | 0.84730085|
| miR-129-2-3p   | -0.0328575     | Down       | 0.62385115 | 0.94925841|
| miR-18b-3p     | -0.032854      | Down       | 0.54621221 | 0.92261663|
| miR-106b-3p    | -0.0328101     | Down       | 0.4171275  | 0.88086907|
| miR-921        | -0.0327982     | Down       | 0.33915794 | 0.85489649|
| miR-609        | -0.032727      | Down       | 0.33862579 | 0.9213181 |
| miR-1911-3p    | -0.0326997     | Down       | 0.46298065 | 0.89396011|
| miR-637        | -0.0326982     | Down       | 0.44135535 | 0.88952595|
| miR-4301       | -0.0326704     | Down       | 0.33862313 | 0.85489649|
| miR-19b-1-5p   | -0.0326675     | Down       | 0.43172229 | 0.88762102|
| miR-6511b-5p   | -0.0324825     | Down       | 0.2042628  | 0.77997491|
| miR-613        | -0.0322523     | Down       | 0.48209927 | 0.9030564 |
| miR-208a-5p    | -0.0322639     | Down       | 0.41564505 | 0.8804535 |
| miR-6892-3p    | -0.0322175     | Down       | 0.65570287 | 0.95321673|
| miR-5010-3p    | -0.0321995     | Down       | 0.49798778 | 0.91028268|
| miR-4737       | -0.0321658     | Down       | 0.14010987 | 0.75376261|
| miR-548a-3p    | -0.0321257     | Down       | 0.53056959 | 0.9213181 |
| miR-4259       | -0.0320631     | Down       | 0.35247129 | 0.8588192 |
| miR-4666b      | -0.0319996     | Down       | 0.31607306 | 0.84917098|
| miR-4747-3p    | -0.0319254     | Down       | 0.41641835 | 0.8804353 |
| miR-6877-5p    | -0.0319219     | Down       | 0.37987848 | 0.86499071|
| miR-548at-3p   | -0.0318171     | Down       | 0.35020919 | 0.8588192 |
| miR-6781-5p    | -0.0317665     | Down       | 0.33930583 | 0.85489649|
| miR-3686       | -0.0317569     | Down       | 0.22396794 | 0.79102241|
| miR-6842-5p    | -0.0317101     | Down       | 0.36890788 | 0.86195374|
| miR-6803-3p    | -0.0314802     | Down       | 0.40146977 | 0.87364718|
| miR-190a-5p    | -0.0314616     | Down       | 0.63180181 | 0.95096807|
| miR-450b-5p    | -0.0314507     | Down       | 0.42557178 | 0.8823614 |
| miR-24-3p      | -0.0314197     | Down       | 0.75498569 | 0.98140055|
| miR-181d-3p    | -0.031391      | Down       | 0.27560752 | 0.83108541|
| miR-4771       | -0.0313002     | Down       | 0.35849906 | 0.8588192 |
| miRNAs  | Log2FoldChange | Regulation | P-value  | P-adj   |
|---------|----------------|------------|----------|---------|
| miR-25-5p | -0.0312979     | Down       | 0.44199334 | 0.88952595 |
| miR-218-5p  | -0.0312859   | Down       | 0.33000051  | 0.85489649  |
| miR-3661    | -0.0312469    | Down       | 0.15243214   | 0.75396664   |
| miR-520b    | -0.0312442    | Down       | 0.44366687   | 0.88952595   |
| miR-889-3p  | -0.0312205    | Down       | 0.64082871   | 0.95096807   |
| miR-1912    | -0.0310354    | Down       | 0.28102885   | 0.83108541   |
| miR-6512-5p | -0.0309975    | Down       | 0.48851369   | 0.90656383   |
| miR-4709-5p | -0.0307474    | Down       | 0.33313348   | 0.85489649   |
| miR-520h    | -0.0306452    | Down       | 0.44723114   | 0.88952595   |
| miR-6797-5p | -0.0306123    | Down       | 0.35491367   | 0.8588192    |
| miR-122-3p  | -0.0306052    | Down       | 0.64051333   | 0.95096807   |
| miR-4328    | -0.0306045    | Down       | 0.30282113   | 0.83872374   |
| miR-548ac   | -0.0304654    | Down       | 0.36242627   | 0.8588192    |
| miR-6077    | -0.0304061    | Down       | 0.33304636   | 0.85489649   |
| miR-6853-5p | -0.0303791    | Down       | 0.3260448    | 0.85489649   |
| miR-129-1-3p | -0.0303223   | Down       | 0.60193873   | 0.93532611   |
| miR-4540    | -0.030299     | Down       | 0.20100239   | 0.77997491   |
| miR-519b-3p | -0.0301566    | Down       | 0.38005484   | 0.86499071   |
| miR-643     | -0.0301015    | Down       | 0.44674239   | 0.88952595   |
| miR-508-5p  | -0.0299621    | Down       | 0.39987343   | 0.87364718   |
| miR-3183    | -0.0299339    | Down       | 0.26463599   | 0.82438552   |
| miR-6863    | -0.0298423    | Down       | 0.25624451   | 0.81102287   |
| miR-5093    | -0.0297343    | Down       | 0.3211177    | 0.85167439   |
| miR-3117-5p | -0.0296979    | Down       | 0.37351236   | 0.86499071   |
| miR-1915-5p | -0.0295722    | Down       | 0.38614591   | 0.86961208   |
| miR-4671-5p | -0.0293784    | Down       | 0.48029366   | 0.90296614   |
| miR-7112-3p | -0.0293444    | Down       | 0.40692661   | 0.87475982   |
| miR-6842-3p | -0.0292299    | Down       | 0.37489059   | 0.86499071   |
| miR-7848-3p | -0.0291606    | Down       | 0.47173691   | 0.89396011   |
| miR-3925-3p | -0.0291496    | Down       | 0.44297755   | 0.88952595   |
| miR-6075    | -0.0290637    | Down       | 0.34793883   | 0.8588192    |
| miR-611     | -0.0290556    | Down       | 0.40338581   | 0.87475982   |
| miR-3688-3p | -0.029053     | Down       | 0.33899315   | 0.85489649   |
| miR-7151-3p | -0.0288311    | Down       | 0.29471257   | 0.83872374   |
| miR-6721-5p | -0.0286954    | Down       | 0.33671486   | 0.85489649   |
| miR-499a-3p | -0.0286779    | Down       | 0.3975788    | 0.87364718   |
| miR-4330    | -0.0285087    | Down       | 0.30886419   | 0.84601313   |
| miR-133a-5p | -0.0284487    | Down       | 0.24051057   | 0.80586181   |
| miR-2110    | -0.0283739    | Down       | 0.33449566   | 0.85489649   |
| miR-6776-5p | -0.0283318    | Down       | 0.39853903   | 0.87364718   |
| miR-93-5p   | -0.028325     | Down       | 0.77082806   | 0.98290443   |
| miR-4305    | -0.0282488    | Down       | 0.45028902   | 0.88964976   |
| miR-411-3p  | -0.0282225    | Down       | 0.61100763   | 0.94386479   |
| miR-3189-5p | -0.0281667    | Down       | 0.21137683   | 0.78263372   |
| miR-6773-3p | -0.028141     | Down       | 0.50601389   | 0.912181     |
| miR-6762-5p | -0.0280596    | Down       | 0.32984973   | 0.85489649   |
| miR-549a    | -0.028046     | Down       | 0.54673169   | 0.92261663   |
| miR-3150a-5p | -0.0280455   | Down       | 0.32033013   | 0.85046325   |
| miR-650     | -0.0279112    | Down       | 0.27951311   | 0.83108541   |
Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value | P-adj    |
|--------------|----------------|------------|---------|----------|
| miR-4731-5p  | -0.0277768     | Down       | 0.36275575 | 0.8588192 |
| miR-4436a    | -0.0276167     | Down       | 0.34953371 | 0.8588192 |
| miR-639      | -0.0275526     | Down       | 0.36815025 | 0.86195734 |
| miR-548av-5p | -0.0275382     | Down       | 0.33395129 | 0.85489649 |
| miR-3913-5p  | -0.0274806     | Down       | 0.42347246 | 0.8823614 |
| miR-4662b    | -0.0274059     | Down       | 0.55883847 | 0.92752078 |
| miR-4511     | -0.027387      | Down       | 0.67203992 | 0.95648223 |
| miR-4650-5p  | -0.0272772     | Down       | 0.49200610 | 0.90695643 |
| miR-4726-3p  | -0.0270911     | Down       | 0.45237699 | 0.89093879 |
| miR-2277-3p  | -0.0270691     | Down       | 0.55095919 | 0.92349191 |
| miR-3201     | -0.0270669     | Down       | 0.21411414 | 0.78498335 |
| miR-612      | -0.0269448     | Down       | 0.42969464 | 0.8669482 |
| miR-621      | -0.0269064     | Down       | 0.51622064 | 0.91376348 |
| miR-4503     | -0.0268456     | Down       | 0.41567275 | 0.8804535 |
| miR-19a-5p   | -0.0268393     | Down       | 0.42780704 | 0.88394447 |
| miR-3939     | -0.0267855     | Down       | 0.56371885 | 0.92988283 |
| miR-6834-3p  | -0.0267572     | Down       | 0.54053286 | 0.9213181 |
| miR-3160-3p  | -0.0267371     | Down       | 0.39258692 | 0.87281803 |
| miR-548j-3p  | -0.026724      | Down       | 0.36033208 | 0.8588192 |
| miR-4264     | -0.0267094     | Down       | 0.46939468 | 0.89396011 |
| miR-2115-5p  | -0.0266976     | Down       | 0.50624103 | 0.912181 |
| miR-6782-3p  | -0.0266664     | Down       | 0.6122267  | 0.94386479 |
| miR-4707-3p  | -0.0266129     | Down       | 0.51175645 | 0.91376348 |
| miR-659-5p   | -0.0266029     | Down       | 0.56371885 | 0.92988283 |
| miR-1273c    | -0.0265915     | Down       | 0.56324824 | 0.92970327 |
| miR-4778-3p  | -0.026464      | Down       | 0.54053286 | 0.9213181 |
| miR-548a-5p  | -0.0263646     | Down       | 0.39074351 | 0.87281803 |
| miR-8076     | -0.0263375     | Down       | 0.21570366 | 0.7853205 |
| miR-6774-3p  | -0.0262921     | Down       | 0.6184354  | 0.94829596 |
| miR-187-3p   | -0.0262687     | Down       | 0.6122267  | 0.94386479 |
| miR-6780-3p  | -0.0262058     | Down       | 0.5359073  | 0.92384946 |
| miR-4654     | -0.0262048     | Down       | 0.40631365 | 0.87475982 |
| miR-4479     | -0.0261019     | Down       | 0.40303872 | 0.87475982 |
| miR-548av-5p | -0.0260327     | Down       | 0.3619964  | 0.8588192 |
| miR-1229-3p  | -0.0259448     | Down       | 0.62982461 | 0.95065239 |
| miR-4999-3p  | -0.0259058     | Down       | 0.51235821 | 0.91376348 |
| miR-6794-5p  | -0.0258639     | Down       | 0.64968367 | 0.95321673 |
| miR-518x-3p  | -0.0258487     | Down       | 0.46803021 | 0.89396011 |
| miR-185-3p   | -0.0257747     | Down       | 0.58499315 | 0.93513803 |
| miR-4667-3p  | -0.0257646     | Down       | 0.38641099 | 0.86961208 |
| NCI_00000197 | -0.0257608     | Down       | 0.53660801 | 0.9213181 |
| miR-200b-5p  | -0.0257468     | Down       | 0.28862915 | 0.8349474 |
| miR-518c-5p  | -0.0257151     | Down       | 0.37392524 | 0.86499071 |
| miR-1911-5p  | -0.0257045     | Down       | 0.47268981 | 0.89396011 |
| miR-3613-5p  | -0.0256137     | Down       | 0.5213217  | 0.91732227 |
| miR-548y     | -0.0255985     | Down       | 0.36507913 | 0.8588192 |
| miR-6755-5p  | -0.0255671     | Down       | 0.39163753 | 0.87281803 |
| miR-548as-5p | -0.0254177     | Down       | 0.34432168 | 0.8588192 |
Table 9 (Continued).

| miRNAs                  | Log2FoldChange | Regulation | P-value    | P-adj     |
|-------------------------|----------------|------------|------------|-----------|
| miR-4668                | −0.0253343     | Down       | 0.50380212 | 0.91147569 |
| miR-4664-5p             | −0.0252439     | Down       | 0.52252164 | 0.91732227 |
| miR-3129-3p             | −0.0252211     | Down       | 0.48803069 | 0.90656383 |
| miR-5484-5p             | −0.0251434     | Down       | 0.52928404 | 0.92119547 |
| miR-6770-3p             | −0.0249958     | Down       | 0.4626474  | 0.89396011 |
| miR-1-5p                | −0.024974      | Down       | 0.54095921 | 0.9213181 |
| miR-6807-3p             | −0.0249379     | Down       | 0.4241687  | 0.8823614 |
| miR-7160-3p             | −0.0249049     | Down       | 0.36478516 | 0.8598192 |
| miR-934                 | −0.0248951     | Down       | 0.36815835 | 0.86195734 |
| miR-7112-3p             | −0.0248867     | Down       | 0.52393019 | 0.9213181 |
| miR-8078                | −0.0247883     | Down       | 0.36500255 | 0.8823614 |
| miR-214-5p              | −0.0247315     | Down       | 0.31406257 | 0.84917098 |
| miR-6814-5p             | −0.0247263     | Down       | 0.46866242 | 0.90650744 |
| miR-2681-3p             | −0.0245218     | Down       | 0.35525362 | 0.8588192 |
| miR-4256                | −0.0245094     | Down       | 0.36413714 | 0.8588192 |
| miR-3619-5p             | −0.0242098     | Down       | 0.57697008 | 0.93390911 |
| miR-6727-3p             | −0.0241848     | Down       | 0.46978366 | 0.89396011 |
| miR-5581-3p             | −0.024105      | Down       | 0.43590749 | 0.88941554 |
| miR-6821-3p             | −0.0240699     | Down       | 0.53920376 | 0.9213181 |
| miR-5191                | −0.0240566     | Down       | 0.34090188 | 0.8551692 |
| miR-6728-3p             | −0.0240234     | Down       | 0.61912168 | 0.94928596 |
| NC200092197             | −0.0239201     | Down       | 0.26857562 | 0.82861865 |
| miR-1286                | −0.0238976     | Down       | 0.42361731 | 0.8823614 |
| miR-5486-5p             | −0.0238883     | Down       | 0.48489172 | 0.90449982 |
| miR-219a-1-3p           | −0.0237329     | Down       | 0.56052984 | 0.92760899 |
| miR-641                 | −0.0237023     | Down       | 0.67361652 | 0.95648223 |
| miR-145-5p              | −0.0236869     | Down       | 0.9434724  | 0.9988712 |
| miR-6744-5p             | −0.0236591     | Down       | 0.54866022 | 0.92261663 |
| miR-4649-5p             | −0.0236051     | Down       | 0.61179602 | 0.94368479 |
| miR-3171                | −0.0235034     | Down       | 0.67350194 | 0.95648223 |
| miR-149-3p              | −0.023432      | Down       | 0.39448524 | 0.87310741 |
| miR-45246-5p            | −0.0234286     | Down       | 0.42410749 | 0.8823614 |
| miR-1265                | −0.0233405     | Down       | 0.49287871 | 0.90695643 |
| miR-7152-3p             | −0.0233004     | Down       | 0.57739485 | 0.93390911 |
| miR-4720-3p             | −0.0233017     | Down       | 0.37809124 | 0.86499071 |
| miR-1537-5p             | −0.0232765     | Down       | 0.63968834 | 0.95096807 |
| miR-4735-3p             | −0.0232067     | Down       | 0.38580088 | 0.86961208 |
| miR-6831-5p             | −0.0231041     | Down       | 0.47232408 | 0.89396011 |
| miR-302c-3p             | −0.0230396     | Down       | 0.36861128 | 0.86195734 |
| miR-617                 | −0.0229629     | Down       | 0.72003158 | 0.96558066 |
| miR-6877-3p             | −0.0229476     | Down       | 0.63855179 | 0.95096807 |
| miR-5692a               | −0.0229447     | Down       | 0.423124   | 0.8823614 |
| miR-640                 | −0.0229348     | Down       | 0.7008013  | 0.96268515 |
| miR-3922-5p             | −0.0228789     | Down       | 0.29212106 | 0.83872374 |
| miR-329-5p              | −0.0228768     | Down       | 0.5137625  | 0.91376348 |
| miR-4797-3p             | −0.0228032     | Down       | 0.33996273 | 0.85489649 |
| miR-591                 | −0.0227442     | Down       | 0.51170058 | 0.91376348 |
| miR-1255b-2-3p          | −0.0227272     | Down       | 0.64792269 | 0.95321673 |
| miR-554                 | −0.0226667     | Down       | 0.5165602  | 0.91376348 |
Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value   | P-adj   |
|------------|----------------|------------|-----------|---------|
| miR-7850-5p | -0.0226549     | Down       | 0.42088471 | 0.8823614 |
| miR-624-3p  | -0.022569      | Down       | 0.44792099 | 0.8896123 |
| miR-501-3p  | -0.022561      | Down       | 0.72779336 | 0.9696367 |
| miR-3178    | -0.0225061     | Down       | 0.35278742 | 0.8588192 |
| miR-511-3p  | -0.0223247     | Down       | 0.47990324 | 0.9028926 |
| miR-4434    | -0.0222334     | Down       | 0.481052   | 0.9030564 |
| miR-6777-3p | -0.022166      | Down       | 0.63978023 | 0.9509607 |
| miR-1207-3p | -0.0219647     | Down       | 0.54804246 | 0.92261663|
| miR-3136-3p | -0.0219553     | Down       | 0.61990964 | 0.94829596|
| miR-8080    | -0.0219457     | Down       | 0.4413316  | 0.88952595|
| miR-6833-3p | -0.0218518     | Down       | 0.61529953 | 0.94689808|
| miR-6511a-3p| -0.0218305     | Down       | 0.62779774 | 0.9498341 |
| miR-4782-3p | -0.021813      | Down       | 0.38913329 | 0.87266367|
| miR-4759    | -0.021747      | Down       | 0.47690937 | 0.89857557|
| miR-6788-3p | -0.0217395     | Down       | 0.42326016 | 0.8823614 |
| miR-4457    | -0.0217289     | Down       | 0.35904329 | 0.8588192 |
| miR-2114-3p | -0.0217087     | Down       | 0.46680529 | 0.89396011|
| miR-208a-3p | -0.0216887     | Down       | 0.57371991 | 0.93390911|
| miR-924     | -0.0216297     | Down       | 0.48498084 | 0.90449982|
| miR-6819-5p | -0.0216207     | Down       | 0.60973131 | 0.94386479|
| miR-4782-5p | -0.0216032     | Down       | 0.53467106 | 0.9213181 |
| miR-6753-5p | -0.0215961     | Down       | 0.513281   | 0.91376348|
| miR-4779    | -0.0215243     | Down       | 0.35563879 | 0.8588192 |
| miR-6847-5p | -0.0214709     | Down       | 0.49314174 | 0.90695643|
| miR-302b-3p | -0.0213073     | Down       | 0.46434411 | 0.89396011|
| miR-583     | -0.0212315     | Down       | 0.56736377 | 0.9303065 |
| miR-6878-3p | -0.0212105     | Down       | 0.36926655 | 0.86195734|
| miR-548ag   | -0.0212064     | Down       | 0.51578333 | 0.91376348|
| miR-3194-5p | -0.021182      | Down       | 0.70234811 | 0.96268515|
| miR-6828-5p | -0.0211656     | Down       | 0.39486429 | 0.8731074 |
| miR-7109-5p | -0.0211595     | Down       | 0.50943748 | 0.91230009|
| miR-1966-3p | -0.0210447     | Down       | 0.55285141 | 0.92384946|
| miR-662     | -0.0210389     | Down       | 0.71800577 | 0.96505269|
| miR-5192    | -0.0209993     | Down       | 0.46504184 | 0.89396011|
| miR-1266-5p | -0.0209397     | Down       | 0.53390601 | 0.92384946|
| miR-548f-5p | -0.020819      | Down       | 0.60725348 | 0.94355588|
| miR-891a-5p | -0.0206623     | Down       | 0.50614706 | 0.912181 |
| miR-514a-5p | -0.0203138     | Down       | 0.49325699 | 0.90695643|
| miR-567     | -0.0203091     | Down       | 0.60896204 | 0.94386479|
| miR-519a-5p | -0.0203012     | Down       | 0.51104339 | 0.91376348|
| miR-6742-5p | -0.0200957     | Down       | 0.53027998 | 0.9213181 |
| miR-5087    | -0.0200794     | Down       | 0.52357825 | 0.9178691 |
| miR-16-1-3p | -0.0200778     | Down       | 0.33434141 | 0.85496949|
| miR-3202    | -0.0200496     | Down       | 0.52892652 | 0.92119547|
| miR-6888-5p | -0.0200418     | Down       | 0.46309567 | 0.89396011|
| miR-2276-5p | -0.0200027     | Down       | 0.47050027 | 0.89396011|
| miR-3714    | -0.0199413     | Down       | 0.45375523 | 0.89093879|
| miR-5708    | -0.0198854     | Down       | 0.48209859 | 0.9030564 |
| miR-208b-3p | -0.0198438     | Down       | 0.43849767 | 0.88952595|

(Continued)
Table 9 (Continued).

| miRNAs            | Log2FoldChange | Regulation | P-value  | P-adj   |
|-------------------|----------------|------------|----------|---------|
| miR-8070          | -0.0198259     | Down       | 0.56288068 | 0.92970327 |
| miR-4524a-5p      | -0.0197501     | Down       | 0.53816235 | 0.9213181 |
| miR-3189-3p       | -0.0196763     | Down       | 0.46691571 | 0.89396011 |
| miR-4695-5p       | -0.0196329     | Down       | 0.72755483 | 0.96963657 |
| miR-519d-3p       | -0.0196262     | Down       | 0.51976908 | 0.91632037 |
| miR-3918          | -0.0196255     | Down       | 0.41137651 | 0.8793356 |
| miR-6883-3p       | -0.0195984     | Down       | 0.64183749 | 0.95128163 |
| miR-298           | -0.0195803     | Down       | 0.55851468 | 0.92752078 |
| miR-5095          | -0.0194938     | Down       | 0.59415038 | 0.93829717 |
| miR-373-3p        | -0.0194035     | Down       | 0.47647192 | 0.89841001 |
| miR-3622b-3p      | -0.0193703     | Down       | 0.67771735 | 0.95648223 |
| miR-3656          | -0.0193481     | Down       | 0.82855543 | 0.99440018 |
| miR-4265          | -0.019335      | Down       | 0.44210537 | 0.89525956 |
| miR-589-3p        | -0.0192968     | Down       | 0.6412559  | 0.95096807 |
| miR-6722-3p       | -0.0192565     | Down       | 0.43605587 | 0.89415544 |
| miR-1248          | -0.0192199     | Down       | 0.48145878 | 0.9030564 |
| miR-8071          | -0.0191373     | Down       | 0.57941186 | 0.93436563 |
| miR-6822-3p       | -0.0190523     | Down       | 0.53678876 | 0.9213181 |
| miR-3689d         | -0.0190456     | Down       | 0.4142069  | 0.8804535 |
| miR-548ar-3p      | -0.0189736     | Down       | 0.55852155 | 0.92752078 |
| miR-548d-5p       | -0.0189594     | Down       | 0.4817617  | 0.9030564 |
| miR-6802-3p       | -0.0189422     | Down       | 0.51874876 | 0.91564857 |
| miR-4504          | -0.0189187     | Down       | 0.49111452 | 0.90695643 |
| miR-6864-3p       | -0.0188964     | Down       | 0.54207416 | 0.92199245 |
| miR-3618          | -0.0187864     | Down       | 0.69179636 | 0.96707402 |
| miR-103b          | -0.0187592     | Down       | 0.57395811 | 0.93390911 |
| miR-6844          | -0.018755      | Down       | 0.77362276 | 0.9852381 |
| miR-431-3p        | -0.0187068     | Down       | 0.79929465 | 0.98820926 |
| miR-1200          | -0.018706      | Down       | 0.56758211 | 0.9303065 |
| miR-7110-3p       | -0.0186295     | Down       | 0.46493742 | 0.89396011 |
| miR-5004-5p       | -0.0186198     | Down       | 0.40300059 | 0.87475982 |
| miR-3617-3p       | -0.0186036     | Down       | 0.66555667 | 0.95557578 |
| miR-6779-5p       | -0.0185894     | Down       | 0.51792705 | 0.91482647 |
| miR-454-3p        | -0.0184822     | Down       | 0.76305689 | 0.98100055 |
| miR-5688          | -0.0183095     | Down       | 0.54890305 | 0.92261663 |
| miR-4777-3p       | -0.0182984     | Down       | 0.58441507 | 0.93513803 |
| miR-138-1-3p      | -0.0182606     | Down       | 0.72136765 | 0.96558066 |
| miR-4671-3p       | -0.0182268     | Down       | 0.69455307 | 0.96174643 |
| miR-4463          | -0.0182222     | Down       | 0.48413004 | 0.90449982 |
| miR-4424          | -0.0181867     | Down       | 0.56815021 | 0.9303065 |
| miR-1268b         | -0.0179837     | Down       | 0.8287958  | 0.99440018 |
| miR-4732-3p       | -0.0179263     | Down       | 0.58509804 | 0.93513803 |
| miR-6746-5p       | -0.0179198     | Down       | 0.58247149 | 0.93436563 |
| miR-6892-5p       | -0.017886      | Down       | 0.59755189 | 0.93869704 |
| miR-381-5p        | -0.0178605     | Down       | 0.65525257 | 0.95321673 |
| miR-1261          | -0.0178075     | Down       | 0.48991008 | 0.90695643 |
| miR-616-3p        | -0.0177903     | Down       | 0.47341623 | 0.89396011 |
| miR-4676-3p       | -0.0177801     | Down       | 0.67441895 | 0.95648223 |
| miR-4645-3p       | -0.017748      | Down       | 0.64695212 | 0.95321673 |
Table 9 (Continued).

| miRNAs        | Log2FoldChange | Regulation | P-value   | P-adj    |
|---------------|----------------|------------|-----------|----------|
| miR-4293      | -0.0177317     | Down       | 0.66240796| 0.95510802|
| miR-6881-3p   | -0.0177258     | Down       | 0.76287968| 0.98140055|
| miR-744-3p    | -0.0176999     | Down       | 0.71123168| 0.96505269|
| miR-216b-3p   | -0.0176221     | Down       | 0.51523309| 0.91376348|
| miR-3622a-3p  | -0.0175364     | Down       | 0.57580661| 0.93390911|
| miR-3919      | -0.0175071     | Down       | 0.5510952 | 0.92349191|
| miR-4701-3p   | -0.0174818     | Down       | 0.45866694| 0.88964976|
| miR-3131      | -0.0174639     | Down       | 0.52596692| 0.91954761|
| miR-4760-5p   | -0.0173869     | Down       | 0.67324921| 0.95648223|
| miR-4433b-3p  | -0.0172945     | Down       | 0.54300728| 0.9222099 |
| miR-4761-5p   | -0.0172715     | Down       | 0.5875354 | 0.93675929|
| miR-892a      | -0.0172692     | Down       | 0.65506354| 0.95321673|
| miR-345-3p    | -0.0172563     | Down       | 0.64008036| 0.95096807|
| miR-3147      | -0.0172107     | Down       | 0.64066451| 0.95096807|
| miR-378h      | -0.0171729     | Down       | 0.50416125| 0.91193213|
| miR-6891-3p   | -0.0171451     | Down       | 0.76246977| 0.98140055|
| miR-188-3p    | -0.0170843     | Down       | 0.65777789| 0.95321673|
| miR-2277-5p   | -0.0170661     | Down       | 0.56519544| 0.9303065 |
| miR-7108-3p   | -0.0170624     | Down       | 0.63080393| 0.95086097|
| miR-6850-5p   | -0.016963      | Down       | 0.81070492| 0.99064883|
| miR-767-3p    | -0.0169514     | Down       | 0.75691552| 0.98140055|
| miR-345-5p    | -0.0168958     | Down       | 0.81256332| 0.99064883|
| miR-6889-5p   | -0.0168908     | Down       | 0.37711739| 0.86499071|
| miR-145-3p    | -0.0168268     | Down       | 0.70862699| 0.96360966|
| miR-4802-3p   | -0.0168272     | Down       | 0.57328301| 0.93390911|
| miR-376a-2-5p | -0.0168259     | Down       | 0.59273245| 0.93770773|
| miR-6133      | -0.0167772     | Down       | 0.50891359| 0.91230009|
| miR-4691-3p   | -0.0165958     | Down       | 0.50664374| 0.912181 |
| miR-4783-5p   | -0.0165943     | Down       | 0.67050849| 0.95648223|
| miR-4514      | -0.0165234     | Down       | 0.54631268| 0.92261663|
| miR-6745      | -0.0165196     | Down       | 0.52870674| 0.92119547|
| miR-548b-3p   | -0.0164887     | Down       | 0.56978174| 0.93210635|
| miR-4435      | -0.0164779     | Down       | 0.56561035| 0.9303065 |
| miR-3165      | -0.0164702     | Down       | 0.5816504 | 0.93436563|
| miR-219b-5p   | -0.0164568     | Down       | 0.59560483| 0.93868471|
| miR-548v      | -0.0164565     | Down       | 0.70844026| 0.96360966|
| miR-2467-3p   | -0.0164015     | Down       | 0.57742474| 0.93390911|
| miR-3924      | -0.0162979     | Down       | 0.70061417| 0.96268515|
| miR-4766-5p   | -0.016287      | Down       | 0.48436282| 0.90449982|
| miR-4673      | -0.0162448     | Down       | 0.59710592| 0.93868471|
| miR-6513-3p   | -0.0162307     | Down       | 0.60967882| 0.94386479|
| miR-4651      | -0.0160382     | Down       | 0.82761866| 0.99430803|
| miR-485-3p    | -0.0160167     | Down       | 0.87943283| 0.99898712|
| miR-4662a-3p  | -0.015971      | Down       | 0.49625711| 0.90968672|
| miR-6845-3p   | -0.0158811     | Down       | 0.67837672| 0.95648223|
| miR-3144-5p   | -0.0158022     | Down       | 0.53056015| 0.9213181 |
| miR-1184      | -0.0158072     | Down       | 0.59828657| 0.93870358|
| miR-6839-5p   | -0.0156551     | Down       | 0.6119096 | 0.94386479|
| miR-1258      | -0.015538      | Down       | 0.58766102| 0.93675929|

(Continued)
Table 9 (Continued).

| miRNAs    | Log2FoldChange | Regulation | P-value  | P-adj    |
|-----------|----------------|------------|----------|----------|
| miR-5697  | -0.0154575     | Down       | 0.68886204 | 0.96036263 |
| miR-8065  | -0.015457     | Down       | 0.74994003 | 0.97742837 |
| miR-6870-5p | -0.0154516   | Down       | 0.66323138 | 0.95110802 |
| miR-206   | -0.0153486    | Down       | 0.55904258 | 0.92752708 |
| miR-4452  | -0.0153427    | Down       | 0.58344668 | 0.93436563 |
| miR-510-3p | -0.0153325    | Down       | 0.66778315 | 0.95631006 |
| miR-146b-3p | -0.0153142   | Down       | 0.57687517 | 0.93390911 |
| miR-4513  | -0.0152798    | Down       | 0.6014067 | 0.93952621 |
| miR-7847-3p | -0.0152761   | Down       | 0.77823881 | 0.985258  |
| miR-6739-5p | -0.0152297   | Down       | 0.7761263 | 0.985258  |
| miR-4646-3p | -0.0151834   | Down       | 0.84117716 | 0.99654281 |
| miR-2116-5p | -0.0151732   | Down       | 0.6849632 | 0.95932176 |
| miR-6817-3p | -0.0150789   | Down       | 0.61008554 | 0.94386479 |
| miR-4660  | -0.0150254    | Down       | 0.50800372 | 0.91230009 |
| miR-3160-5p | -0.0149645   | Down       | 0.67722872 | 0.95648223 |
| miR-5011-5p | -0.0149335   | Down       | 0.59054265 | 0.93675929 |
| miR-5685  | -0.0149228    | Down       | 0.59141154 | 0.93707007 |
| miR-4729  | -0.0149005    | Down       | 0.74047795 | 0.97402999 |
| miR-585-3p | -0.0148846    | Down       | 0.741324   | 0.97402999 |
| miR-3181  | -0.0148665    | Down       | 0.57151784 | 0.93363213 |
| miR-7159-5p | -0.0148501    | Down       | 0.60210514 | 0.93952621 |
| miR-1236-5p | -0.0148479    | Down       | 0.73719766 | 0.97354829 |
| miR-655-3p | -0.0148337    | Down       | 0.67655901 | 0.95648223 |
| miR-6773-3p | -0.0148148    | Down       | 0.63769818 | 0.95096807 |
| miR-452-3p | -0.0146011    | Down       | 0.62426449 | 0.9493253  |
| miR-4532  | -0.0145244    | Down       | 0.79484255 | 0.98759926 |
| miR-1276  | -0.0145182    | Down       | 0.66431616 | 0.95510802 |
| miR-495-5p | -0.014511     | Down       | 0.64839579 | 0.95321673 |
| miR-3184-5p | -0.0144988    | Down       | 0.67280274 | 0.95648223 |
| miR-6873-5p | -0.0144971    | Down       | 0.63738698 | 0.95096807 |
| miR-1237-5p | -0.014493     | Down       | 0.63860474 | 0.95096807 |
| miR-605-5p | -0.0144929    | Down       | 0.64097092 | 0.95096807 |
| miR-548b-5p | -0.0144614    | Down       | 0.76570467 | 0.98147681 |
| miR-7856-5p | -0.0143765    | Down       | 0.72382632 | 0.96691758 |
| miR-5382-3p | -0.0143693    | Down       | 0.65392278 | 0.95321673 |
| miR-6786-3p | -0.0143516    | Down       | 0.6934944  | 0.96137172 |
| miR-4723-3p | -0.0140957    | Down       | 0.88560625 | 0.99897872 |
| miR-6855-5p | -0.0140764    | Down       | 0.68879875 | 0.96036263 |
| miR-146a-3p | -0.0140732    | Down       | 0.63408847 | 0.95096807 |
| miR-4726-5p | -0.0140357    | Down       | 0.62034801 | 0.94829596 |
| miR-6782-5p | -0.0140077    | Down       | 0.4999732  | 0.91121111 |
| miR-1278  | -0.013964     | Down       | 0.81623945 | 0.99127826 |
| miR-346   | -0.0139568    | Down       | 0.57180427 | 0.93363213 |
| miR-190b  | -0.0139451    | Down       | 0.55975316 | 0.9276427 |
| miR-887-3p | -0.0138433    | Down       | 0.80365516 | 0.90063213 |
| miR-6068  | -0.0137686    | Down       | 0.82973935 | 0.99489095 |
| miR-631   | -0.0137437    | Down       | 0.67728143 | 0.95648223 |
| miR-6737-5p | -0.0137008    | Down       | 0.74839715 | 0.9742837 |
| miR-7702  | -0.0136451    | Down       | 0.68775489 | 0.96036263 |

(Continued)
Table 9 (Continued).

| miRNAs          | Log2FoldChange | Regulation | P-value | P-adj  |
|-----------------|----------------|------------|---------|--------|
| miR-4709-3p     | -0.0135279     | Down       | 0.57658086 | 0.93390911 |
| miR-6874-3p     | -0.0135163     | Down       | 0.59284104 | 0.93770773 |
| miR-6846-5p     | -0.0134762     | Down       | 0.6527056  | 0.95321673 |
| miR-2278        | -0.0133521     | Down       | 0.576741   | 0.93390911 |
| miR-130a-5p     | -0.013298      | Down       | 0.70637716 | 0.96360966 |
| miR-6836-5p     | -0.0131042     | Down       | 0.54763293 | 0.92261663 |
| miR-6882-5p     | -0.0130684     | Down       | 0.5242369  | 0.91825968 |
| miR-3193        | -0.0130581     | Down       | 0.59827391 | 0.93870358 |
| miR-6812-3p     | -0.013037      | Down       | 0.826037   | 0.99340905 |
| miR-6819-3p     | -0.012997      | Down       | 0.80469099 | 0.99064883 |
| miR-6857-5p     | -0.0129467     | Down       | 0.69145376 | 0.96077402 |
| miR-4655-5p     | -0.0129251     | Down       | 0.6878741  | 0.96036263 |
| miR-4418        | -0.0129231     | Down       | 0.53214975 | 0.9213181 |
| miR-8066        | -0.0128877     | Down       | 0.79360278 | 0.98694309 |
| miR-128-1-5p    | -0.0128078     | Down       | 0.87264725 | 0.99898712 |
| miR-4701-5p     | -0.0127842     | Down       | 0.75883109 | 0.98140055 |
| miR-6750-3p     | -0.0127744     | Down       | 0.70392756 | 0.96360966 |
| miR-130b-5p     | -0.0127465     | Down       | 0.75751851 | 0.98140055 |
| miR-3653-5p     | -0.0127035     | Down       | 0.79715681 | 0.98759926 |
| miR-1199-5p     | -0.0126985     | Down       | 0.71040964 | 0.96505269 |
| miR-548b        | -0.0126651     | Down       | 0.74107714 | 0.97402999 |
| miR-4799-5p     | -0.0126574     | Down       | 0.70117911 | 0.96268515 |
| miR-665         | -0.0126447     | Down       | 0.69642239 | 0.96226104 |
| miR-548d-3p     | -0.0126426     | Down       | 0.71618248 | 0.96505269 |
| miR-5047        | -0.0126237     | Down       | 0.6538641  | 0.95321673 |
| miR-214-3p      | -0.0125973     | Down       | 0.66824257 | 0.95631006 |
| miR-5007-5p     | -0.0125917     | Down       | 0.64514439 | 0.95321673 |
| miR-6824-5p     | -0.0125551     | Down       | 0.77703408 | 0.985258  |
| miR-6835-5p     | -0.0125379     | Down       | 0.66382121 | 0.95510802 |
| miR-3976        | -0.0125279     | Down       | 0.67920619 | 0.9566446 |
| miR-5706        | -0.0125053     | Down       | 0.69376627 | 0.96137172 |
| miR-187-5p      | -0.0124375     | Down       | 0.72563224 | 0.96826128 |
| miR-5571-5p     | -0.0124326     | Down       | 0.8552683  | 0.99898712 |
| miR-6862-3p     | -0.0124127     | Down       | 0.74999562 | 0.97742837 |
| miR-2276-3p     | -0.0123549     | Down       | 0.65208401 | 0.95321673 |
| miR-5579-3p     | -0.0123529     | Down       | 0.6752284  | 0.95648223 |
| miR-6501-5p     | -0.0123046     | Down       | 0.61453806 | 0.94686019 |
| miR-183-5p      | -0.0122913     | Down       | 0.761594   | 0.98140055 |
| miR-3123        | -0.012244      | Down       | 0.6669721  | 0.95631006 |
| miR-519e-5p     | -0.0122324     | Down       | 0.58007819 | 0.93436563 |
| miR-5587-5p     | -0.0122294     | Down       | 0.65197791 | 0.95321673 |
| miR-4423-5p     | -0.0121935     | Down       | 0.73278235 | 0.9725372 |
| miR-378c        | -0.0121663     | Down       | 0.65008801 | 0.95321673 |
| miR-4758-5p     | -0.0121174     | Down       | 0.77102542 | 0.98290443 |
| miR-1468-3p     | -0.0120833     | Down       | 0.78243923 | 0.98664743 |
| miR-7855-5p     | -0.0120272     | Down       | 0.76376796 | 0.98140055 |
| miR-4647        | -0.0119836     | Down       | 0.75647451 | 0.98140055 |
| miR-506-5p      | -0.0119826     | Down       | 0.74052913 | 0.97402999 |
| miR-4776-3p     | -0.0119525     | Down       | 0.71186538 | 0.96505269 |
| miRNAs          | Log2FoldChange | Regulation | P-value  | P-adj  |
|-----------------|----------------|------------|----------|--------|
| miR-3666        | -0.0119274     | Down       | 0.58255769 | 0.93436563 |
| miR-6827-5p     | -0.011866      | Down       | 0.68812192 | 0.96036263 |
| miR-6790-3p     | -0.011811      | Down       | 0.7844565  | 0.98667434 |
| miR-5583-3p     | -0.0117971     | Down       | 0.79156515 | 0.98667434 |
| miR-1295b-5p    | -0.0117206     | Down       | 0.6919816  | 0.96077402 |
| miR-3677-3p     | -0.0117104     | Down       | 0.67769257 | 0.95648223 |
| miR-4527        | -0.0116914     | Down       | 0.57519673 | 0.93390911 |
| miR-3115        | -0.0116471     | Down       | 0.79078548 | 0.98667434 |
| miR-143-5p      | -0.0116368     | Down       | 0.73628333 | 0.97354829 |
| miR-4637        | -0.0115636     | Down       | 0.71639324 | 0.96505269 |
| miR-1182        | -0.0114596     | Down       | 0.74557094 | 0.9764091  |
| miR-548c-5p     | -0.0114263     | Down       | 0.72567052 | 0.96826128 |
| miR-4260        | -0.0114243     | Down       | 0.71608133 | 0.96505269 |
| miR-520g-5p     | -0.0113337     | Down       | 0.71718692 | 0.96505269 |
| miR-605-3p      | -0.0113136     | Down       | 0.68422057 | 0.95880418 |
| miR-873-3p      | -0.0112921     | Down       | 0.73299788 | 0.9725372 |
| miR-1244        | -0.0112603     | Down       | 0.6232706  | 0.94925841 |
| miR-8055        | -0.0109754     | Down       | 0.66758111 | 0.9561006 |
| miR-3662        | -0.0109397     | Down       | 0.69726598 | 0.96239183 |
| miR-6862-5p     | -0.010841      | Down       | 0.72132034 | 0.96558066 |
| miR-4658        | -0.0108322     | Down       | 0.70165965 | 0.96268515 |
| miR-6767-3p     | -0.0108203     | Down       | 0.74011199 | 0.97402999 |
| miR-99a-3p      | -0.0107907     | Down       | 0.96731243 | 0.99898712 |
| miR-6768-3p     | -0.0106522     | Down       | 0.78842766 | 0.98667434 |
| miR-4659a-5p    | -0.0106451     | Down       | 0.79792473 | 0.98759926 |
| miR-2117        | -0.0106433     | Down       | 0.77501288 | 0.985258 |
| miR-6735-5p     | -0.0105937     | Down       | 0.68319041 | 0.9585044 |
| miR-3135a       | -0.0105893     | Down       | 0.69622559 | 0.96226104 |
| miR-4295        | -0.010552      | Down       | 0.72600758 | 0.96826128 |
| miR-7107-3p     | -0.0105176     | Down       | 0.84626259 | 0.99654281 |
| miR-128-2-5p    | -0.0105075     | Down       | 0.66830072 | 0.95631006 |
| miR-6859-5p     | -0.0104776     | Down       | 0.75078712 | 0.97770354 |
| miR-3684        | -0.0104013     | Down       | 0.83539086 | 0.99654281 |
| miR-30d-3p      | -0.0103853     | Down       | 0.71051835 | 0.96505269 |
| miR-4638-5p     | -0.0103425     | Down       | 0.70833184 | 0.96360966 |
| miR-4789-3p     | -0.0103283     | Down       | 0.74613358 | 0.9764091 |
| miR-190a-3p     | -0.0102881     | Down       | 0.84773027 | 0.99654281 |
| miR-3689f       | -0.0101659     | Down       | 0.70864679 | 0.96360966 |
| miR-3913-3p     | -0.0101642     | Down       | 0.72958913 | 0.97152542 |
| miR-4633-3p     | -0.0101254     | Down       | 0.85388096 | 0.99898712 |
| miR-486-5p      | -0.0099604     | Down       | 0.95866057 | 0.99898712 |
| miR-6747-3p     | -0.0099557     | Down       | 0.64086171 | 0.95096807 |
| miR-1251-3p     | -0.0099478     | Down       | 0.74176683 | 0.9741382 |
| miR-10a-3p      | -0.0098892     | Down       | 0.78024065 | 0.98667434 |
| miR-658         | -0.0098766     | Down       | 0.7897364  | 0.98667434 |
| miR-944         | -0.0098706     | Down       | 0.81797369 | 0.99127826 |
| miR-4713-5p     | -0.0098246     | Down       | 0.83457819 | 0.99622199 |
| miR-5006-3p     | -0.009715      | Down       | 0.78606427 | 0.98667434 |
| miR-373-5p      | -0.0095526     | Down       | 0.73271645 | 0.9725372 |

(Continued)
Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value   | P-adj     |
|------------|----------------|------------|-----------|-----------|
| miR-3169   | -0.0095199     | Down       | 0.71712341| 0.96505269|
| miR-518a-5p| -0.0094811     | Down       | 0.76918477| 0.98237037|
| miR-4641   | -0.0094703     | Down       | 0.81044806| 0.99064883|
| miR-3692-5p| -0.0093147     | Down       | 0.76433074| 0.98140055|
| miR-3126-5p| -0.0093056     | Down       | 0.65614493| 0.95321673|
| miR-576-3p | -0.009283      | Down       | 0.78846763| 0.98667434|
| miR-1285-5p| -0.0092817     | Down       | 0.7864442 | 0.98667434|
| miR-4784   | -0.009158      | Down       | 0.69256634| 0.96106669|
| miR-498    | -0.0091545     | Down       | 0.82074845| 0.99168948|
| miR-219a-2-3p| -0.0090465     | Down       | 0.85244841| 0.99898712|
| miR-450b-3p| -0.0090186     | Down       | 0.80687156| 0.99064883|
| miR-615-3p | -0.009012      | Down       | 0.82772197| 0.99252298|
| miR-657    | -0.009012      | Down       | 0.70445092| 0.96360966|
| miR-5011-3p| -0.0089942     | Down       | 0.83702003| 0.99452821|
| miR-4792   | -0.008984      | Down       | 0.81317265| 0.99092163|
| miR-3944-3p| -0.0089698     | Down       | 0.92653983| 0.99898712|
| miR-4769-3p| -0.008894      | Down       | 0.78310298| 0.98667434|
| miR-6872-5p| -0.0088936     | Down       | 0.75998162| 0.98140055|
| miR-6876-5p| -0.0088756     | Down       | 0.6575788 | 0.95321673|
| miR-205-5p | -0.0088591     | Down       | 0.81959201| 0.99127826|
| miR-494-5p | -0.0088706     | Down       | 0.8596073 | 0.99898712|
| miR-2335-3p| -0.0086358     | Down       | 0.7670393 | 0.98227692|
| miR-4474-3p| -0.008608      | Down       | 0.73513737| 0.97354829|
| miR-7852-3p| -0.0085958     | Down       | 0.85496752| 0.99898712|
| miR-383-5p | -0.0085243     | Down       | 0.8839679 | 0.99898712|
| miR-875-5p | -0.0082844     | Down       | 0.81901427| 0.99127826|
| miR-6822-5p| -0.0082025     | Down       | 0.78963006| 0.98667434|
| miR-5691   | -0.0081525     | Down       | 0.79710014| 0.98759926|
| miR-7155-3p| -0.0081318     | Down       | 0.71750381| 0.96505269|
| miR-4448   | -0.0080719     | Down       | 0.7367675 | 0.97354829|
| miR-3182   | -0.0080707     | Down       | 0.816367 | 0.99127826|
| miR-5680   | -0.0080072     | Down       | 0.87347525| 0.99898712|
| miR-654-5p | -0.0079851     | Down       | 0.81536599| 0.99122915|
| miR-4794   | -0.0079826     | Down       | 0.80753955| 0.99064883|
| miR-4772-5p| -0.0078341     | Down       | 0.98391904| 0.99898712|
| miR-100-5p | -0.0077228     | Down       | 0.75985452| 0.98140055|
| let-7g-3p  | -0.0076142     | Down       | 0.82812993| 0.99440018|
| miR-4645-5p| -0.0076122     | Down       | 0.87948853| 0.99898712|
| miR-188-5p | -0.0076115     | Down       | 0.81671067| 0.99127826|
| miR-338-5p | -0.0075769     | Down       | 0.84311541| 0.99654281|
| miR-708-5p | -0.0075666     | Down       | 0.92606518| 0.99898712|
| miR-6789-5p| -0.0075105     | Down       | 0.89165272| 0.99898712|
| miR-6787-3p| -0.0074763     | Down       | 0.8164637 | 0.99127826|
| miR-6815-5p| -0.0074274     | Down       | 0.83027884| 0.99489095|
| miR-718    | -0.0073929     | Down       | 0.83149808| 0.99505896|
| miR-3622a-5p| -0.0073902     | Down       | 0.90441834| 0.99898712|

(Continued)
| miRNAs          | Log2FoldChange | Regulation | P-value     | P-adj     |
|----------------|----------------|------------|-------------|-----------|
| miR-4318       | -0.0071434     | Down       | 0.79009082  | 0.98667434 |
| miR-1224-3p    | -0.0071228     | Down       | 0.89904345  | 0.9998712  |
| miR-3681-5p    | -0.0071212     | Down       | 0.85999628  | 0.9998712  |
| miR-5580-5p    | -0.0070837     | Down       | 0.87394584  | 0.9998712  |
| miR-767-3p     | -0.0070818     | Down       | 0.78482358  | 0.98667434 |
| miR-8067       | -0.0070745     | Down       | 0.78450315  | 0.98667434 |
| miR-6751-5p    | -0.0070414     | Down       | 0.82126495  | 0.99185328 |
| miR-6748-3p    | -0.0069865     | Down       | 0.77607548  | 0.985258   |
| miR-374a-3p    | -0.006964      | Down       | 0.8671137   | 0.9998712  |
| miR-1247-5p    | -0.0069552     | Down       | 0.79780852  | 0.98759926 |
| miR-1206       | -0.0069354     | Down       | 0.88342507  | 0.9998712  |
| miR-6716-3p    | -0.0069342     | Down       | 0.88604018  | 0.9998712  |
| miR-7153-3p    | -0.0068762     | Down       | 0.80682369  | 0.99064883 |
| miR-635        | -0.0068419     | Down       | 0.87010589  | 0.9998712  |
| miR-616-5p     | -0.0067948     | Down       | 0.87844038  | 0.9998712  |
| miR-548q       | -0.0067864     | Down       | 0.80815498  | 0.99064883 |
| miR-6832-5p    | -0.0067224     | Down       | 0.85778301  | 0.9998712  |
| miR-2682-3p    | -0.0066297     | Down       | 0.79941131  | 0.98820926 |
| miR-412-5p     | -0.00662       | Down       | 0.89035774  | 0.9998712  |
| miR-302f       | -0.0066155     | Down       | 0.88132151  | 0.9998712  |
| miR-3064-3p    | -0.0065595     | Down       | 0.82587428  | 0.99340905 |
| miR-34a-3p     | -0.0063862     | Down       | 0.87642148  | 0.9998712  |
| miR-6810-5p    | -0.0063765     | Down       | 0.84789718  | 0.99654281 |
| miR-6512-3p    | -0.0063262     | Down       | 0.81724812  | 0.99127826 |
| miR-4756-3p    | -0.0062289     | Down       | 0.86071954  | 0.9998712  |
| miR-6772-3p    | -0.0062016     | Down       | 0.8176216   | 0.99127826 |
| miR-1178-3p    | -0.0060641     | Down       | 0.83603672  | 0.99654281 |
| miR-3156-3p    | -0.0060097     | Down       | 0.87659355  | 0.9998712  |
| miR-92a-2-5p   | -0.0059985     | Down       | 0.89337705  | 0.9998712  |
| miR-3192-5p    | -0.0059849     | Down       | 0.85140192  | 0.9998712  |
| miR-3616-5p    | -0.005916      | Down       | 0.87556977  | 0.9998712  |
| miR-216b-5p    | -0.0059046     | Down       | 0.78988169  | 0.98674343 |
| miR-1273g-5p   | -0.0058234     | Down       | 0.84875466  | 0.9903761 |
| miR-454-5p     | -0.0056392     | Down       | 0.87659395  | 0.9998712  |
| miR-604        | -0.0056228     | Down       | 0.84115808  | 0.99654281 |
| miR-5003-3p    | -0.0055939     | Down       | 0.77709499  | 0.985258   |
| miR-4646-5p    | -0.0055568     | Down       | 0.91343785  | 0.9998712  |
| miR-1185-5p    | -0.0054925     | Down       | 0.8750581   | 0.9998712  |
| miR-6809-3p    | -0.0054802     | Down       | 0.90618848  | 0.9998712  |
| miR-5695       | -0.0054138     | Down       | 0.84065578  | 0.99654281 |
| miR-1976       | -0.0053957     | Down       | 0.89787741  | 0.9998712  |
| miR-563        | -0.0053882     | Down       | 0.91226822  | 0.9998712  |
| miR-6734-3p    | -0.0053774     | Down       | 0.87471748  | 0.9998712  |
| miR-4319       | -0.0053747     | Down       | 0.86232995  | 0.9998712  |
| miR-342-3p     | -0.0052338     | Down       | 0.97293249  | 0.9998712  |
| miR-6895-5p    | -0.005215      | Down       | 0.8608465   | 0.9998712  |
| miR-4723-5p    | -0.0051688     | Down       | 0.81224515  | 0.99064883 |
| miR-4528       | -0.0051614     | Down       | 0.92980523  | 0.9998712  |
| NC2_00079215   | -0.0051563     | Down       | 0.87570139  | 0.9998712  |

(Continued)
### Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value     | P-adj       |
|--------------|----------------|------------|-------------|-------------|
| miR-1538     | -0.0050997     | Down       | 0.87810329  | 0.99898712  |
| miR-6872-3p  | -0.0050274     | Down       | 0.88748977  | 0.99898712  |
| miR-3668     | -0.0050174     | Down       | 0.90089115  | 0.99898712  |
| miR-4420     | -0.004945      | Down       | 0.85326     | 0.99898712  |
| miR-371a-5p  | -0.0049431     | Down       | 0.81677945  | 0.99127826  |
| miR-200c-5p  | -0.0048674     | Down       | 0.86744806  | 0.99898712  |
| miR-155-3p   | -0.0047673     | Down       | 0.92489206  | 0.99898712  |
| miR-6806-5p  | -0.0047274     | Down       | 0.87138368  | 0.99898712  |
| miR-920      | -0.0047252     | Down       | 0.86831937  | 0.99898712  |
| miR-1538     | -0.004718      | Down       | 0.86831937  | 0.99898712  |
| miR-4420     | -0.0047001     | Down       | 0.91499362  | 0.99898712  |
| miR-155-3p   | -0.0046743     | Down       | 0.83192388  | 0.99622199  |
| miR-6872-3p  | -0.0046459     | Down       | 0.88067889  | 0.99898712  |
| miR-3668     | -0.0043974     | Down       | 0.90204635  | 0.99898712  |
| miR-4420     | -0.0042257     | Down       | 0.89460988  | 0.99898712  |
| miR-920      | -0.0041515     | Down       | 0.86674611  | 0.99898712  |
| miR-1538     | -0.0041155     | Down       | 0.91117932  | 0.99898712  |
| miR-4420     | -0.0040522     | Down       | 0.89608593  | 0.99898712  |
| miR-920      | -0.0040192     | Down       | 0.89469173  | 0.99898712  |
| miR-1538     | -0.0039418     | Down       | 0.89105691  | 0.99898712  |
| miR-4420     | -0.0039263     | Down       | 0.90249915  | 0.99898712  |
| miR-183-3p   | -0.0039116     | Down       | 0.90249053  | 0.99898712  |
| miR-770-5p   | -0.0038988     | Down       | 0.90826697  | 0.99898712  |
| miR-3064-5p  | -0.0038875     | Down       | 0.8904142   | 0.99898712  |
| miR-634      | -0.0038805     | Down       | 0.96723926  | 0.99898712  |
| miR-660-3p   | -0.0038712     | Down       | 0.9097167   | 0.99898712  |
| miR-644a     | -0.0038296     | Down       | 0.9175064   | 0.99898712  |
| miR-5586-3p  | -0.0038126     | Down       | 0.86274889  | 0.99898712  |
| miR-3659     | -0.0037935     | Down       | 0.90826795  | 0.99898712  |
| miR-512-5p   | -0.0037682     | Down       | 0.92327364  | 0.99898712  |
| miR-572      | -0.0037248     | Down       | 0.9145349   | 0.99898712  |
| miR-3138     | -0.0037108     | Down       | 0.91265307  | 0.99898712  |
| miR-7703     | -0.0037       | Down       | 0.9192547   | 0.99898712  |
| miR-659-3p   | -0.0036919     | Down       | 0.90801691  | 0.99898712  |
| miR-3921     | -0.0036138     | Down       | 0.91702854  | 0.99898712  |
| miR-23c      | -0.0035461     | Down       | 0.93580094  | 0.99898712  |
| miR-6769a-5p | -0.003528      | Down       | 0.92503826  | 0.99898712  |
| miR-941      | -0.0035254     | Down       | 0.9033374   | 0.99898712  |
| miR-1323     | -0.0035254     | Down       | 0.9254549   | 0.99898712  |
| miR-490-3p   | -0.0035039     | Down       | 0.90591256  | 0.99898712  |
| miR-6504-3p  | -0.0034827     | Down       | 0.90968611  | 0.99898712  |
| miR-1263     | -0.0034603     | Down       | 0.91408589  | 0.99898712  |
| miR-449a     | -0.0034566     | Down       | 0.90031562  | 0.99898712  |
| miR-3944-5p  | -0.003421      | Down       | 0.91384492  | 0.99898712  |
| miR-1199-3p  | -0.003396      | Down       | 0.92236772  | 0.99898712  |
| miR-3674     | -0.003396      | Down       | 0.9206664   | 0.99898712  |
| miR-4659b-5p | -0.0033209     | Down       | 0.93880961  | 0.99898712  |
| miRNAs         | Log2FoldChange | Regulation | P-value       | P-adj        |
|---------------|----------------|------------|---------------|--------------|
| miR-3200-3p   | -0.0032855     | Down       | 0.92266612    | 0.99989712   |
| miR-450a-1-3p | -0.0032779     | Down       | 0.94125452    | 0.99989712   |
| miR-30c-1-3p  | -0.0031641     | Down       | 0.93461856    | 0.99989712   |
| miR-548w      | -0.0031582     | Down       | 0.92357786    | 0.99989712   |
| miR-4690-3p   | -0.0031051     | Down       | 0.92408199    | 0.99989712   |
| miR-6849-5p   | -0.0030846     | Down       | 0.91722387    | 0.99989712   |
| miR-7113-3p   | -0.0030742     | Down       | 0.93227711    | 0.99989712   |
| miR-606       | -0.0030314     | Down       | 0.91699444    | 0.99989712   |
| miR-455-5p    | -0.0030307     | Down       | 0.94950521    | 0.99989712   |
| miR-5197-5p   | -0.0030231     | Down       | 0.96329908    | 0.99989712   |
| miR-6726-5p   | -0.0030115     | Down       | 0.89240213    | 0.99989712   |
| miR-135b-3p   | -0.0029845     | Down       | 0.93259063    | 0.99989712   |
| miR-4451      | -0.0029258     | Down       | 0.90566083    | 0.99989712   |
| miR-5196-3p   | -0.0028833     | Down       | 0.9410239     | 0.99989712   |
| miR-30a-3p    | -0.0028798     | Down       | 0.96173026    | 0.99989712   |
| miR-7139-3p   | -0.0028746     | Down       | 0.93108389    | 0.99989712   |
| miR-144-5p    | -0.0028729     | Down       | 0.98291237    | 0.99989712   |
| miR-204-5p    | -0.0027756     | Down       | 0.96390565    | 0.99989712   |
| miR-6729-5p   | -0.0027536     | Down       | 0.9342249     | 0.99989712   |
| miR-524-3p    | -0.0027175     | Down       | 0.93463267    | 0.99989712   |
| miR-4692      | -0.0027174     | Down       | 0.93330804    | 0.99989712   |
| miR-4254      | -0.0027026     | Down       | 0.94607389    | 0.99989712   |
| miR-197-3p    | -0.0026814     | Down       | 0.97446832    | 0.99989712   |
| miR-6808-5p   | -0.0026431     | Down       | 0.94498915    | 0.99989712   |
| miR-6795-5p   | -0.0026283     | Down       | 0.91449896    | 0.99989712   |
| miR-4324      | -0.00262       | Down       | 0.9400151     | 0.99989712   |
| miR-513b-3p   | -0.0024873     | Down       | 0.93432363    | 0.99989712   |
| miR-193b-3p   | -0.0024777     | Down       | 0.98359496    | 0.99989712   |
| miR-3664-3p   | -0.0024542     | Down       | 0.92943662    | 0.99989712   |
| miR-6743-5p   | -0.0024529     | Down       | 0.9027108     | 0.99989712   |
| miR-6507-5p   | -0.0024365     | Down       | 0.93017877    | 0.99989712   |
| miR-5692b     | -0.0024253     | Down       | 0.90975261    | 0.99989712   |
| miR-3158-5p   | -0.0024079     | Down       | 0.93792342    | 0.99989712   |
| miR-758-5p    | -0.0023229     | Down       | 0.95116671    | 0.99989712   |
| miR-1283      | -0.0023082     | Down       | 0.95634844    | 0.99989712   |
| miR-6510-3p   | -0.0022771     | Down       | 0.94891395    | 0.99989712   |
| miR-3121-5p   | -0.0022103     | Down       | 0.97235279    | 0.99989712   |
| miR-25-3p     | -0.0021921     | Down       | 0.97945036    | 0.99989712   |
| miR-3681-3p   | -0.0021322     | Down       | 0.9550712     | 0.99989712   |
| miR-6887-3p   | -0.0020516     | Down       | 0.95483442    | 0.99989712   |
| miR-101-5p    | -0.0020024     | Down       | 0.96328694    | 0.99989712   |
| miR-6799-5p   | -0.0019956     | Down       | 0.96608755    | 0.99989712   |
| miR-219b-3p   | -0.0019641     | Down       | 0.95601519    | 0.99989712   |
| miR-580-3p    | -0.0019317     | Down       | 0.94837611    | 0.99989712   |
| miR-6792-3p   | -0.0019166     | Down       | 0.956652      | 0.99989712   |
| NC1_00000215  | -0.0018841     | Down       | 0.96373938    | 0.99989712   |
| miR-6811-5p   | -0.0018232     | Down       | 0.96188232    | 0.99989712   |
| miR-4704-3p   | -0.0017889     | Down       | 0.96132284    | 0.99989712   |
| miR-4309      | -0.0017661     | Down       | 0.95105748    | 0.99989712   |

(Continued)
Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value   | P-adj   |
|--------------|----------------|------------|-----------|---------|
| miR-2392     | -0.0017598     | Down       | 0.980127  | 0.99898712 |
| miR-4632-3p  | -0.0017532     | Down       | 0.94929584 | 0.99898712 |
| miR-218-2-3p | -0.0017235     | Down       | 0.9674829  | 0.99898712 |
| miR-711      | -0.0016486     | Down       | 0.95731286 | 0.99898712 |
| miR-4290     | -0.0016305     | Down       | 0.97739464 | 0.99898712 |
| miR-5189-5p  | -0.0016252     | Down       | 0.96215081 | 0.99898712 |
| miR-500b-5p  | -0.001612      | Down       | 0.95268854 | 0.99898712 |
| miR-3648     | -0.0014824     | Down       | 0.96589432 | 0.99898712 |
| miR-4674     | -0.0014518     | Down       | 0.94880466 | 0.99898712 |
| miR-1208     | -0.0013905     | Down       | 0.96583714 | 0.99898712 |
| miR-4751     | -0.0013897     | Down       | 0.95352909 | 0.99898712 |
| miR-433-3p   | -0.0013693     | Down       | 0.97819644 | 0.99898712 |
| miR-4308     | -0.0013122     | Down       | 0.95611105 | 0.99898712 |
| miR-548j-5p  | -0.0012819     | Down       | 0.97553329 | 0.99898712 |
| miR-8068     | -0.0012147     | Down       | 0.95925337 | 0.99898712 |
| miR-6759-5p  | -0.0011223     | Down       | 0.96731    | 0.99898712 |
| miR-6715b-3p | -0.0011213     | Down       | 0.97036889 | 0.99898712 |
| miR-548an    | -0.0011134     | Down       | 0.96318494 | 0.99898712 |
| miR-6715b-5p | -0.0010821     | Down       | 0.9703719  | 0.99898712 |
| miR-510-5p   | -0.0010532     | Down       | 0.97075147 | 0.99898712 |
| miR-4694-5p  | -0.0010357     | Down       | 0.98024922 | 0.99898712 |
| miR-6817-5p  | -0.0010043     | Down       | 0.96991745 | 0.99898712 |
| miR-3606-3p  | -0.0009922     | Down       | 0.98932447 | 0.99904195 |
| miR-3609     | -0.0009853     | Down       | 0.97323962 | 0.99898712 |
| miR-518b     | -0.000889      | Down       | 0.98279757 | 0.99898712 |
| miR-124-3p   | -0.0008157     | Down       | 0.97080446 | 0.99898712 |
| miR-1204     | -0.0007893     | Down       | 0.98561309 | 0.99898712 |
| miR-1255b-5p | -0.0007106     | Down       | 0.98083044 | 0.99898712 |
| miR-6837-5p  | -0.0006794     | Down       | 0.98080458 | 0.99898712 |
| miR-507      | -0.0006167     | Down       | 0.98680757 | 0.99904195 |
| miR-96-3p    | -0.0005904     | Down       | 0.98939967 | 0.99904195 |
| miR-3186-5p  | -0.0005172     | Down       | 0.98303093 | 0.99898712 |
| miR-370-5p   | -0.0005016     | Down       | 0.98540341 | 0.99898712 |
| miR-4273     | -0.000445      | Down       | 0.99087488 | 0.99904195 |
| miR-6798-3p  | -0.0004329     | Down       | 0.99242048 | 0.99904195 |
| miR-3122     | -0.0004157     | Down       | 0.98547863 | 0.99898712 |
| miR-3911     | -0.0003118     | Down       | 0.99522027 | 0.99904195 |
| miR-371b-3p  | -0.0003055     | Down       | 0.99364604 | 0.99904195 |
| miR-6868-5p  | -0.0002811     | Down       | 0.99205446 | 0.99904195 |
| miR-299-3p   | -0.0002789     | Down       | 0.99354178 | 0.99904195 |
| miR-302c-5p  | -0.0002069     | Down       | 0.99238835 | 0.99904195 |
| miR-6505-3p  | -0.0002018     | Down       | 0.99670956 | 0.99904195 |
| miR-548b-3p  | 4.80×10⁻⁵      | Up         | 0.99920946 | 0.99904195 |
| miR-627-3p   | 4.86×10⁻⁵      | Up         | 0.99946876 | 0.99904195 |
| miR-6718-5p  | 0.00012601     | Up         | 0.99652509 | 0.99904195 |
| miR-6790-5p  | 0.00014766     | Up         | 0.9958867  | 0.99904195 |
| miR-466a-3p  | 0.00017412     | Up         | 0.99603995 | 0.99904195 |
| miR-302e     | 0.00019522     | Up         | 0.99636872 | 0.99904195 |
| miR-6787-5p  | 0.00026324     | Up         | 0.99312444 | 0.99904195 |

(Continued)
| miRNAs       | Log2FoldChange | Regulation | P-value  | P-adj     |
|-------------|---------------|------------|----------|-----------|
| miR-147b    | 0.00029406    | Up         | 0.99417609 | 0.99904195 |
| miR-4740-5p | 0.00029998    | Up         | 0.99473955 | 0.99904195 |
| miR-4800-3p | 0.0003067     | Up         | 0.99309816 | 0.99904195 |
| miR-3683    | 0.00036807    | Up         | 0.9902761  | 0.99904195 |
| miR-3689a-5p| 0.00038906    | Up         | 0.98808154 | 0.99904195 |
| miR-6827-3p | 0.00039472    | Up         | 0.98677094 | 0.99904195 |
| miR-4791    | 0.00046421    | Up         | 0.98246602 | 0.99904195 |
| miR-3146    | 0.00052485    | Up         | 0.97570083 | 0.99904195 |
| miR-4798-3p | 0.00052915    | Up         | 0.98085346 | 0.99904195 |
| miR-7845-5p | 0.00054149    | Up         | 0.9840955  | 0.99904195 |
| miR-587     | 0.00056284    | Up         | 0.9875682  | 0.99904195 |
| miR-4706    | 0.00057658    | Up         | 0.9896598  | 0.99904195 |
| miR-3650    | 0.00060113    | Up         | 0.98246602 | 0.99904195 |
| miR-4537    | 0.00062976    | Up         | 0.98562082 | 0.99904195 |
| miR-6129    | 0.00065819    | Up         | 0.97570083 | 0.99904195 |
| miR-4798-3p | 0.00069812    | Up         | 0.98055025 | 0.99904195 |
| miR-7161-3p | 0.00079577    | Up         | 0.98055025 | 0.99904195 |
| miR-587     | 0.00079607    | Up         | 0.98562082 | 0.99904195 |
| miR-1298-5p | 0.00083155    | Up         | 0.98562082 | 0.99904195 |
| miR-3655    | 0.00087755    | Up         | 0.98068497 | 0.99904195 |
| miR-6806-3p | 0.0009646    | Up         | 0.97337242 | 0.99904195 |
| miR-1298-5p | 0.0010153    | Up         | 0.96964137 | 0.99904195 |
| miR-3148    | 0.00104513   | Up         | 0.96629547 | 0.99904195 |
| miR-1298-3p | 0.00116617   | Up         | 0.96964137 | 0.99904195 |
| miR-378a-5p | 0.00119067   | Up         | 0.96964137 | 0.99904195 |
| miR-7161-3p | 0.0012234    | Up         | 0.96964137 | 0.99904195 |
| miR-23a-3p  | 0.00125302   | Up         | 0.96964137 | 0.99904195 |
| miR-6806-3p | 0.00127333   | Up         | 0.96964137 | 0.99904195 |
| miR-3191-5p | 0.00129186   | Up         | 0.96964137 | 0.99904195 |
| miR-4699-5p | 0.00129705   | Up         | 0.96964137 | 0.99904195 |
| miR-3126-3p | 0.00139265   | Up         | 0.96964137 | 0.99904195 |
| miR-3140-5p | 0.00140044   | Up         | 0.96964137 | 0.99904195 |
| miR-6723-5p | 0.00142556   | Up         | 0.96964137 | 0.99904195 |
| miR-573     | 0.00142671   | Up         | 0.96964137 | 0.99904195 |
| miR-4733-5p | 0.00143716   | Up         | 0.96964137 | 0.99904195 |
| miR-92b-3p  | 0.00146746   | Up         | 0.96964137 | 0.99904195 |
| miR-1180-5p | 0.00147286   | Up         | 0.96964137 | 0.99904195 |
| miR-4768-3p | 0.00148174   | Up         | 0.96964137 | 0.99904195 |
| miR-6804-3p | 0.00150997   | Up         | 0.96964137 | 0.99904195 |
| miR-5010-5p | 0.00153164   | Up         | 0.96964137 | 0.99904195 |

Table 9 (Continued).
Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value   | P-adj    |
|--------------|----------------|------------|-----------|----------|
| miR-7153-5p  | 0.00153251     | Up         | 0.95803798| 0.99898712|
| miR-4789-5p  | 0.00153826     | Up         | 0.97000256| 0.99898712|
| miR-149-5p   | 0.00169817     | Up         | 0.95691905| 0.99898712|
| miR-8077     | 0.00173739     | Up         | 0.96228581| 0.99898712|
| miR-127-5p   | 0.00173908     | Up         | 0.95183069| 0.99898712|
| miR-4501     | 0.00175705     | Up         | 0.95082433| 0.99898712|
| miR-376a-5p  | 0.00176507     | Up         | 0.96843308| 0.99898712|
| miR-4279     | 0.00182263     | Up         | 0.97743092| 0.99898712|
| miR-1282     | 0.0018404      | Up         | 0.95314944| 0.99898712|
| miR-5583-5p  | 0.00185753     | Up         | 0.94002562| 0.99898712|
| miR-4437     | 0.00191567     | Up         | 0.96952875| 0.99898712|
| miR-5583-5p  | 0.00192048     | Up         | 0.96868055| 0.99898712|
| miR-1228-5p  | 0.00201888     | Up         | 0.92703988| 0.99898712|
| miR-5687     | 0.0020738      | Up         | 0.96196251| 0.99898712|
| miR-6816-3p  | 0.00215482     | Up         | 0.95631146| 0.99898712|
| miR-519c-3p  | 0.00215986     | Up         | 0.95475733| 0.99898712|
| miR-4703-3p  | 0.00216083     | Up         | 0.96161646| 0.99898712|
| miR-4655-3p  | 0.00219685     | Up         | 0.94525282| 0.99898712|
| miR-1295a    | 0.00219999     | Up         | 0.93784315| 0.99898712|
| miR-3940-3p  | 0.00229041     | Up         | 0.96273026| 0.99898712|
| miR-4719     | 0.00229203     | Up         | 0.96646563| 0.99898712|
| miR-4677-5p  | 0.0022962      | Up         | 0.94525282| 0.99898712|
| miR-6847-3p  | 0.00230232     | Up         | 0.96283202| 0.99898712|
| miR-4763-5p  | 0.00238533     | Up         | 0.93039316| 0.99898712|
| miR-4289     | 0.00239412     | Up         | 0.95728448| 0.99898712|
| miR-300      | 0.00239907     | Up         | 0.94468572| 0.99898712|
| miR-629-3p   | 0.00243816     | Up         | 0.92961757| 0.99898712|
| miR-4432     | 0.00245061     | Up         | 0.90864201| 0.99898712|
| miR-4524b-3p | 0.002466       | Up         | 0.94444986| 0.99898712|
| miR-552-5p   | 0.00249528     | Up         | 0.94630486| 0.99898712|
| miR-1247-3p  | 0.00258503     | Up         | 0.9230124 | 0.99898712|
| miR-4417     | 0.0027244      | Up         | 0.94819632| 0.99898712|
| miR-195-3p   | 0.00280151     | Up         | 0.94134865| 0.99898712|
| miR-4763-5p  | 0.00283221     | Up         | 0.94567128| 0.99898712|
| miR-559      | 0.00283475     | Up         | 0.93246615| 0.99898712|
| miR-1288-5p  | 0.00287294     | Up         | 0.91069106| 0.99898712|
| miR-3128     | 0.00290191     | Up         | 0.9164185 | 0.99898712|
| miR-335-3p   | 0.0030629      | Up         | 0.96743191| 0.99898712|
| miR-92a-3p   | 0.00309934     | Up         | 0.96666665| 0.99898712|
| miR-328-5p   | 0.00318751     | Up         | 0.91969491| 0.99898712|
| miR-8058     | 0.00322494     | Up         | 0.93576164| 0.99898712|
| miR-3654     | 0.00324715     | Up         | 0.9154113 | 0.99898712|
| miR-330-5p   | 0.00325701     | Up         | 0.94317225| 0.99898712|
| miR-5089-3p  | 0.00328345     | Up         | 0.92178001| 0.99898712|
| miR-6830-3p  | 0.0032993      | Up         | 0.92150396| 0.99898712|

(Continued)
| miRNAs       | Log2FoldChange | Regulation | P-value | P-adj  |
|--------------|----------------|------------|---------|--------|
| miR-4752     | 0.00330367     | Up         | 0.93028464 | 0.99898712 |
| miR-331-5p   | 0.00331525     | Up         | 0.92813569 | 0.99898712 |
| miR-663b     | 0.00331973     | Up         | 0.91301131 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| let-7b-3p    | 0.00337109     | Up         | 0.93884878 | 0.99898712 |
| miR-548aw    | 0.00338056     | Up         | 0.93891524 | 0.99898712 |
| miR-1271-3p  | 0.00338477     | Up         | 0.92848311 | 0.99898712 |
| miR-663b     | 0.00338463     | Up         | 0.93474718 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| let-7b-3p    | 0.00337109     | Up         | 0.93884878 | 0.99898712 |
| miR-548aw    | 0.00338056     | Up         | 0.93891524 | 0.99898712 |
| miR-1271-3p  | 0.00338477     | Up         | 0.92848311 | 0.99898712 |
| miR-663b     | 0.00338463     | Up         | 0.93474718 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| let-7b-3p    | 0.00337109     | Up         | 0.93884878 | 0.99898712 |
| miR-548aw    | 0.00338056     | Up         | 0.93891524 | 0.99898712 |
| miR-1271-3p  | 0.00338477     | Up         | 0.92848311 | 0.99898712 |
| miR-663b     | 0.00338463     | Up         | 0.93474718 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| let-7b-3p    | 0.00337109     | Up         | 0.93884878 | 0.99898712 |
| miR-548aw    | 0.00338056     | Up         | 0.93891524 | 0.99898712 |
| miR-1271-3p  | 0.00338477     | Up         | 0.92848311 | 0.99898712 |
| miR-663b     | 0.00338463     | Up         | 0.93474718 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| let-7b-3p    | 0.00337109     | Up         | 0.93884878 | 0.99898712 |
| miR-548aw    | 0.00338056     | Up         | 0.93891524 | 0.99898712 |
| miR-1271-3p  | 0.00338477     | Up         | 0.92848311 | 0.99898712 |
| miR-663b     | 0.00338463     | Up         | 0.93474718 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| let-7b-3p    | 0.00337109     | Up         | 0.93884878 | 0.99898712 |
| miR-548aw    | 0.00338056     | Up         | 0.93891524 | 0.99898712 |
| miR-1271-3p  | 0.00338477     | Up         | 0.92848311 | 0.99898712 |
| miR-663b     | 0.00338463     | Up         | 0.93474718 | 0.99898712 |
| miR-4764-3p  | 0.00336323     | Up         | 0.93474718 | 0.99898712 |
| miRNAs         | Log2FoldChange | Regulation | P-value  | P-adj   |
|---------------|----------------|------------|----------|---------|
| miR-3915      | 0.00526613     | Up         | 0.83166795 | 0.99505896 |
| miR-6719-3p   | 0.00527162     | Up         | 0.88640055 | 0.99898712 |
| miR-4436b-3p  | 0.00527661     | Up         | 0.84266097 | 0.99654281 |
| miR-4283      | 0.00527869     | Up         | 0.8450852  | 0.99654281 |
| miR-593-5p    | 0.00531576     | Up         | 0.84789014 | 0.99654281 |
| miR-6719-5p   | 0.00532191     | Up         | 0.87262952 | 0.99898712 |
| miR-4436b-5p  | 0.00532661     | Up         | 0.8450852  | 0.99654281 |
| miR-3927-5p   | 0.00548928     | Up         | 0.86784757 | 0.99898712 |
| miR-626       | 0.0055202      | Up         | 0.82249207 | 0.99252298 |
| miR-6070      | 0.00553692     | Up         | 0.86897821 | 0.99898712 |
| miR-6074      | 0.00554496     | Up         | 0.83968303 | 0.99654281 |
| miR-548ak     | 0.00559526     | Up         | 0.86340327 | 0.99898712 |
| miR-26a-2-3p  | 0.00561578     | Up         | 0.93206718 | 0.99898712 |
| miR-6758-5p   | 0.00567841     | Up         | 0.81085101 | 0.99064883 |
| miR-3713      | 0.00577598     | Up         | 0.77736592 | 0.985258  |
| miR-2116-3p   | 0.00580625     | Up         | 0.90984233 | 0.99898712 |
| miR-7851-3p   | 0.00588184     | Up         | 0.8415095  | 0.99654281 |
| miR-4803      | 0.00597366     | Up         | 0.88088685 | 0.99898712 |
| miR-514a-3p   | 0.00604114     | Up         | 0.86688525 | 0.99898712 |
| miR-1972      | 0.00604884     | Up         | 0.91631474 | 0.99898712 |
| miR-875-3p    | 0.00605147     | Up         | 0.81226805 | 0.99064883 |
| miR-302d-5p   | 0.00609671     | Up         | 0.82642356 | 0.99340905 |
| miR-6791-3p   | 0.00611437     | Up         | 0.82015659 | 0.99144047 |
| miR-23a-5p    | 0.00611826     | Up         | 0.84035989 | 0.99654281 |
| miR-4690-5p   | 0.00627341     | Up         | 0.88491742 | 0.99898712 |
| miR-6851-5p   | 0.0064148      | Up         | 0.91852166 | 0.99898712 |
| miR-548x-3p   | 0.00647126     | Up         | 0.78597976 | 0.98664734 |
| miR-4263      | 0.00647493     | Up         | 0.82323114 | 0.99252298 |
| miR-30c-2-3p  | 0.00658433     | Up         | 0.78325746 | 0.98664734 |
| miR-4253      | 0.00662912     | Up         | 0.86666295 | 0.99898712 |
| miR-8085      | 0.0066686      | Up         | 0.8078958  | 0.99064883 |
| miR-514a-5p   | 0.00667439     | Up         | 0.83230378 | 0.9955233  |
| miR-4469-5p   | 0.00667776     | Up         | 0.87862251 | 0.99898712 |
| miR-3127-3p   | 0.00671663     | Up         | 0.8253678  | 0.99340905 |
| miR-548x-3p   | 0.00675695     | Up         | 0.8391941  | 0.99654281 |
| miR-4469      | 0.00679696     | Up         | 0.79739667 | 0.98759926 |
| miR-4678      | 0.00682196     | Up         | 0.84156448 | 0.99654281 |
| miR-6843-3p   | 0.00693783     | Up         | 0.81870342 | 0.99127826 |
| miR-5590-5p   | 0.00699154     | Up         | 0.88519385 | 0.99898712 |
| miR-367-5p    | 0.00701992     | Up         | 0.7621473  | 0.98140055 |
| miR-3675      | 0.00705138     | Up         | 0.86781429 | 0.99898712 |
| miR-6500-5p   | 0.00709102     | Up         | 0.88389959 | 0.99898712 |
| miR-7109-3p   | 0.00715258     | Up         | 0.86817229 | 0.99898712 |
| miR-761       | 0.00725141     | Up         | 0.80469338 | 0.99064883 |
| miR-3685      | 0.00726365     | Up         | 0.79280404 | 0.98676309 |
| miR-4714-3p   | 0.00729509     | Up         | 0.85892014 | 0.99898712 |
| miR-6866-5p   | 0.00730567     | Up         | 0.84621505 | 0.99654281 |
| miR-4526      | 0.00733506     | Up         | 0.76375104 | 0.98140055 |
| miR-4436b-5p  | 0.00741513     | Up         | 0.88151895 | 0.99898712 |

(Continued)
| miRNAs     | Log2FoldChange | Regulation | P-value       | P-adj       |
|------------|----------------|------------|---------------|-------------|
| miR-3153   | 0.0074168      | Up         | 0.7694721     | 0.98237037  |
| miR-4772-3p| 0.0075411      | Up         | 0.81766753    | 0.99127826  |
| miR-3663-5p| 0.00762725     | Up         | 0.80974872    | 0.99064883  |
| miR-3065-5p| 0.00770806     | Up         | 0.73065485    | 0.97193735  |
| miR-3141   | 0.00776054     | Up         | 0.90607938    | 0.99898712  |
| miR-1292-3p| 0.00776917     | Up         | 0.81851928    | 0.99127826  |
| miR-4756-5p| 0.00780377     | Up         | 0.79286606    | 0.98676309  |
| miR-7976   | 0.00782671     | Up         | 0.8670542     | 0.99898712  |
| miR-3140-3p| 0.0078855      | Up         | 0.79720547    | 0.98759926  |
| miR-1284   | 0.00799964     | Up         | 0.8215816     | 0.99654281  |
| miR-3174   | 0.00810481     | Up         | 0.87470817    | 0.99898712  |
| miR-6720-5p| 0.00818865     | Up         | 0.84626862    | 0.99654281  |
| miR-4304   | 0.0082361      | Up         | 0.79025258    | 0.98664734  |
| miR-1264   | 0.00861208     | Up         | 0.8411249     | 0.99654281  |
| miR-3912-3p| 0.00863814     | Up         | 0.8743044     | 0.99898712  |
| miR-4506   | 0.00870046     | Up         | 0.90793938    | 0.99898712  |
| miR-1284   | 0.008722       | Up         | 0.79085209    | 0.98664734  |
| miR-5681b  | 0.00876411     | Up         | 0.8584131     | 0.99898712  |
| miR-548aa  | 0.00890056     | Up         | 0.84798854    | 0.99654281  |
| miR-4269   | 0.00892899     | Up         | 0.81451598    | 0.99122915  |
| miR-7158-5p| 0.00894845     | Up         | 0.86729561    | 0.99898712  |
| miR-452-5p | 0.00895862     | Up         | 0.85771099    | 0.99898712  |
| miR-4490   | 0.0089673      | Up         | 0.73250027    | 0.9725372   |
| miR-655-5p | 0.00904604     | Up         | 0.74753094    | 0.97721563  |
| miR-6506-5p| 0.00904757     | Up         | 0.67599786    | 0.95648223  |
| miR-4755-5p| 0.0090802      | Up         | 0.76114498    | 0.98140055  |
| miR-1273a  | 0.00909625     | Up         | 0.70701626    | 0.96360966  |
| miR-6878-5p| 0.00916874     | Up         | 0.83254408    | 0.9955233   |
| miR-6840-5p| 0.00917447     | Up         | 0.78853145    | 0.98664734  |
| miR-888-5p | 0.00930898     | Up         | 0.6728992     | 0.9548223   |
| miR-4494   | 0.00934109     | Up         | 0.65694105    | 0.95321673  |
| miR-3689b-3p| 0.00939617    | Up         | 0.78293383    | 0.98664734  |
| miR-6804-5p| 0.00939724     | Up         | 0.65264057    | 0.95321673  |
| miR-4698   | 0.00943298     | Up         | 0.84142941    | 0.99654281  |
| miR-3134   | 0.00954703     | Up         | 0.73284844    | 0.9725372   |
| miR-6880-5p| 0.00956249     | Up         | 0.84058856    | 0.99654281  |
| miR-6764-3p| 0.00958155     | Up         | 0.7778236     | 0.985258    |
| miR-6840-3p| 0.00960503     | Up         | 0.8008763     | 0.98907164  |
| miR-596    | 0.009634       | Up         | 0.6972447     | 0.96239183  |
| miR-6823-3p| 0.0096698      | Up         | 0.83033428    | 0.99489005  |
| miR-3200-5p| 0.00979753     | Up         | 0.82584554    | 0.99340905  |
| miR-6828-3p| 0.00987954     | Up         | 0.76981499    | 0.98237037  |
| miR-4783-3p| 0.00995837     | Up         | 0.73689972    | 0.97354829  |
| miR-4670-5p| 0.01004604     | Up         | 0.76449957    | 0.98140055  |
| miR-136-3p | 0.01006505     | Up         | 0.85730812    | 0.99898712  |
| miR-365a-5p| 0.01010965     | Up         | 0.7008463     | 0.96268515  |
| miR-4748   | 0.01013589     | Up         | 0.79150405    | 0.98664734  |
| miR-4742-3p| 0.0101833      | Up         | 0.77805094    | 0.985258    |
Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value    | P-adj       |
|------------|----------------|------------|------------|-------------|
| miR-4520-5p| 0.0102179      | Up         | 0.8304177  | 0.99448905  |
| miR-1180-3p| 0.01021945     | Up         | 0.66003638 | 0.95397723  |
| miR-3691-5p| 0.01022646     | Up         | 0.72226246 | 0.96627512  |
| miR-2681-5p| 0.01028915     | Up         | 0.71152528 | 0.96505269  |
| miR-203a-5p| 0.01029073     | Up         | 0.79814929 | 0.98759926  |
| miR-4536-5p| 0.01032611     | Up         | 0.7659882  | 0.98213308  |
| miR-1180-3p| 0.01032611     | Up         | 0.72387137 | 0.96691758  |
| miR-3691-5p| 0.01032611     | Up         | 0.72226246 | 0.96627512  |
| miR-2681-5p| 0.01032611     | Up         | 0.71152528 | 0.96505269  |
| miR-203a-5p| 0.01032611     | Up         | 0.79814929 | 0.98759926  |
| miR-3691-5p| 0.01032611     | Up         | 0.7659882  | 0.98213308  |
| miR-2681-5p| 0.01032611     | Up         | 0.72387137 | 0.96691758  |
| miR-203a-5p| 0.01032611     | Up         | 0.79814929 | 0.98759926  |
| miR-3691-5p| 0.01032611     | Up         | 0.7659882  | 0.98213308  |
| miR-2681-5p| 0.01032611     | Up         | 0.72387137 | 0.96691758  |
| miR-203a-5p| 0.01032611     | Up         | 0.79814929 | 0.98759926  |
| miR-3691-5p| 0.01032611     | Up         | 0.7659882  | 0.98213308  |
| miR-2681-5p| 0.01032611     | Up         | 0.72387137 | 0.96691758  |
| miR-203a-5p| 0.01032611     | Up         | 0.79814929 | 0.98759926  |
| miR-3691-5p| 0.01032611     | Up         | 0.7659882  | 0.98213308  |
Table 9 (Continued).

| miRNAs                  | Log2FoldChange | Regulation | P-value    | P-adj     |
|-------------------------|----------------|------------|------------|-----------|
| miR-4781-3p             | 0.01182106     | Up         | 0.71425667 | 0.96505269 |
| miR-4502                | 0.01188395     | Up         | 0.66321265 | 0.9510802  |
| miR-3149                | 0.01193411     | Up         | 0.75330525 | 0.9775429  |
| miR-4712-5p             | 0.01193425     | Up         | 0.77741809 | 0.985258   |
| miR-3310-3p             | 0.01198522     | Up         | 0.72070737 | 0.9658066  |
| miR-4473                | 0.01201285     | Up         | 0.61156537 | 0.94386479 |
| miR-3142                | 0.01202439     | Up         | 0.82632704 | 0.99340905 |
| miR-1910-5p             | 0.01204555     | Up         | 0.86979935 | 0.9989712  |
| miR-5008-5p             | 0.01210927     | Up         | 0.67184466 | 0.9564823  |
| miR-6769a-3p            | 0.01213759     | Up         | 0.67377095 | 0.9564823  |
| miR-550b-2-5p           | 0.0123235      | Up         | 0.6803527  | 0.95756103 |
| miR-132-5p              | 0.01239979     | Up         | 0.62785584 | 0.9498341  |
| miR-377-5p              | 0.01243349     | Up         | 0.73963553 | 0.97402999 |
| miR-3612                | 0.01246368     | Up         | 0.75708145 | 0.98140055 |
| miR-3908                | 0.01253284     | Up         | 0.71684988 | 0.96505269 |
| miR-34c-5p              | 0.01254468     | Up         | 0.7048188  | 0.9630966  |
| miR-6765-5p             | 0.01255238     | Up         | 0.67419733 | 0.9564823  |
| miR-4745-3p             | 0.01256461     | Up         | 0.69898791 | 0.96268515 |
| miR-4738-3p             | 0.01276161     | Up         | 0.59320033 | 0.93770773 |
| miR-4638-3p             | 0.01277387     | Up         | 0.59292589 | 0.93770773 |
| miR-1914-5p             | 0.01282594     | Up         | 0.73045802 | 0.97193735 |
| miR-129-5p              | 0.01283002     | Up         | 0.63258914 | 0.95096807 |
| miR-544a                | 0.01283799     | Up         | 0.74617411 | 0.9764091  |
| miR-579-5p              | 0.01285453     | Up         | 0.62994592 | 0.9565239  |
| miR-3914                | 0.01286086     | Up         | 0.62464601 | 0.94934372 |
| miR-651-3p              | 0.01287047     | Up         | 0.69538348 | 0.96185982 |
| miR-6084                | 0.01293593     | Up         | 0.65583838 | 0.95321673 |
| miR-181b-3p             | 0.01306301     | Up         | 0.78935621 | 0.98667434 |
| miR-410-5p              | 0.01310405     | Up         | 0.51984245 | 0.91632037 |
| miR-323b-5p             | 0.01310415     | Up         | 0.69390838 | 0.96137172 |
| miR-7849-3p             | 0.0131112      | Up         | 0.61849336 | 0.94829596 |
| miR-597-3p              | 0.01311716     | Up         | 0.71900872 | 0.96505269 |
| miR-124-5p              | 0.0131234      | Up         | 0.79377874 | 0.98694309 |
| miR-363-5p              | 0.01318634     | Up         | 0.76210555 | 0.98140055 |
| miR-3934-3p             | 0.01322045     | Up         | 0.67932933 | 0.9566446  |
| miR-3687                | 0.01324644     | Up         | 0.58548597 | 0.93868471 |
| miR-3167                | 0.01330917     | Up         | 0.63645436 | 0.95096807 |
| miR-4710                | 0.01333306     | Up         | 0.52796647 | 0.92119547 |
| miR-4307                | 0.01336258     | Up         | 0.70482576 | 0.9630966  |
| miR-4775                | 0.01343595     | Up         | 0.54052103 | 0.9213181  |
| miR-3928-5p             | 0.01351781     | Up         | 0.80368404 | 0.99063213 |
| miR-92a-1-5p            | 0.01356483     | Up         | 0.75096762 | 0.97770354 |
| miR-517-5p              | 0.01361653     | Up         | 0.66420343 | 0.95510802 |
| miR-1292-5p             | 0.01366842     | Up         | 0.63710706 | 0.95096807 |
| miR-202-3p              | 0.01377676     | Up         | 0.62199514 | 0.94868101 |
| miR-8056                | 0.01404629     | Up         | 0.65642876 | 0.95321673 |
| miR-3936                | 0.01405122     | Up         | 0.69131766 | 0.96077402 |
| miR-4661-3p             | 0.01406232     | Up         | 0.53649807 | 0.9213181  |
| miR-4481                | 0.01414048     | Up         | 0.65872097 | 0.95321673 |

(Continued)
Table 9 (Continued).

| miRNAs              | Log2FoldChange | Regulation | P-value     | P-adj       |
|---------------------|----------------|------------|-------------|-------------|
| miR-1298-5p         | 0.01414814     | Up         | 0.70116334  | 0.96268515  |
| miR-429             | 0.01419675     | Up         | 0.57850214  | 0.9346563   |
| miR-4774-3p         | 0.0142617      | Up         | 0.64602929  | 0.95321673  |
| miR-548ad-5p        | 0.01427071     | Up         | 0.56433017  | 0.93029412  |
| miR-4472            | 0.01428134     | Up         | 0.54467602  | 0.92261663  |
| miR-4517            | 0.01429999     | Up         | 0.65536784  | 0.9321673   |
| miR-99b-3p          | 0.01433655     | Up         | 0.54153182  | 0.92167998  |
| miR-4644            | 0.0143617      | Up         | 0.64547146  | 0.95321673  |
| miR-1250-5p         | 0.01443761     | Up         | 0.53908047  | 0.9213181   |
| miR-372-3p          | 0.01455139     | Up         | 0.80755313  | 0.99064883  |
| miR-4640-3p         | 0.01456831     | Up         | 0.78150428  | 0.9867434   |
| miR-105-3p          | 0.01458433     | Up         | 0.55080673  | 0.92349191  |
| miR-4498            | 0.01458433     | Up         | 0.60334631  | 0.94089807  |
| miR-3688-5p         | 0.01464264     | Up         | 0.61124878  | 0.94386479  |
| miR-6801-5p         | 0.01464637     | Up         | 0.60580933  | 0.94188142  |
| miR-4656            | 0.01466241     | Up         | 0.89012295  | 0.99898712  |
| miR-6856-5p         | 0.01469675     | Up         | 0.5891102   | 0.93675929  |
| miR-5586-5p         | 0.01477128     | Up         | 0.67846969  | 0.95648223  |
| miR-4640-3p         | 0.0148236      | Up         | 0.84494113  | 0.99654281  |
| miR-6729-3p         | 0.01483882     | Up         | 0.76047908  | 0.98140055  |
| miR-4531            | 0.01488447     | Up         | 0.59076862  | 0.93675929  |
| miR-3937            | 0.01490706     | Up         | 0.73739196  | 0.97354829  |
| miR-3607-5p         | 0.01492801     | Up         | 0.68988789  | 0.96032633  |
| miR-4744            | 0.01496713     | Up         | 0.58205836  | 0.93464563  |
| miR-1537-3p         | 0.01497413     | Up         | 0.74459679  | 0.97515801  |
| miR-5584-5p         | 0.015004       | Up         | 0.6648476   | 0.95510802  |
| miR-4778-5p         | 0.01507405     | Up         | 0.7091484   | 0.96369664  |
| miR-6852-3p         | 0.01514938     | Up         | 0.63028111  | 0.95086097  |
| miR-938             | 0.01520606     | Up         | 0.65801777  | 0.95321673  |
| miR-3177-5p         | 0.01524968     | Up         | 0.5169696   | 0.91376348  |
| miR-3199            | 0.01580960     | Up         | 0.80976632  | 0.99064883  |
| miR-1185-2-3p       | 0.01550201     | Up         | 0.65535348  | 0.95321673  |
| miR-6509-3p         | 0.01565998     | Up         | 0.44533113  | 0.8892595   |
| miR-6884-5p         | 0.01570405     | Up         | 0.49293956  | 0.90695643  |
| miR-4477a           | 0.01570405     | Up         | 0.49293956  | 0.90695643  |
| miR-1185-2-3p       | 0.01534462     | Up         | 0.71296587  | 0.96502569  |
| miR-6509-3p         | 0.01541891     | Up         | 0.73653953  | 0.97354829  |
| miR-6884-5p         | 0.01565998     | Up         | 0.44533113  | 0.8892595   |
| miR-4426            | 0.0155663      | Up         | 0.60204571  | 0.94829596  |
| miR-4311            | 0.01562945     | Up         | 0.66323241  | 0.95510802  |
| miR-6730-3p         | 0.01579544     | Up         | 0.63661012  | 0.95096807  |
| miR-4796-5p         | 0.01579621     | Up         | 0.81253151  | 0.99064883  |
| miR-378j            | 0.01582298     | Up         | 0.59044664  | 0.93675929  |
| miR-4276            | 0.01582809     | Up         | 0.49987739  | 0.91121111  |
| miR-5091            | 0.01587546     | Up         | 0.51631719  | 0.91376348  |
| miR-622             | 0.01587548     | Up         | 0.65431659  | 0.95321673  |

(Continued)
Table 9 (Continued).

| miRNAs    | Log2FoldChange | Regulation | P-value    | P-adj      |
|-----------|----------------|------------|------------|------------|
| miR-4477b | 0.01595427     | Up         | 0.67510492 | 0.95648223 |
| miR-4480  | 0.01605291     | Up         | 0.68121945 | 0.95825614 |
| miR-6730-5p| 0.0160569      | Up         | 0.6543226  | 0.95321673 |
| miR-4653-5p| 0.01607326     | Up         | 0.60565483 | 0.94188142 |
| miR-3934-5p| 0.01611412     | Up         | 0.64022393 | 0.95096807 |
| miR-4642  | 0.01621443     | Up         | 0.61120826 | 0.94386479 |
| miR-6871-3p| 0.01624775     | Up         | 0.68349862 | 0.95853044 |
| miR-211-5p| 0.01631686     | Up         | 0.78984502 | 0.98667434 |
| miR-448   | 0.01636933     | Up         | 0.68645874 | 0.96036263 |
| miR-548ai | 0.01646598     | Up         | 0.76498329 | 0.98147681 |
| miR-6502-3p| 0.01660247     | Up         | 0.75312865 | 0.97975429 |
| miR-4430  | 0.01667968     | Up         | 0.87860394 | 0.9989712  |
| miR-6740-3p| 0.01668376     | Up         | 0.71732029 | 0.96505269 |
| miR-4727-5p| 0.01670733     | Up         | 0.5998042  | 0.93953261 |
| miR-5684  | 0.01673479     | Up         | 0.78501761 | 0.98667434 |
| miR-5002-3p| 0.01677134     | Up         | 0.66415873 | 0.95321673 |
| miR-1203  | 0.01680127     | Up         | 0.66528781 | 0.95557578 |
| miR-369-3p| 0.01686971     | Up         | 0.60979891 | 0.9436479  |
| miR-200a-3p| 0.01701242     | Up         | 0.52452216 | 0.91825968 |
| miR-375   | 0.01706379     | Up         | 0.55983417 | 0.9276427  |
| miR-30d-5p| 0.01708292     | Up         | 0.7998693  | 0.9830004  |
| miR-3689a-3p| 0.01718387    | Up         | 0.49300838 | 0.90694634 |
| miR-1909-5p| 0.01737509     | Up         | 0.80972313 | 0.99064883 |
| miR-4750-3p| 0.01746273     | Up         | 0.69856279 | 0.96268515 |
| miR-6775-5p| 0.01746273     | Up         | 0.71605815 | 0.96505269 |
| miR-497-3p| 0.0174979      | Up         | 0.50358715 | 0.91147569 |
| miR-4500  | 0.01753437     | Up         | 0.62783916 | 0.949341    |
| miR-139-3p| 0.01757692     | Up         | 0.86938452 | 0.9989712  |
| miR-3194-3p| 0.01763165     | Up         | 0.80799992 | 0.91121111 |
| miR-4679  | 0.01782269     | Up         | 0.5908509  | 0.9367929  |
| miR-27a-5p| 0.01792569     | Up         | 0.56305474 | 0.82970327 |
| miR-1296-5p| 0.01793662     | Up         | 0.58790108 | 0.9367929  |
| miR-4755-3p| 0.01795334     | Up         | 0.54032429 | 0.9213181 |
| miR-671-5p| 0.01798175     | Up         | 0.91512111 | 0.9989712  |
| miR-520e  | 0.01806457     | Up         | 0.70204427 | 0.96268515 |
| miR-670-3p| 0.0181048      | Up         | 0.63264444 | 0.95096807 |
| miR-3929  | 0.01811785     | Up         | 0.52196244 | 0.91732227 |
| miR-936   | 0.01818701     | Up         | 0.50295729 | 0.91147569 |
| miR-203b-5p| 0.0183307      | Up         | 0.54804896 | 0.92261663 |
| miR-6776-3p| 0.01834543     | Up         | 0.70605908 | 0.96360966 |
| miR-3611  | 0.01837621     | Up         | 0.62549396 | 0.9498341  |
| miR-376b-5p| 0.0184051      | Up         | 0.58970873 | 0.9367929  |
| miR-148b-5p| 0.01843913     | Up         | 0.62829493 | 0.9498341  |
| miR-153-3p| 0.01846882     | Up         | 0.60505783 | 0.94188142 |
| miR-4795-5p| 0.01849838     | Up         | 0.62346004 | 0.94925841 |

(Continued)
Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value     | P-adj     |
|--------------|----------------|------------|-------------|-----------|
| miR-551b-5p  | 0.01851548     | Up         | 0.47290103  | 0.89396011|
| miR-6083     | 0.0185183      | Up         | 0.49043732  | 0.90695643|
| miR-6829-5p  | 0.0185316      | Up         | 0.68941596  | 0.96036263|
| miR-1245b-3p | 0.01889982     | Up         | 0.59437657  | 0.93829717|
| miR-323a-5p  | 0.01897084     | Up         | 0.57029425  | 0.93235129|
| miR-4635     | 0.01898759     | Up         | 0.51382454  | 0.91376348|
| miR-5001-3p  | 0.01900715     | Up         | 0.6053071   | 0.94188142|
| miR-939-3p   | 0.01900859     | Up         | 0.68941596  | 0.96036263|
| miR-64       | 0.01904427     | Up         | 0.50975211  | 0.91230009|
| miR-4724-5p  | 0.01904875     | Up         | 0.46392595  | 0.93829717|
| miR-6731-3p  | 0.01906737     | Up         | 0.72346229  | 0.96691758|
| miR-516b-5p  | 0.01910255     | Up         | 0.48676275  | 0.90650744|
| miR-646      | 0.01916462     | Up         | 0.62653619  | 0.9498341 |
| miR-4482-5p  | 0.01920295     | Up         | 0.54096071  | 0.9213181 |
| miR-6823-5p  | 0.01923855     | Up         | 0.46136863  | 0.93856365|
| miR-6801-3p  | 0.01934473     | Up         | 0.71769458  | 0.96505269|
| miR-520c-3p  | 0.01935136     | Up         | 0.59704876  | 0.93868471|
| miR-6815-3p  | 0.01936625     | Up         | 0.76197125  | 0.98140055|
| miR-6514-3p  | 0.01937438     | Up         | 0.4584095   | 0.9213181 |
| miR-6861-5p  | 0.01947914     | Up         | 0.53968436  | 0.9213181 |
| miR-3119     | 0.01953288     | Up         | 0.36524879  | 0.8588192 |
| miR-4700-5p  | 0.01954516     | Up         | 0.39732241  | 0.87364718|
| miR-6795-3p  | 0.01964065     | Up         | 0.7047127   | 0.9668515 |
| miR-5698     | 0.01965235     | Up         | 0.43796949  | 0.88952595|
| miR-4508     | 0.01972715     | Up         | 0.40121234  | 0.87364718|
| miR-551a     | 0.01972754     | Up         | 0.61849932  | 0.94829596|
| miR-1279     | 0.01986827     | Up         | 0.59078677  | 0.93675929|
| miR-3644-5p  | 0.019903       | Up         | 0.45946349  | 0.89360111|
| miR-6741-3p  | 0.01992061     | Up         | 0.58584764  | 0.93575415|
| miR-6130     | 0.02000124     | Up         | 0.41972578  | 0.8823614 |
| miR-3127-5p  | 0.02001376     | Up         | 0.66753131  | 0.95631006|
| miR-3973     | 0.02007343     | Up         | 0.46691545  | 0.89360111|
| miR-6854-5p  | 0.02017661     | Up         | 0.53693007  | 0.9213181 |
| miR-520a-5p  | 0.02025704     | Up         | 0.46924916  | 0.89360111|
| miR-6805-5p  | 0.02026553     | Up         | 0.52305157  | 0.9175171 |
| miR-4294     | 0.02033504     | Up         | 0.35358085  | 0.8588192 |
| miR-93-3p    | 0.02033835     | Up         | 0.76260214  | 0.98140055|
| miR-4684-3p  | 0.02043351     | Up         | 0.43276033  | 0.88833759|
| miR-433-5p   | 0.02044078     | Up         | 0.37902916  | 0.86499071|
| miR-4757-3p  | 0.02046866     | Up         | 0.35122046  | 0.92349191|
| miR-506-3p   | 0.02048703     | Up         | 0.63777341  | 0.95096807|
| miR-517a-3p  | 0.02049334     | Up         | 0.71781101  | 0.96505269|
| miR-548ar-5p | 0.02056456     | Up         | 0.52876085  | 0.92119547|
| miR-544b     | 0.02064575     | Up         | 0.50912217  | 0.91230009|
| miR-194-3p   | 0.02077382     | Up         | 0.39578604  | 0.87310741|
| miR-708-3p   | 0.02098796     | Up         | 0.40708667  | 0.87475982|
| miR-4764-5p  | 0.02118715     | Up         | 0.56812303  | 0.9303065 |
| miR-599      | 0.02121295     | Up         | 0.43535852  | 0.88941554|
| miR-5003-5p  | 0.02124741     | Up         | 0.44566007  | 0.88952595|

(Continued)
| miRNAs      | Log2FoldChange | Regulation | P-value  | P-adj      |
|------------|---------------|------------|----------|------------|
| miR-1226-3p| 0.02132186    | Up         | 0.53242448 | 0.9213181 |
| miR-325    | 0.02133066    | Up         | 0.52051665 | 0.8952595 |
| miR-548a   | 0.02148162    | Up         | 0.44559008 | 0.8952595 |
| miR-6874-5p| 0.02148592    | Up         | 0.54504845 | 0.92261663 |
| miR-7151-5p| 0.02163544    | Up         | 0.30004361 | 0.83872374 |
| miR-499a-5p| 0.02164053    | Up         | 0.5426569  | 0.9222099 |
| miR-4491   | 0.02166487    | Up         | 0.47154073 | 0.89396011 |
| miR-518f-3p| 0.02169151    | Up         | 0.6831004  | 0.95853044 |
| miR-6811-3p| 0.02180674    | Up         | 0.60084548 | 0.93953261 |
| miR-3184-3p| 0.02185842    | Up         | 0.5673034  | 0.9303656 |
| miR-6874-5p| 0.02186425    | Up         | 0.65344952 | 0.95321673 |
| miR-7151-5p| 0.02187098    | Up         | 0.63387065 | 0.95096807 |
| miR-499a-5p| 0.02190151    | Up         | 0.5097307  | 0.9121111 |
| miR-5693   | 0.02206122    | Up         | 0.50386992 | 0.9147569 |
| miR-499b-3p| 0.02210218    | Up         | 0.58322926 | 0.93436563 |
| miR-5700   | 0.02218527    | Up         | 0.38994367 | 0.93679299 |
| miR-4787-5p| 0.02221382    | Up         | 0.65864707 | 0.95321673 |
| miR-4676-5p| 0.02222161    | Up         | 0.47930937 | 0.90243596 |
| miR-6820-5p| 0.0222336    | Up         | 0.58319465 | 0.93436563 |
| miR-4804-5p| 0.02223079    | Up         | 0.49202453 | 0.9069643 |
| miR-380-5p | 0.02227146    | Up         | 0.51536985 | 0.93736348 |
| miR-6742-3p| 0.02237604    | Up         | 0.58352064 | 0.93436563 |
| miR-6833-5p| 0.02243951    | Up         | 0.50926238 | 0.91230009 |
| miR-6871-5p| 0.02248366    | Up         | 0.4268147  | 0.88249386 |
| miR-19b-2-3p| 0.02252117 | Up         | 0.6484582  | 0.95321673 |
| miR-3671   | 0.0225583     | Up         | 0.56831954 | 0.9303656 |
| miR-4447   | 0.02263427    | Up         | 0.4397869  | 0.88952595 |
| miR-525-3p | 0.02266101    | Up         | 0.62137369 | 0.9489596 |
| miR-6861-3p| 0.02274475    | Up         | 0.58950393 | 0.93679299 |
| miR-1275   | 0.02289121    | Up         | 0.91458073 | 0.9989712 |
| miR-518e-5p| 0.02294105    | Up         | 0.45597788 | 0.89182889 |
| miR-1287-3p| 0.02310958    | Up         | 0.4553913  | 0.891297 |
| miR-3617-5p| 0.02323344    | Up         | 0.64968436 | 0.95321673 |
| miR-6783-5p| 0.0233775     | Up         | 0.4356048  | 0.88941554 |
| miR-7160-5p| 0.02343496    | Up         | 0.5065038  | 0.912181 |
| miR-5579-5p| 0.02344538    | Up         | 0.55670065 | 0.9269334 |
| miR-6760-3p| 0.02347367    | Up         | 0.7386143  | 0.97402999 |
| miR-7154-3p| 0.02348532    | Up         | 0.4548674  | 0.891297 |
| miR-4292   | 0.02355298    | Up         | 0.4574619  | 0.89244441 |
| miR-4753-5p| 0.02367013    | Up         | 0.42523878 | 0.8823614 |
| miR-4715-3p| 0.02377472    | Up         | 0.6720246  | 0.95648223 |
| miR-2467-5p| 0.02382854    | Up         | 0.48887473 | 0.90656383 |
| miR-8054   | 0.02383556    | Up         | 0.4418897  | 0.88952595 |
| miR-4313   | 0.02387812    | Up         | 0.6997027  | 0.96268515 |
| miR-6761-5p| 0.02391023    | Up         | 0.46096324 | 0.89396011 |
| miR-1272   | 0.02407068    | Up         | 0.4083297  | 0.87603742 |
| miR-942-3p | 0.02408566    | Up         | 0.40786434 | 0.8756987 |
| miR-4251   | 0.02411161    | Up         | 0.54820586 | 0.92261663 |
| miR-210-5p | 0.02422365    | Up         | 0.47292638 | 0.89396011 |

(Continued)
Table 9 (Continued).

| miRNAs      | Log2FoldChange | Regulation | P-value  | P-adj     |
|-------------|----------------|------------|----------|-----------|
| miR-3927-3p | 0.02423045     | Up         | 0.6019432| 0.93953261|
| miR-553     | 0.02423263     | Up         | 0.56057921| 0.92768099|
| miR-6869-3p | 0.02424035     | Up         | 0.52250599| 0.91732227|
| miR-4999-5p | 0.02427566     | Up         | 0.49857628| 0.91012268|
| miR-324-3p  | 0.02431653     | Up         | 0.71762607| 0.96505269|
| miR-1226-5p | 0.02438006     | Up         | 0.41293737| 0.8804535 |
| miR-3619-3p | 0.02440371     | Up         | 0.44753193| 0.8995259 |
| miR-4999-5p | 0.02441946     | Up         | 0.3989277 | 0.87364718|
| miR-553     | 0.02442544     | Up         | 0.46980283| 0.89396011|
| miR-504-5p  | 0.0244978      | Up         | 0.4506903 | 0.88964976|
| miR-4704-5p | 0.02457118     | Up         | 0.35223335| 0.8588192 |
| miR-504-5p  | 0.02467118     | Up         | 0.4506903 | 0.88964976|
| miR-4746-5p | 0.02469827     | Up         | 0.35698033| 0.92696334|
| miR-20b-3p  | 0.024709       | Up         | 0.36485338| 0.8588192 |
| miR-4461    | 0.02476583     | Up         | 0.55720606| 0.92696334|
| miR-138-5p  | 0.02479871     | Up         | 0.48787964| 0.90656383|
| miR-5481-3p | 0.02480375     | Up         | 0.6616726 | 0.95510802|
| miR-5002-5p | 0.02480824     | Up         | 0.32490062| 0.85489649|
| miR-378e    | 0.0248163      | Up         | 0.44638568| 0.8895259 |
| miR-555     | 0.02482369     | Up         | 0.47334371| 0.89396011|
| miR-4315    | 0.02486687     | Up         | 0.49577156| 0.90944534|
| miR-182-3p  | 0.02490835     | Up         | 0.4216688 | 0.8823614 |
| miR-6780a-5p| 0.02508612     | Up         | 0.65978153| 0.95397723|
| miR-153-5p  | 0.02513058     | Up         | 0.50956146| 0.91230009|
| miR-6774-5p | 0.0252508      | Up         | 0.38578973| 0.86961208|
| miR-372-5p  | 0.025309       | Up         | 0.40036325| 0.87364718|
| miR-3159    | 0.02532184     | Up         | 0.4205062 | 0.8823614 |
| miR-4467    | 0.02533118     | Up         | 0.37976904| 0.86499071|
| miR-3168    | 0.02534439     | Up         | 0.4408406 | 0.8895259 |
| miR-6889-3p | 0.02542975     | Up         | 0.79127667| 0.98667434|
| miR-3150b-3p| 0.02552629     | Up         | 0.42472941| 0.8823614 |
| miR-3614-3p | 0.02580515     | Up         | 0.3249311 | 0.9875125 |
| miR-4724-3p | 0.02587713     | Up         | 0.55314262| 0.92384946|
| miR-3679-3p | 0.02591213     | Up         | 0.71514096| 0.96505269|
| miR-4694-3p | 0.0260404      | Up         | 0.2976176 | 0.83872374|
| miR-4252    | 0.02617889     | Up         | 0.41182256| 0.8793356 |
| miR-4774-5p | 0.02618218     | Up         | 0.37549511| 0.86499071|
| miR-548p    | 0.02618724     | Up         | 0.39523775| 0.87310741|
| miR-6514-5p | 0.02620675     | Up         | 0.37788582| 0.86499071|
| miR-4534    | 0.02621799     | Up         | 0.5168833 | 0.91376348|
| miR-6715a-3p| 0.02624311     | Up         | 0.38614243| 0.86961208|
| miR-3920    | 0.02624926     | Up         | 0.69772176| 0.96250398|
| miR-7113-5p | 0.02634294     | Up         | 0.27562149| 0.83108541|
| miR-4277    | 0.02639359     | Up         | 0.39676404| 0.87358687|
| miR-208b-5p | 0.02643533     | Up         | 0.53329665| 0.91213181|
| miR-449c-3p | 0.02644331     | Up         | 0.29568464| 0.83872374|
| miR-6128    | 0.02667642     | Up         | 0.50234964| 0.91147569|
| miR-548n    | 0.02670062     | Up         | 0.31152037| 0.8475125 |
| miR-6783-3p | 0.02681328     | Up         | 0.33060759| 0.85489649|
| miR-4427    | 0.0268181      | Up         | 0.43559298| 0.88941534|
| miRNAs     | Log2FoldChange | Regulation | P-value  | P-adj   |
|-----------|---------------|------------|----------|---------|
| miR-6802-5p | 0.02693858    | Up         | 0.34140218 | 0.85516921 |
| miR-4529-5p | 0.02695070    | Up         | 0.5346817 | 0.9213181 |
| miR-137    | 0.02707829    | Up         | 0.45509436 | 0.891297 |
| miR-4440   | 0.02709012    | Up         | 0.34362873 | 0.85823697 |
| miR-7515   | 0.02711302    | Up         | 0.30891275 | 0.84601313 |
| miR-7154-5p | 0.02714240   | Up         | 0.37609847 | 0.86499071 |
| miR-4529-3p | 0.02715907    | Up         | 0.5677343 | 0.9303065 |
| miR-6508-3p | 0.02716898    | Up         | 0.54595956 | 0.92261663 |
| miR-620    | 0.02720751    | Up         | 0.49055899 | 0.9065643 |
| miR-1293   | 0.02723147    | Up         | 0.35380018 | 0.8588192 |
| let-7e-3p  | 0.02727251    | Up         | 0.44949219 | 0.8894976 |
| miR-4740-3p | 0.02728007    | Up         | 0.49873931 | 0.91032268 |
| miR-548i   | 0.02728987    | Up         | 0.26610662 | 0.82438552 |
| miR-103a-2-5p | 0.02729507   | Up         | 0.31530614 | 0.84917098 |
| miR-6749-3p | 0.02808208    | Up         | 0.34686008 | 0.8588192 |
| miR-4421   | 0.02826019    | Up         | 0.27679993 | 0.83108541 |
| miR-483-5p | 0.02826129    | Up         | 0.6279789 | 0.9498341 |
| miR-6134   | 0.02834864    | Up         | 0.38783827 | 0.87128003 |
| miR-1294   | 0.02837677    | Up         | 0.26190277 | 0.81988914 |
| miR-1257   | 0.02865524    | Up         | 0.3398032 | 0.85489649 |
| miR-6509-5p | 0.02865937    | Up         | 0.38183201 | 0.8612247 |
| miR-2909   | 0.02885471    | Up         | 0.40484157 | 0.87475982 |
| miR-202-5p | 0.02889478    | Up         | 0.6327852 | 0.9222099 |
| miR-4786-3p | 0.02906531    | Up         | 0.4179162 | 0.8811004 |
| miR-633    | 0.02906807    | Up         | 0.34516107 | 0.8588192 |
| miR-4736   | 0.02909211    | Up         | 0.46430733 | 0.89396011 |
| miR-548ao-3p | 0.0292578     | Up         | 0.41656785 | 0.8804353 |
| miR-6836-3p | 0.0293377     | Up         | 0.53348041 | 0.9213181 |
| miR-525-5p | 0.02937872    | Up         | 0.22645561 | 0.79102241 |
| miR-1251-5p | 0.02938206    | Up         | 0.38217233 | 0.8661247 |
| miR-1306-3p | 0.02940317    | Up         | 0.39092904 | 0.87364718 |
| miR-1231   | 0.02946145    | Up         | 0.23748454 | 0.8038192 |
| miR-4302   | 0.02947784    | Up         | 0.52691064 | 0.92051728 |
| miR-485-5p | 0.02948993    | Up         | 0.37777111 | 0.86499071 |
| miR-561-3p | 0.02950395    | Up         | 0.50098883 | 0.9121111 |
| miR-892c-5p | 0.02953377    | Up         | 0.40024462 | 0.87364718 |
| miR-7159-3p | 0.02955477    | Up         | 0.31285611 | 0.8475125 |
| miR-3124-3p | 0.02959642    | Up         | 0.19296399 | 0.77974911 |
| miR-4476   | 0.02966598    | Up         | 0.53982754 | 0.9213181 |
| miR-5195-3p | 0.02973844    | Up         | 0.3286761 | 0.85489649 |
| miR-6798-5p | 0.02986807    | Up         | 0.53816839 | 0.9213181 |
| miR-4741   | 0.02987025    | Up         | 0.6334498 | 0.9506807 |
| miR-3620-5p | 0.02992468    | Up         | 0.30789948 | 0.8433031 |
| miR-3116   | 0.03005477    | Up         | 0.25045141 | 0.80715125 |
| miR-7973   | 0.03005652    | Up         | 0.3268339 | 0.85489649 |
| miR-5001-5p | 0.0300737     | Up         | 0.53332437 | 0.92389496 |

(Continued)
Table 9 (Continued).

| miRNAs          | Log2FoldChange | Regulation | P-value   | P-adj     |
|-----------------|----------------|------------|-----------|-----------|
| miR-3591-5p     | 0.03027396     | Up         | 0.25123175| 0.80715125|
| miR-6788-5p     | 0.03031197     | Up         | 0.25476983| 0.81031406|
| miR-4770        | 0.03031384     | Up         | 0.17626762| 0.77062416|
| miR-4722-5p     | 0.03041055     | Up         | 0.27028076| 0.83107769|
| miR-670-5p      | 0.03047355     | Up         | 0.20259859| 0.77997491|
| miR-4681        | 0.03050059     | Up         | 0.20091977| 0.77997491|
| miR-218-1-3p    | 0.03054934     | Up         | 0.28342391| 0.83107769|
| miR-6788-5p     | 0.0306498      | Up         | 0.2948952 | 0.83872374|
| miR-4770        | 0.03065132     | Up         | 0.39212471| 0.87281803|
| miR-670-5p      | 0.03066423     | Up         | 0.82336926| 0.99252298|
| miR-4681        | 0.0306804      | Up         | 0.68602982| 0.96029228|
| miR-218-1-3p    | 0.03073293     | Up         | 0.218466  | 0.78840757|
| miR-6788-5p     | 0.03080711     | Up         | 0.44476972| 0.88952595|
| miR-4770        | 0.03094721     | Up         | 0.34121026| 0.85516921|
| miR-670-5p      | 0.03105401     | Up         | 0.43070548| 0.88759074|
| miR-4681        | 0.03113862     | Up         | 0.14257113| 0.75376261|
| miR-218-1-3p    | 0.03130364     | Up         | 0.36743134| 0.86195734|
| miR-6788-5p     | 0.0313145      | Up         | 0.41109277| 0.87913536|
| miR-4770        | 0.03155607     | Up         | 0.40519275| 0.87475982|
| miR-6788-5p     | 0.03161619     | Up         | 0.4213246 | 0.8823614|
| miR-4770        | 0.03161724     | Up         | 0.4996733 | 0.8894976|
| miR-6788-5p     | 0.03164575     | Up         | 0.334798  | 0.9213181|
| miR-4770        | 0.0317454      | Up         | 0.3013818 | 0.83872374|
| miR-6788-5p     | 0.03182286     | Up         | 0.40658308| 0.87475982|
| miR-4770        | 0.03184083     | Up         | 0.34095019| 0.85516921|
| miR-6788-5p     | 0.0318701      | Up         | 0.44743825| 0.88952595|
| miR-4770        | 0.03190043     | Up         | 0.3655651 | 0.8588192|
| miR-6788-5p     | 0.03219936     | Up         | 0.3201688 | 0.85046325|
| miR-4770        | 0.03223689     | Up         | 0.27668467| 0.83108541|
| miR-6788-5p     | 0.03234506     | Up         | 0.17163503| 0.77062416|
| miR-6788-5p     | 0.03246089     | Up         | 0.23035881| 0.79466058|
| miR-6788-5p     | 0.03253566     | Up         | 0.50166291| 0.91147569|
| miR-6788-5p     | 0.03254509     | Up         | 0.46426145| 0.89396011|
| miR-6788-5p     | 0.03257163     | Up         | 0.24382571| 0.80715125|
| miR-6788-5p     | 0.03259034     | Up         | 0.83963668| 0.99654281|
| miR-6788-5p     | 0.03263465     | Up         | 0.24121568| 0.80614344|
| miR-6788-5p     | 0.0326443      | Up         | 0.22658673| 0.79102241|
| miR-6788-5p     | 0.03265373     | Up         | 0.16032466| 0.76082142|
| miR-6788-5p     | 0.03279131     | Up         | 0.8542697 | 0.99898712|
| miR-6788-5p     | 0.03282655     | Up         | 0.8403079 | 0.99654281|
| miR-6788-5p     | 0.03283932     | Up         | 0.57655026| 0.93390911|
| miR-6788-5p     | 0.03285515     | Up         | 0.1695905 | 0.77062416|
| miR-6788-5p     | 0.03289378     | Up         | 0.4132006 | 0.8804535|
| miR-6788-5p     | 0.03299145     | Up         | 0.31753409| 0.84917098|
| miR-6788-5p     | 0.03301146     | Up         | 0.29107891| 0.83872374|

(Continued)
Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value    | P-adj     |
|------------|----------------|------------|------------|-----------|
| miR-5000-3p | 0.0312279      | Up         | 0.20177441 | 0.77997491|
| miR-1193    | 0.0318041      | Up         | 0.11602809 | 0.7422488 |
| miR-3942-3p | 0.0318391      | Up         | 0.49335607 | 0.90695643|
| miR-6845-5p | 0.0321475      | Up         | 0.46960894 | 0.89396011|
| miR-889-5p  | 0.0324309      | Up         | 0.28522198 | 0.83289761|
| miR-1471    | 0.0333836      | Up         | 0.31115147 | 0.8475125 |
| miR-585-5p  | 0.0336345      | Up         | 0.36213281 | 0.8588192 |
| miR-6513-5p | 0.0337839      | Up         | 0.29886864 | 0.83872374|
| miR-8074    | 0.03352439     | Up         | 0.35286528 | 0.8588192 |
| miR-3907    | 0.03355366     | Up         | 0.31295306 | 0.8475125 |
| miR-3170    | 0.03361297     | Up         | 0.28328304 | 0.83193599|
| miR-4761-3p | 0.03364893     | Up         | 0.3031921  | 0.83872374|
| miR-4695-3p | 0.03374892     | Up         | 0.33789055 | 0.85489649|
| miR-487a-5p | 0.03377349     | Up         | 0.46369411 | 0.89396011|
| miR-3942-5p | 0.03395729     | Up         | 0.42275918 | 0.8823614 |
| miR-8088    | 0.03395917     | Up         | 0.12762754 | 0.74892227|
| miR-4326    | 0.03399485     | Up         | 0.39471249 | 0.87310741|
| miR-155-5p  | 0.03404459     | Up         | 0.80932045 | 0.99064883|
| miR-3690    | 0.03409675     | Up         | 0.39488925 | 0.87310741|
| miR-4685-3p | 0.03416231     | Up         | 0.45768161 | 0.89244441|
| miR-1302    | 0.03425043     | Up         | 0.22811873 | 0.79102241|
| miR-7-2-3p  | 0.03440461     | Up         | 0.33154051 | 0.85489649|
| miR-4677-3p | 0.03441566     | Up         | 0.30226843 | 0.83872374|
| miR-3660    | 0.03459958     | Up         | 0.30226843 | 0.83872374|
| miR-1229-5p | 0.03468552     | Up         | 0.2813402  | 0.83108541|
| miR-5009-5p | 0.03469731     | Up         | 0.2813402  | 0.83108541|
| miR-4766-3p | 0.03472279     | Up         | 0.17886448 | 0.77062416|
| miR-4664-3p | 0.0347848      | Up         | 0.42348632 | 0.8823614 |
| miR-4296    | 0.03478611     | Up         | 0.28471996 | 0.83193599|
| miR-6841-5p | 0.03480077     | Up         | 0.36207326 | 0.8588192 |
| miR-4699-3p | 0.03485191     | Up         | 0.2789268  | 0.83108541|
| miR-105-5p  | 0.03492293     | Up         | 0.43276212 | 0.88833759|
| miR-1229-5p | 0.0350583      | Up         | 0.70680678 | 0.96360966|
| miR-1205    | 0.03512762     | Up         | 0.17645303 | 0.77062416|
| miR-8082    | 0.03537106     | Up         | 0.28859008 | 0.84394974|
| miR-6778-3p | 0.03537593     | Up         | 0.35862587 | 0.8588192 |
| miR-8075    | 0.03548293     | Up         | 0.23935284 | 0.80380192|
| miR-520d-3p | 0.03557657     | Up         | 0.20689493 | 0.78263372|
| miR-5187-5p | 0.03560641     | Up         | 0.19413706 | 0.77997491|
| miR-6736-3p | 0.03566937     | Up         | 0.29870046 | 0.83872374|
| miR-548ac-5p| 0.03573935     | Up         | 0.30468684 | 0.83927672|
| miR-551-3p  | 0.03574804     | Up         | 0.25145867 | 0.80715125|
| miR-7853-5p | 0.0357678      | Up         | 0.1331583  | 0.74892227|
| miR-29b-2-5p| 0.03586254     | Up         | 0.30415974 | 0.83872374|
| miR-7844-5p | 0.03587377     | Up         | 0.22386382 | 0.79102241|

(Continued)
Table 9 (Continued).

| miRNAs        | Log2FoldChange | Regulation | P-value    | P-adj       |
|---------------|----------------|------------|------------|-------------|
| miR-196a-3p   | 0.03601832     | Up         | 0.17803967 | 0.77062416  |
| miR-4693-3p   | 0.03607285     | Up         | 0.19938898 | 0.77997491  |
| miR-496       | 0.03608936     | Up         | 0.32422293 | 0.85489649  |
| miR-6894-5p   | 0.03610148     | Up         | 0.18941797 | 0.77997491  |
| miR-7157-3p   | 0.03625689     | Up         | 0.18909666 | 0.77997491  |
| miR-1914-3p   | 0.03627463     | Up         | 0.62987625 | 0.95065239  |
| miR-6860      | 0.03627669     | Up         | 0.14979885 | 0.75376261  |
| miR-6750-5p   | 0.03627802     | Up         | 0.2160179  | 0.7853205   |
| miR-6886-5p   | 0.03652277     | Up         | 0.27957753 | 0.83108541  |
| miR-7157-3p   | 0.03658935     | Up         | 0.43662861 | 0.88952595  |
| miR-4720-5p   | 0.03681332     | Up         | 0.13035282 | 0.74892227  |
| miR-122-5p    | 0.03687171     | Up         | 0.14472276 | 0.75376261  |
| miR-1909-3p   | 0.03687211     | Up         | 0.1819375  | 0.77344537  |
| miR-1243      | 0.03695111     | Up         | 0.34756238 | 0.8588192   |
| miR-6848-5p   | 0.03696994     | Up         | 0.27240881 | 0.83108541  |
| miR-6736-5p   | 0.03706158     | Up         | 0.32377062 | 0.85489649  |
| miR-34b-3p    | 0.03734561     | Up         | 0.73754807 | 0.97354829  |
| miR-4720-5p   | 0.03761332     | Up         | 0.29379641 | 0.83872374  |
| miR-6882-3p   | 0.03761332     | Up         | 0.15777935 | 0.75988515  |
| miR-4474-5p   | 0.03763137     | Up         | 0.30910752 | 0.84601313  |
| miR-1236-3p   | 0.03773461     | Up         | 0.37922698 | 0.86499071  |
| miR-5681a     | 0.03801933     | Up         | 0.24815225 | 0.80715125  |
| miR-3910      | 0.03804647     | Up         | 0.2806822  | 0.83108541  |
| miR-3678-3p   | 0.03807823     | Up         | 0.36396818 | 0.8588192   |
| miR-6838-5p   | 0.03811724     | Up         | 0.13604868 | 0.75376261  |
| miR-4661-5p   | 0.03820281     | Up         | 0.23108332 | 0.79502561  |
| miR-598-5p    | 0.03830432     | Up         | 0.15547245 | 0.75588563  |
| miR-6825-5p   | 0.03837002     | Up         | 0.18588078 | 0.7767007   |
| miR-579-3p    | 0.0383978      | Up         | 0.10369361 | 0.74226488  |
| miR-6768-5p   | 0.03840336     | Up         | 0.29653583 | 0.83872374  |
| miR-607       | 0.03844626     | Up         | 0.43070991 | 0.88759074  |
| miR-514b-5p   | 0.03847919     | Up         | 0.12575112 | 0.74465526  |
| miR-376c-5p   | 0.03868361     | Up         | 0.3609705  | 0.8588192   |
| miR-6771-3p   | 0.03868435     | Up         | 0.39572746 | 0.87310741  |
| miR-671-3p    | 0.03879676     | Up         | 0.4395678  | 0.88952595  |
| miR-7974      | 0.0388885      | Up         | 0.2018095  | 0.77997491  |
| miR-523-3p    | 0.03900629     | Up         | 0.14829019 | 0.75376261  |
| miR-4760-3p   | 0.03917813     | Up         | 0.39896188 | 0.87364718  |
| miR-675-3p    | 0.03922992     | Up         | 0.34598835 | 0.8588192   |
| miR-1233-3p   | 0.03932368     | Up         | 0.49662437 | 0.90971108  |
| miR-500a-3p   | 0.03935554     | Up         | 0.61879455 | 0.94829596  |
| miR-3180      | 0.03941221     | Up         | 0.16395796 | 0.76892691  |
| miR-33b-5p    | 0.03959734     | Up         | 0.31606259 | 0.84917098  |
| miR-4711-3p   | 0.03964566     | Up         | 0.25101393 | 0.80715125  |
| miR-4750-5p   | 0.03971147     | Up         | 0.08287334 | 0.69839839  |
| miR-367-3p    | 0.03984679     | Up         | 0.25183159 | 0.80715125  |
| miR-323b-3p   | 0.03990502     | Up         | 0.17721599 | 0.77062416  |

(Continued)
| miRNAs          | Log2FoldChange | Regulation | P-value       | P-adj       |
|-----------------|----------------|------------|---------------|-------------|
| miR-1321        | 0.0402516      | Up         | 0.13375694    | 0.74892227  |
| miR-18a-3p      | 0.04010365     | Up         | 0.37562221    | 0.86499071  |
| miR-6072        | 0.04010963     | Up         | 0.33186263    | 0.85489649  |
| miR-449b-3p     | 0.0401152      | Up         | 0.19401484    | 0.77997491  |
| miR-3173-3p     | 0.04036297     | Up         | 0.24825061    | 0.80715125  |
| miR-3156-5p     | 0.04040939     | Up         | 0.38153022    | 0.86612247  |
| miR-4471        | 0.04042235     | Up         | 0.33978286    | 0.85489649  |
| miR-580-5p      | 0.04056515     | Up         | 0.25071618    | 0.80715125  |
| miR-427         | 0.04060488     | Up         | 0.26624124    | 0.82438552  |
| miR-548h-3p     | 0.04066678     | Up         | 0.18575176    | 0.77677007  |
| miR-6765-3p     | 0.0407351      | Up         | 0.16606324    | 0.76915081  |
| miR-6846-3p     | 0.04074924     | Up         | 0.30408928    | 0.8372374  |
| miR-6807-5p     | 0.04078216     | Up         | 0.53160743    | 0.92261663  |
| miR-6846-3p     | 0.04078605     | Up         | 0.39033207    | 0.87281803  |
| miR-4518        | 0.04082069     | Up         | 0.45761716    | 0.89244441  |
| miR-100-3p      | 0.04085695     | Up         | 0.35794546    | 0.8588192   |
| miR-4327        | 0.04091817     | Up         | 0.27666692    | 0.83105841  |
| miR-6818-5p     | 0.04097196     | Up         | 0.18757745    | 0.77997491  |
| miR-19a-3p      | 0.04102357     | Up         | 0.27666692    | 0.83105841  |
| miR-548h-3p     | 0.04107351     | Up         | 0.18575176    | 0.77677007  |
| miR-6876-3p     | 0.04118224     | Up         | 0.29757035    | 0.83872374  |
| miR-556-3p      | 0.04120505     | Up         | 0.19401484    | 0.77997491  |
| miR-548h-3p     | 0.04123633     | Up         | 0.18207566    | 0.77344537  |
| miR-5705        | 0.04125884     | Up         | 0.14766333    | 0.75372614  |
| miR-3605-5p     | 0.04127629     | Up         | 0.13916892    | 0.75372614  |
| miR-3621        | 0.04129921     | Up         | 0.15845074    | 0.7988515   |
| miR-3621        | 0.04132926     | Up         | 0.20318418    | 0.77994791  |
| miR-380-3p      | 0.04133196     | Up         | 0.22292684    | 0.79102241  |
| miR-3605-5p     | 0.0413505      | Up         | 0.54518596    | 0.9261663   |
| miR-5705        | 0.04141633     | Up         | 0.18207566    | 0.77344537  |
| miR-3605-5p     | 0.04147755     | Up         | 0.20989329    | 0.78263372  |
| miR-5591-5p     | 0.04159962     | Up         | 0.30032934    | 0.83872374  |
| miR-5195-5p     | 0.04165547     | Up         | 0.19401484    | 0.77997491  |
| miR-3621        | 0.04165547     | Up         | 0.16972762    | 0.77062416  |
| miR-1250-3p     | 0.04170601     | Up         | 0.27258916    | 0.83107769  |
| miR-491-5p      | 0.04204882     | Up         | 0.09714365    | 0.73085631  |
| miR-556-3p      | 0.04206638     | Up         | 0.44931883    | 0.88964976  |
| miR-6799-3p     | 0.04207906     | Up         | 0.31704859    | 0.84917098  |
| miR-19a-3p      | 0.04217759     | Up         | 0.20989329    | 0.78263372  |
| miR-3154        | 0.04223574     | Up         | 0.12130399    | 0.74226488  |
| miR-6813-3p     | 0.04224463     | Up         | 0.39270768    | 0.8730612   |
| miR-3925-5p     | 0.04246307     | Up         | 0.27258916    | 0.83108541  |
| miR-3670        | 0.04253471     | Up         | 0.11670866    | 0.74226488  |
| miR-4453        | 0.04258259     | Up         | 0.05055003    | 0.62458446  |
| miR-4271        | 0.0429164      | Up         | 0.55251367    | 0.92384946  |
| miR-6799-3p     | 0.04300684     | Up         | 0.07858756    | 0.68910078  |
| miR-4529-3p     | 0.04328269     | Up         | 0.16597797    | 0.76915081  |

(Continued)
| miRNAs          | Log2FoldChange | Regulation | P-value  | P-adj    |
|-----------------|----------------|------------|----------|----------|
| miR-6733-5p     | 0.04335371     | Up         | 0.20559661 | 0.78047751       |
| miR-5209-5p     | 0.04339194     | Up         | 0.25109345 | 0.80715125       |
| miR-4325        | 0.04340191     | Up         | 0.15424249 | 0.75393664       |
| miR-3667-5p     | 0.04350045     | Up         | 0.63222897 | 0.95096807       |
| miR-3186-3p     | 0.0435136      | Up         | 0.23530151 | 0.80202237       |
| miR-6501-3p     | 0.0435136      | Up         | 0.09379904 | 0.72555728       |
| miR-1253        | 0.04375056     | Up         | 0.1151096  | 0.74226488       |
| miR-6781-3p     | 0.04381511     | Up         | 0.07438659 | 0.83107769       |
| miR-5589-3p     | 0.04405912     | Up         | 0.2724389  | 0.8406327        |
| miR-764         | 0.04417422     | Up         | 0.11500808 | 0.74226488       |
| miR-3186-3p     | 0.0444632      | Up         | 0.28593611 | 0.83289761       |
| miR-939-5p      | 0.0444632      | Up         | 0.14541416 | 0.75376261       |
| miR-4648        | 0.04450342     | Up         | 0.73455339 | 0.97354829       |
| miR-5701        | 0.04456045     | Up         | 0.21082098 | 0.7623372        |
| miR-6818-3p     | 0.04464997     | Up         | 0.23921914 | 0.80380192       |
| miR-4777-5p     | 0.0448246      | Up         | 0.20999917 | 0.78263372       |
| miR-597-5p      | 0.04495122     | Up         | 0.17466302 | 0.77062416       |
| miR-4262        | 0.04497037     | Up         | 0.13341303 | 0.74892227       |
| miR-6814-3p     | 0.04498088     | Up         | 0.27863126 | 0.83108541       |
| miR-4733-3p     | 0.04515748     | Up         | 0.10700953 | 0.74226488       |
| miR-198         | 0.04517199     | Up         | 0.1050005  | 0.74226488       |
| miR-4510        | 0.04528562     | Up         | 0.11425075 | 0.74226488       |
| miR-4743-3p     | 0.0454178      | Up         | 0.6957496  | 0.67187824       |
| miR-548az-3p    | 0.04548397     | Up         | 0.16890955 | 0.77062416       |
| miR-7843-5p     | 0.04554652     | Up         | 0.06781769 | 0.86270515       |
| miR-4672        | 0.045715       | Up         | 0.638909   | 0.95096807       |
| miR-6894-3p     | 0.04580143     | Up         | 0.22915805 | 0.79158088       |
| miR-3176        | 0.04606993     | Up         | 0.09281998 | 0.72287071       |
| miR-6893-3p     | 0.04622563     | Up         | 0.210879   | 0.78263372       |
| miR-3137        | 0.04657398     | Up         | 0.388545   | 0.87210628       |
| miR-6780a-3p    | 0.04669084     | Up         | 0.32606651 | 0.85489649       |
| miR-5696        | 0.04708647     | Up         | 0.3910817  | 0.87281803       |
| miR-296-5p      | 0.0472118      | Up         | 0.28288192 | 0.83193599       |
| miR-6762-3p     | 0.04725137     | Up         | 0.29769649 | 0.83872374       |
| miR-6747-5p     | 0.04725775     | Up         | 0.24707509 | 0.80715125       |
| miR-8053        | 0.0473133      | Up         | 0.20270231 | 0.77979491       |
| miR-3152-5p     | 0.04732823     | Up         | 0.19598155 | 0.77979491       |
| miR-571         | 0.04734154     | Up         | 0.84533752 | 0.99654281       |
| miR-378b        | 0.04739432     | Up         | 0.06860943 | 0.66790237       |
| miR-499b-5p     | 0.04800234     | Up         | 0.27937448 | 0.83108541       |
| miR-147a        | 0.04818405     | Up         | 0.06618544 | 0.65890175       |
| miR-892c-3p     | 0.04821604     | Up         | 0.27352161 | 0.83107769       |
| miR-6762-3p     | 0.04841079     | Up         | 0.08410509 | 0.70009532       |
| miR-6747-5p     | 0.04842416     | Up         | 0.05041196 | 0.62129395       |
| miR-4523        | 0.04855634     | Up         | 0.0620686  | 0.65108692       |

(Continued)
Table 9 (Continued).

| miRNAs          | Log2FoldChange | Regulation | P-value     | P-adj     |
|-----------------|----------------|------------|-------------|-----------|
| miR-215-3p      | 0.04857459     | Up         | 0.35706226  | 0.8588192 |
| miR-3675-5p     | 0.04879536     | Up         | 0.25507552  | 0.81031406|
| miR-488-5p      | 0.04908388     | Up         | 0.08417489  | 0.70009532|
| miR-548au-5p    | 0.04911752     | Up         | 0.08315561  | 0.69839839|
| miR-4475        | 0.04922564     | Up         | 0.24552818  | 0.80715125|
| miR-4538        | 0.04929697     | Up         | 0.15188194  | 0.75393664|
| miR-4524a-3p    | 0.04931592     | Up         | 0.13022476  | 0.7492227 |
| miR-1297        | 0.04951592     | Up         | 0.08417489  | 0.70009532|
| miR-4475        | 0.04952140     | Up         | 0.21665067  | 0.7853205 |
| miR-1827        | 0.04962680     | Up         | 0.25624536  | 0.81102287|
| miR-1297        | 0.04984516     | Up         | 0.24492201  | 0.80715125|
| miR-3675-5p     | 0.04991254     | Up         | 0.19551925  | 0.77997491|
| miR-488-5p      | 0.050037082    | Up         | 0.06076089  | 0.64823335|
| miR-4524a-3p    | 0.05036927     | Up         | 0.21258503  | 0.78263372|
| miR-1297        | 0.05069856     | Up         | 0.12083398  | 0.74226488|
| miR-3675-5p     | 0.05096148     | Up         | 0.67354792  | 0.95648223|
| miR-548au-5p    | 0.05113808     | Up         | 0.06047598  | 0.64823335|
| miR-1297        | 0.05115466     | Up         | 0.12549433  | 0.74465526|
| miR-4475        | 0.05115494     | Up         | 0.0665464   | 0.6590175 |
| miR-4475        | 0.05123612     | Up         | 0.2768576   | 0.83105841|
| miR-4521        | 0.05149196     | Up         | 0.17417833  | 0.77062416|
| miR-3157-3p     | 0.05171743     | Up         | 0.67825049  | 0.95648223|
| miR-4475        | 0.05175787     | Up         | 0.12086294  | 0.74226488|
| miR-3180-5p     | 0.05205933     | Up         | 0.22745616  | 0.79102241|
| miR-1273f       | 0.05273566     | Up         | 0.3795035   | 0.86499071|
| miR-4675        | 0.05273927     | Up         | 0.14291919  | 0.74465526|
| miR-4475        | 0.05273927     | Up         | 0.14291919  | 0.74465526|
| miR-3157-3p     | 0.05273464     | Up         | 0.43527281  | 0.88941554|
| miR-569         | 0.0527518      | Up         | 0.15673419  | 0.75715578|
| miR-2113        | 0.05283136     | Up         | 0.18308273  | 0.77350881|
| miR-4696        | 0.05289934     | Up         | 0.06296921  | 0.65539395|
| miR-216a-3p     | 0.05300228     | Up         | 0.11694725  | 0.74226488|
| miR-8069        | 0.05327677     | Up         | 0.74385134  | 0.97549977|
| miR-378f        | 0.0532519      | Up         | 0.33432056  | 0.85489649|
| miR-378f        | 0.05334213     | Up         | 0.20140266  | 0.77997491|
| miR-6372-3p     | 0.05336692     | Up         | 0.2016338   | 0.77997491|
| miR-569         | 0.05340195     | Up         | 0.22409885  | 0.79102241|
| miR-135b-5p     | 0.05351659     | Up         | 0.20225766  | 0.77997491|
| miR-589-5p      | 0.05379551     | Up         | 0.0891464   | 0.71411286|
| miR-348m        | 0.05393355     | Up         | 0.35513747  | 0.8588192 |
| miR-4316        | 0.05396877     | Up         | 0.13140033  | 0.74892227|
| miR-7108-5p     | 0.05421148     | Up         | 0.58185476  | 0.93436563|
| miR-4758-3p     | 0.05427522     | Up         | 0.40499182  | 0.87475982|
| miR-3974        | 0.05440058     | Up         | 0.03934144  | 0.59871978|
| miR-6499-3p     | 0.05455931     | Up         | 0.19238152  | 0.77997491|

(Continued)
Table 9 (Continued).

| miRNAs          | Log2FoldChange | Regulation | P-value  | P-adj    |
|-----------------|----------------|------------|----------|----------|
| miR-7156-3p     | 0.05474298     | Up         | 0.11579842 | 0.74226488 |
| miR-3677-5p     | 0.05477731     | Up         | 0.11357964 | 0.74226488 |
| miR-4802-5p     | 0.05510145     | Up         | 0.12191501 | 0.74423174 |
| miR-512-3p      | 0.05528425     | Up         | 0.28071561 | 0.83108541 |
| miR-548g-3p     | 0.05529729     | Up         | 0.42571423 | 0.8823614  |
| miR-4768-5p     | 0.05542136     | Up         | 0.25826154 | 0.81339724 |
| miR-548ad-3p    | 0.05542262     | Up         | 0.18370678 | 0.77350881 |
| miR-4795-3p     | 0.05570005     | Up         | 0.1924634  | 0.74226488 |
| miR-512-5p      | 0.05571431     | Up         | 0.42571423 | 0.8823614  |
| miR-548ad-3p    | 0.05577899     | Up         | 0.04674782 | 0.61412501 |
| miR-4795-3p     | 0.05581371     | Up         | 0.04063447 | 0.60118096 |
| miR-1469        | 0.05584382     | Up         | 0.22861872 | 0.78047751 |
| miR-3652        | 0.05590099     | Up         | 0.2054363  | 0.78047751 |
| miR-933         | 0.05596346     | Up         | 0.12011652 | 0.74226488 |
| miR-3117-3p     | 0.05603267     | Up         | 0.12113369 | 0.74226488 |
| miR-3190-5p     | 0.05608432     | Up         | 0.22861872 | 0.79102241 |
| miR-6761-3p     | 0.05610884     | Up         | 0.16210545 | 0.76582906 |
| miR-6835-3p     | 0.05627694     | Up         | 0.27628877 | 0.83108541 |
| miR-6080        | 0.05677708     | Up         | 0.17847595 | 0.77062416 |
| miR-4300        | 0.05678393     | Up         | 0.05365624 | 0.63883244 |
| miR-4429        | 0.05677899     | Up         | 0.04674782 | 0.61412501 |
| miR-1270        | 0.05688983     | Up         | 0.01208124 | 0.44354507 |
| miR-526b-5p     | 0.0569863      | Up         | 0.10278829 | 0.74226488 |
| miR-4639-5p     | 0.05691153     | Up         | 0.14529474 | 0.75376261 |
| miR-5588-5p     | 0.05692605     | Up         | 0.03581121 | 0.59871978 |
| miR-615-5p      | 0.05703646     | Up         | 0.1150281  | 0.74226488 |
| miR-1249-5p     | 0.05710084     | Up         | 0.16210545 | 0.76582906 |
| miR-1252-5p     | 0.05722112     | Up         | 0.10268676 | 0.73922664 |
| miR-150-3p      | 0.05725973     | Up         | 0.25826154 | 0.81339724 |
| miR-4790-5p     | 0.05730035     | Up         | 0.10614619 | 0.74226488 |
| miR-3678-5p     | 0.05766581     | Up         | 0.30176797 | 0.83872374 |
| miR-222-3p      | 0.0587964      | Up         | 0.31819131 | 0.84917098 |
| miR-4765-5p     | 0.0587769      | Up         | 0.08817894 | 0.71090561 |
| miR-6812-5p     | 0.05917651     | Up         | 0.56525274 | 0.93030656 |
| miR-3145-3p     | 0.05928081     | Up         | 0.17130088 | 0.77062416 |
| miR-601         | 0.05930908     | Up         | 0.1151752  | 0.74226488 |
| miR-450a-2-3p   | 0.0594454      | Up         | 0.1464859  | 0.75376261 |
| miR-32-3p       | 0.05951562     | Up         | 0.14474059 | 0.75376261 |
| miR-1908-3p     | 0.05961361     | Up         | 0.43830338 | 0.88952959 |
| miR-3162-5p     | 0.05982246     | Up         | 0.45070972 | 0.89864976 |
| miR-664b-3p     | 0.05992559     | Up         | 0.79741636 | 0.98759926 |
| miR-3922-3p     | 0.0599527      | Up         | 0.15889256 | 0.75988515 |
| miR-4458        | 0.06003594     | Up         | 0.09890351 | 0.73085631 |
| miR-6826-3p     | 0.06023102     | Up         | 0.13036518 | 0.74892227 |
| miR-3605-3p     | 0.06051898     | Up         | 0.16045339 | 0.76082142 |
| miR-548bl       | 0.06052741     | Up         | 0.10733331 | 0.74226488 |
| miR-501-3p      | 0.06053351     | Up         | 0.16686685 | 0.76915081 |
| miR-512-5p      | 0.06055698     | Up         | 0.110184   | 0.74226488 |
| miR-6775-3p     | 0.06081053     | Up         | 0.32525563 | 0.85489649 |
| miR-24-2-5p     | 0.06086829     | Up         | 0.27107456 | 0.83107769 |
| miR-4745-5p     | 0.06148174     | Up         | 0.26320069 | 0.82197281 |

(Continued)
| miRNAs         | Log2FoldChange | Regulation | P-value       | P-adj       |
|---------------|----------------|------------|---------------|-------------|
| miR-142-5p    | 0.0615305      | Up         | 0.74062343    | 0.97402999  |
| miR-3145-5p   | 0.06155958     | Up         | 0.27053651    | 0.83107769  |
| miR-619-3p    | 0.06190106     | Up         | 0.04090207    | 0.60118096  |
| miR-4697-3p   | 0.06193714     | Up         | 0.03581024    | 0.59871978  |
| mir-1913      | 0.06196023     | Up         | 0.14965706    | 0.75393664  |
| miR-1227-3p   | 0.0624576      | Up         | 0.26520529    | 0.82438552  |
| miR-619-3p    | 0.06249059     | Up         | 0.23882079    | 0.80380192  |
| miR-6857-3p   | 0.06254411     | Up         | 0.0762451     | 0.68910078  |
| miR-1913      | 0.0627565      | Up         | 0.0762451     | 0.68910078  |
| miR-1227-3p   | 0.06254411     | Up         | 0.24890997    | 0.80715125  |
| miR-7977      | 0.06354694     | Up         | 0.74952299    | 0.97742837  |
| miR-3622b-5p  | 0.06364311     | Up         | 0.0940119     | 0.6142501   |
| miR-1273h-3p  | 0.06364311     | Up         | 0.0940119     | 0.6142501   |
| miR-7977      | 0.06381373     | Up         | 0.30201312    | 0.83872374  |
| miR-6867-3p   | 0.06424523     | Up         | 0.17909857    | 0.77062416  |
| miR-4663      | 0.06432453     | Up         | 0.02836095    | 0.59282645  |
| miR-4715-5p   | 0.06496711     | Up         | 0.03872527    | 0.59871978  |
| miR-6508-5p   | 0.06483137     | Up         | 0.51403325    | 0.91376348  |
| miR-3935      | 0.06495576     | Up         | 0.3347485     | 0.85486949  |
| miR-6867-3p   | 0.06507568     | Up         | 0.04850407    | 0.6142501   |
| miR-492       | 0.06516851     | Up         | 0.04991087    | 0.62129395  |
| miR-5094      | 0.06523354     | Up         | 0.32183809    | 0.85270505  |
| miR-6865-3p   | 0.06524252     | Up         | 0.21168754    | 0.78263372  |
| miR-4715-5p   | 0.06642453     | Up         | 0.1302163     | 0.7492227   |
| miR-4663      | 0.06642453     | Up         | 0.1302163     | 0.7492227   |
| miR-4715-5p   | 0.06683348     | Up         | 0.0299282     | 0.59616038  |
| miR-4663      | 0.06683348     | Up         | 0.0299282     | 0.59616038  |
| miR-4715-5p   | 0.06690942     | Up         | 0.30201312    | 0.83872374  |
| miR-4715-5p   | 0.06690942     | Up         | 0.30201312    | 0.83872374  |
| miR-4288      | 0.06765074     | Up         | 0.11109946    | 0.7426488   |
| miR-4288      | 0.06765074     | Up         | 0.11109946    | 0.7426488   |
| miR-3120-5p   | 0.0678456      | Up         | 0.07987684    | 0.6910078   |
| miR-7114-5p   | 0.06800749     | Up         | 0.6569214     | 0.95321673  |
| miR-548ah-5p  | 0.06819495     | Up         | 0.07413876    | 0.68406327  |
| miR-4663      | 0.06843293     | Up         | 0.40487621    | 0.87475982  |
| miR-513c-5p   | 0.06854085     | Up         | 0.18053401    | 0.77062416  |
| miR-4716-5p   | 0.06872344     | Up         | 0.20833359    | 0.78263372  |
| miR-4787-3p   | 0.06876198     | Up         | 0.50943723    | 0.91230009  |
| miR-600       | 0.06877777     | Up         | 0.07989689    | 0.6910078   |
| miR-71150     | 0.06879546     | Up         | 0.26528174    | 0.82438552  |
| miR-29a-5p    | 0.06883865     | Up         | 0.14662388    | 0.75376261  |
| miR-184       | 0.06888405     | Up         | 0.01862817    | 0.53734625  |
| miR-6870-3p   | 0.06911219     | Up         | 0.23957676    | 0.80380192  |
| miR-6850-3p   | 0.06919394     | Up         | 0.25777855    | 0.81287224  |
| miR-4657      | 0.06968547     | Up         | 0.12522401    | 0.74465526  |
| miR-371b-5p   | 0.06969313     | Up         | 0.23932344    | 0.80380192  |
| miR-4680-5p   | 0.06974422     | Up         | 0.03404741    | 0.59871978  |
| miR-6499-5p   | 0.07006264     | Up         | 0.04920309    | 0.61683874  |
| miR-6810-3p   | 0.0701419      | Up         | 0.06035347    | 0.64832335  |
| miR-3682-3p   | 0.07039938     | Up         | 0.17881596    | 0.77062416  |
| miR-6126      | 0.0704907      | Up         | 0.28825395    | 0.83439474  |
| miR-653-5p    | 0.07088698     | Up         | 0.03087676    | 0.59781471  |
| miR-382-3p    | 0.07116744     | Up         | 0.18031035    | 0.77062416  |

(Continued)
| miRNAs    | Log2FoldChange | Regulation | P-value     | P-adj     |
|-----------|----------------|------------|-------------|-----------|
| miR-6858-3p | 0.07117186     | Up         | 0.38553306  | 0.86961208 |
| miR-4499   | 0.07122958     | Up         | 0.24841121  | 0.80715125 |
| miR-5187-3p | 0.07144019     | Up         | 0.0212432   | 0.53734625 |
| miR-557    | 0.07164553     | Up         | 0.04546064  | 0.61412501 |
| miR-1281   | 0.07198433     | Up         | 0.40118929  | 0.87364718 |
| miR-6786-5p | 0.07206845     | Up         | 0.12343738  | 0.74454632 |
| miR-455-3p | 0.07226377     | Up         | 0.1834791   | 0.7730881  |
| miR-518d-3p | 0.07256516     | Up         | 0.35615086  | 0.8588192  |
| miR-2861   | 0.07270619     | Up         | 0.03799809  | 0.59871978 |
| miR-648    | 0.07279229     | Up         | 0.08596047  | 0.70807179 |
| miR-4329   | 0.07336799     | Up         | 0.0736192   | 0.68406327 |
| miR-4652-5p | 0.0737191      | Up         | 0.20576632  | 0.55959148 |
| miR-935    | 0.07375817     | Up         | 0.18143568  | 0.77328308 |
| miR-4738-5p | 0.07367855     | Up         | 0.01998951  | 0.53734625 |
| miR-6784-3p | 0.07382632     | Up         | 0.3657297   | 0.59871978 |
| miR-500a-5p | 0.07412535     | Up         | 0.1346475   | 0.75226974 |
| miR-2053   | 0.07445664     | Up         | 0.06375711  | 0.65542311 |
| miR-6800-3p | 0.07499394     | Up         | 0.1424747   | 0.75376261 |
| miR-5581-5p | 0.07511844     | Up         | 0.21009407  | 0.78263372 |
| miR-642b-3p | 0.07598197     | Up         | 0.36915419  | 0.86195734 |
| miR-371a-3p | 0.07664063     | Up         | 0.08711322  | 0.70907074 |
| miR-548ae-3p | 0.07679238     | Up         | 0.21885135  | 0.78840757 |
| miR-4753-3p | 0.07704808     | Up         | 0.0061694   | 0.40213598 |
| miR-4632-3p | 0.07749111     | Up         | 0.12336065  | 0.74454632 |
| miR-550a-5p | 0.07848882     | Up         | 0.24791286  | 0.80715125 |
| miR-509-3p  | 0.07856046     | Up         | 0.03093376  | 0.59781471 |
| miR-3607-3p | 0.07871814     | Up         | 0.6208883   | 0.94829596 |
| miR-3620-3p | 0.07893846     | Up         | 0.04506553  | 0.61412501 |
| miR-3943   | 0.07894053     | Up         | 0.02604419  | 0.55959148 |
| miR-6502-5p | 0.07908038     | Up         | 0.20157974  | 0.77997491 |
| miR-3151-3p | 0.07967298     | Up         | 0.12119654  | 0.74264888 |
| miR-1255a  | 0.07973658     | Up         | 0.05181195  | 0.63253996 |
| miR-34c-3p  | 0.07994349     | Up         | 0.09180651  | 0.72153737 |
| miR-1252-3p | 0.08011389     | Up         | 0.03880862  | 0.59871978 |
| miR-186-3p  | 0.08026808     | Up         | 0.03610748  | 0.59871978 |
| miR-6891-5p | 0.08058981     | Up         | 0.28582416  | 0.83289761 |
| miR-3646   | 0.0809914      | Up         | 0.41406383  | 0.8804535  |
| miR-7110-5p | 0.08143144     | Up         | 0.17902444  | 0.77062416 |
| miR-6824-3p | 0.08146995     | Up         | 0.12843883  | 0.74892227 |
| miR-135a-3p | 0.08192344     | Up         | 0.26560242  | 0.82438552 |
| miR-144-3p  | 0.08254493     | Up         | 0.81458209  | 0.99129215 |
| miR-3195   | 0.08270457     | Up         | 0.24420862  | 0.80715125 |
| miR-548ae-5p | 0.08303471     | Up         | 0.0395986   | 0.59871978 |
| miR-3945   | 0.08394863     | Up         | 0.12433998  | 0.74454632 |
| miR-3139   | 0.08450308     | Up         | 0.02320834  | 0.53734625 |
| miR-6791-5p | 0.08464489     | Up         | 0.4183558   | 0.88201345 |
| miR-1915-3p | 0.08517208     | Up         | 0.53746958  | 0.9213181  |

(Continued)
| miRNAs       | Log2FoldChange | Regulation | P-value     | P-adj     |
|--------------|----------------|------------|-------------|-----------|
| miR-542-5p   | 0.08526668     | Up         | 0.46783284  | 0.89396011|
| miR-519e-3p  | 0.08576418     | Up         | 0.11759491  | 0.74224888|
| miR-5585-3p  | 0.08579912     | Up         | 0.46178841  | 0.89396011|
| miR-378g     | 0.08622678     | Up         | 0.05316056  | 0.63842356|
| miR-548h-5p  | 0.08641971     | Up         | 0.18294233  | 0.77350881|
| miR-6895-3p  | 0.08645486     | Up         | 0.02529787  | 0.55568816|
| miR-8060     | 0.08676058     | Up         | 0.07990351  | 0.68910078|
| miR-6738-3p  | 0.08676132     | Up         | 0.02294984  | 0.53734625|
| miR-7162-3p  | 0.08705854     | Up         | 0.25604062  | 0.81102287|
| miR-6737-3p  | 0.08722144     | Up         | 0.05940578  | 0.64832335|
| miR-8061     | 0.08729181     | Up         | 0.0940578   | 0.64832335|
| miR-7162-3p  | 0.0873125      | Up         | 0.01084837  | 0.43937422|
| miR-651-5p   | 0.08842998     | Up         | 0.00854575  | 0.40696367|
| let-7c-5p    | 0.08921252     | Up         | 0.50684609  | 0.912181  |
| miR-377-3p   | 0.08929848     | Up         | 0.61601294  | 0.94741169|
| miR-602      | 0.08990339     | Up         | 0.0499877   | 0.70240141|
| miR-4691-5p  | 0.09233981     | Up         | 0.06685589  | 0.65890175|
| miR-876-3p   | 0.09288635     | Up         | 0.04792887  | 0.61412501|
| miR-23b-5p   | 0.0930458      | Up         | 0.03197789  | 0.59871978|
| miR-548am-3p | 0.09494395     | Up         | 0.00255307  | 0.34045223|
| miR-96-5p    | 0.09510759     | Up         | 0.13818989  | 0.75376261|
| miR-614      | 0.09555571     | Up         | 0.02218303  | 0.53734625|
| miR-29a-3p   | 0.09570771     | Up         | 0.31794301  | 0.8497098 |
| miR-532-5p   | 0.09574706     | Up         | 0.53567007  | 0.9213181 |
| miR-135a-5p  | 0.09654651     | Up         | 0.0829293   | 0.69839839|
| miR-193a-5p  | 0.09719116     | Up         | 0.09703079  | 0.73085631|
| miR-4497     | 0.09803222     | Up         | 0.17758974  | 0.77062416|
| miR-4433a-5p | 0.09851921     | Up         | 0.03675037  | 0.59871978|
| miR-1277-3p  | 0.09875703     | Up         | 0.03483406  | 0.59871978|
| miR-6507-3p  | 0.09886526     | Up         | 0.09969864  | 0.73085631|
| miR-890      | 0.09952414     | Up         | 0.0034835   | 0.34045223|
| miR-1234-3p  | 0.09955079     | Up         | 0.36352269  | 0.8588192 |
| miR-6851-3p  | 0.09975676     | Up         | 0.19181651  | 0.77997491|
| miR-8084     | 0.09976723     | Up         | 0.00359751  | 0.34045223|
| miR-4725-5p  | 0.09978071     | Up         | 0.21267843  | 0.78263727|
| miR-3155b    | 0.09979122     | Up         | 0.00278283  | 0.34045223|
| miR-501-5p   | 0.10032761     | Up         | 0.39061255  | 0.87281803|
| miR-4507     | 0.10099259     | Up         | 0.31915037  | 0.84972893|
| miR-181b-5p  | 0.10183856     | Up         | 0.35637515  | 0.8588192 |
| miR-4800-5p  | 0.10217379     | Up         | 0.22684006  | 0.79102241|
| miR-1973     | 0.10318636     | Up         | 0.27355317  | 0.83107769|
| miR-876-5p   | 0.10322575     | Up         | 0.00648836  | 0.40231598|
| miR-4689     | 0.10347357     | Up         | 0.15000646  | 0.75393664|
| miR-4485-5p  | 0.10376712     | Up         | 0.42637587  | 0.88249386|
| miR-1470     | 0.1042914      | Up         | 0.14840618  | 0.75376261|
| miR-4536-3p  | 0.10440502     | Up         | 0.00797512  | 0.40696367|
| miR-4478     | 0.10495        | Up         | 0.0747843   | 0.68406327|

(Continued)
### Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value  | P-adj       |
|--------------|----------------|------------|----------|-------------|
| miR-4310     | 0.1058934      | Up         | 0.10095486 | 0.73085631 |
| miR-98-3p    | 0.10626554     | Up         | 0.02112264 | 0.53734625 |
| miR-575      | 0.1064784      | Up         | 0.35501009 | 0.8588192  |
| miR-15a-5p   | 0.10652983     | Up         | 0.35983269 | 0.8588192  |
| miR-6858-5p  | 0.10799872     | Up         | 0.14672844 | 0.75376261 |
| miR-224-3p   | 0.10808806     | Up         | 0.11591039 | 0.74226488 |
| miR-98-3p    | 0.1082694      | Up         | 0.0138673  | 0.46600109 |
| miR-660-5p   | 0.10883293     | Up         | 0.46688213 | 0.89396011 |
| miR-663a     | 0.10974097     | Up         | 0.2834328  | 0.83193599 |
| miR-15a-5p   | 0.11034519     | Up         | 0.0134139  | 0.49284222 |
| miR-6858-5p  | 0.11195401     | Up         | 0.49477477 | 0.90848159 |
| miR-224-3p   | 0.1126684      | Up         | 0.06065803 | 0.64832335 |
| miR-3118     | 0.1131561      | Up         | 0.04582227 | 0.88952595 |
| miR-660-5p   | 0.11359411     | Up         | 0.11445403 | 0.74226488 |
| miR-342-5p   | 0.11363261     | Up         | 0.46550933 | 0.89396011 |
| miR-548c-3p  | 0.11421243     | Up         | 0.0425739  | 0.60118096 |
| miR-638      | 0.11490044     | Up         | 0.1093756  | 0.73589757 |
| miR-937-5p   | 0.11590295     | Up         | 0.16926304 | 0.77062416 |
| miR-483-3p   | 0.11606504     | Up         | 0.00061825 | 0.15302397 |
| miR-1825     | 0.11729768     | Up         | 0.05740226 | 0.64832335 |
| miR-6797-3p  | 0.11835638     | Up         | 0.1600133  | 0.76915081 |
| miR-1181     | 0.12038883     | Up         | 0.00197048 | 0.50670832 |
| miR-6821-5p  | 0.1209839      | Up         | 0.11464818 | 0.74226488 |
| miR-1238-3p  | 0.12126773     | Up         | 0.02485249 | 0.85568816 |
| miR-425-3p   | 0.12135814     | Up         | 0.07479447 | 0.68406327 |
| miR-6515-3p  | 0.12361515     | Up         | 0.29894341 | 0.83872374 |
| miR-3125     | 0.12402533     | Up         | 0.15451361 | 0.75393664 |
| miR-1825     | 0.12479268     | Up         | 0.05740226 | 0.64832335 |
| miR-6797-3p  | 0.12603538     | Up         | 0.1600133  | 0.76915081 |
| miR-1181     | 0.12738883     | Up         | 0.12071581 | 0.74226488 |
| miR-6821-5p  | 0.12909406     | Up         | 0.3717957  | 0.86499071 |
| miR-1238-3p  | 0.13297531     | Up         | 0.0877201  | 0.71650331 |
| miR-6890-3p  | 0.13318201     | Up         | 0.00293306 | 0.34045223 |
| miR-1260a    | 0.13372082     | Up         | 0.32936032 | 0.85489649 |
| miR-8072     | 0.13401883     | Up         | 0.00902604 | 0.46963667 |
| miR-6880-3p  | 0.13423449     | Up         | 0.0186311  | 0.53734625 |
| miR-6734-5p  | 0.13476722     | Up         | 0.0209457  | 0.53734625 |
| miR-5580-3p  | 0.13672314     | Up         | 0.05083706 | 0.62512553 |
| miR-1304-3p  | 0.1371615      | Up         | 0.0040137  | 0.34045223 |
| miR-199b-5p  | 0.13739765     | Up         | 0.5988003  | 0.93906184 |
| miR-4465     | 0.13988188     | Up         | 0.3513979  | 0.8588192  |
| miR-4746-3p  | 0.14158648     | Up         | 0.02080845 | 0.53734625 |
| miR-6759-3p  | 0.14532219     | Up         | 0.0813556  | 0.69819839 |
| let-7b-5p    | 0.14614295     | Up         | 0.35081789 | 0.8588192  |
| miR-4634     | 0.14754824     | Up         | 0.14617632 | 0.75376261 |
| miR-4505     | 0.14761153     | Up         | 0.04246345 | 0.60118096 |
| miR-502-3p   | 0.14790681     | Up         | 0.1566901  | 0.75715578 |

(Continued)
| miRNAs          | Log2FoldChange | Regulation | P-value  | P-adj     |
|-----------------|----------------|------------|----------|-----------|
| miR-4649-3p     | 0.14788706     | Up         | 0.01102337 | 0.43937422 |
| miR-6124        | 0.15010733     | Up         | 0.20156221 | 0.77997491 |
| miR-4687-3p     | 0.15063161     | Up         | 0.33744806 | 0.85486469 |
| let-7f-1-3p     | 0.15074119     | Up         | 0.05525242 | 0.64056718 |
| miR-636         | 0.15213534     | Up         | 0.00198209 | 0.32405862 |
| miR-762         | 0.15570984     | Up         | 0.08053749 | 0.68993782 |
| miR-1228-3p     | 0.15582107     | Up         | 0.16159926 | 0.76484365 |
| let-7i-5p       | 0.1564672      | Up         | 0.04506864 | 0.61412501 |
| miR-6803-5p     | 0.15994903     | Up         | 0.11245159 | 0.75988515 |
| miR-6893-5p     | 0.16407042     | Up         | 0.01102337 | 0.43937422 |
| let-7i-5p       | 0.16733719     | Up         | 0.14386933 | 0.75376261 |
| miR-636         | 0.16739733     | Up         | 0.04603336 | 0.8745982 |
| miR-3655        | 0.16909089     | Up         | 0.03060868 | 0.4981375 |
| miR-140-3p      | 0.17052129     | Up         | 0.039837   | 0.59871978 |
| miR-3196        | 0.17113537     | Up         | 0.21620731 | 0.7853205 |
| miR-191-3p      | 0.17179396     | Up         | 0.04487927 | 0.61412501 |
| miR-4515        | 0.17261046     | Up         | 0.01939174 | 0.53734625 |
| miR-125b-5p     | 0.17326977     | Up         | 0.58039482 | 0.93436563 |
| miR-4284        | 0.17499241     | Up         | 0.13111512 | 0.74892227 |
| miR-6717-5p     | 0.17647607     | Up         | 0.07006357 | 0.67187824 |
| miR-4455        | 0.17661528     | Up         | 0.05721903 | 0.64832335 |
| miR-4767        | 0.17813392     | Up         | 0.00704444 | 0.40231598 |
| miR-7107-5p     | 0.17892282     | Up         | 0.21620731 | 0.7853205 |
| miR-1260b       | 0.17907235     | Up         | 0.14017212 | 0.75376261 |
| miR-3198        | 0.17929237     | Up         | 0.02123337 | 0.53734625 |
| miR-1290        | 0.18046083     | Up         | 0.03967176 | 0.59871978 |
| miR-4485-3p     | 0.18146467     | Up         | 0.07340574 | 0.68406327 |
| miR-6503-3p     | 0.18796968     | Up         | 0.28804023 | 0.83439474 |
| miR-582-5p      | 0.19045558     | Up         | 0.62677845 | 0.9498341 |
| miR-3940-5p     | 0.19057902     | Up         | 0.06848205 | 0.70907074 |
| miR-6879-5p     | 0.19106394     | Up         | 0.1196758 | 0.74226488 |
| miR-6125        | 0.19120639     | Up         | 0.02231673 | 0.53734625 |
| miR-3162-3p     | 0.19253767     | Up         | 0.06057967 | 0.68432335 |
| miR-4442        | 0.19371999     | Up         | 0.02357392 | 0.54093726 |
| miR-4669        | 0.19873977     | Up         | 0.05279268 | 0.68432335 |
| miR-8063        | 0.19905207     | Up         | 0.33357986 | 0.85486469 |
| miRNABrightCorner30 | 0.20171928 | Up | 0.3490045 | 0.8588192 |
| miR-378d        | 0.20715078     | Up         | 0.16934925 | 0.77062416 |
| dmr_285         | 0.20740733     | Up         | 0.13348728 | 0.74892227 |
| miR-4281        | 0.21053809     | Up         | 0.14469165 | 0.75376261 |
| miR-3653-3p     | 0.21583612     | Up         | 0.20986195 | 0.78263372 |
| dmr_31a         | 0.21728525     | Up         | 0.18051196 | 0.77062416 |
| miR-6800-5p     | 0.21733255     | Up         | 0.1072548 | 0.74226488 |
| miR-8485        | 0.21842128     | Up         | 0.1324725 | 0.74892227 |
| miR-532-3p      | 0.22031918     | Up         | 0.17750992 | 0.77062416 |
| miR-29b-1-5p    | 0.22084105     | Up         | 0.22324885 | 0.79102241 |
| miR-6069        | 0.22136576     | Up         | 0.00413241 | 0.34045223 |

(Continued)
Table 9 (Continued).

| miRNAs       | Log2FoldChange | Regulation | P-value  | P-adj    |
|--------------|----------------|------------|----------|----------|
| miR-574-5p   | 0.22143706     | Up         | 0.09257117 | 0.72287071 |
| miR-4739     | 0.22479676     | Up         | 0.46193717 | 0.89396011 |
| miR-7975     | 0.22883797     | Up         | 0.21088885 | 0.78263372 |
| miR-4721     | 0.2307112      | Up         | 0.0365265  | 0.59871978 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-4721     | 0.2307112      | Up         | 0.0365265  | 0.59871978 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
| miR-1207-5p  | 0.23240555     | Up         | 0.24200969 | 0.80715125 |
| miR-4530     | 0.23343011     | Up         | 0.13226628 | 0.74892227 |
only related to M1 macrophage activation induced exacerbation of inflammatory responses but also related to the absolute insulin deficiency caused by pancreatic β-cells destruction. This study only studies the former, and the effect of these differentially expressed genes on the latter needs further studies.

### Table 9 (Continued).

| miRNAs     | Log2FoldChange | Regulation | P-value     | P-adj      |
|------------|----------------|------------|-------------|------------|
| miR-494-3p | 0.52730171     | Up         | 0.00892038  | 0.40696367 |
| miR-21-3p  | 0.55990013     | Up         | 0.21932847  | 0.78840757 |
| miR-7641   | 0.60997261     | Up         | 5.26×10^{-5} | 0.06753368 |
| miR-378a-3p| 0.65466586     | Up         | 0.07470725  | 0.68406327 |
| miR-378i   | 0.67902917     | Up         | 0.06336176  | 0.6553995  |
| miR-3130-5p| 0.7469237      | Up         | 0.31234802  | 0.8475125  |
| miR-4516   | 0.75421011     | Up         | 0.12234989  | 0.74454632 |
| miR-6769b-5p| 1.16196437    | Up         | 0.00062927  | 0.15302397 |

**Conclusions**

In conclusion, we identified differentially expressed circRNAs, lncRNAs, and mRNAs in the PBMCs from T1DM patients and healthy patients and established a T1DM-related circRNA-lncRNA-miRNA-mRNA ceRNA regulatory network for the first time. The construction of

![Figure 6](https://doi.org/10.2147/DMSO.S315488)
the ceRNA network can help to further analyze the interaction between ncRNAs and mRNAs and provide new insights into the molecular mechanisms in T1DM. The new ceRNA network in this study will contribute to the diagnosis and treatment of T1DM. Of course, our research findings are only the first step. In the follow-up experimental verification study, we will rely on multiple levels, including clinical tissue samples, cell line studies, and animal models, to analyze the internal function mechanism.

Abbreviations
BP, biological processes; CAP, c-Cbl-associated protein; CC, cellular components; circRNA, circular RNA; ceRNA, competitive endogenous RNA; DEcircRNAs, differentially expressed circRNAs; DElncRNAs, differentially expressed IncRNAs; DEGs, differentially expressed genes; DEMRNAs, differentially expressed mRNAs; ECM, extracellular matrix components; GEO, Gene Expression Omnibus; GO, Gene Ontology; IFN-I, type I interferon; KEGG, Kyoto Encyclopedia of Genes and Genomes; lncRNA, long non-coding RNA; miRNA, microRNA; MRE, miRNA response element; MF, molecular functions; ncRNA, non-coding RNA; PBMCs, peripheral blood mononuclear cells; PMA, phorbol 12-myristate 13-acetate; qRT-PCR, Quantitative real-time PCR; T1DM, Type 1 diabetes mellitus.

Author Contributions
Both authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure
The authors declare that they have no conflicts of interest for this work.

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