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ORIGINAL RESEARCH

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

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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.[22,33] 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/) was employed for microarray analysis. The "affy" package was used for normalizing microarray expression profiles as described before.[37] Then, empirical Bayes moderated *t*-test in the "limma" package[38] was applied to screen the differentially expressed genes (DEGs) between T1DM samples and normal samples with P value < 0.05 and log2 (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/) analysis and KEGG (http://www.kegg.jp/) pathway analysis of the differentially expressed circRNA, lncRNA, and mRNAs was

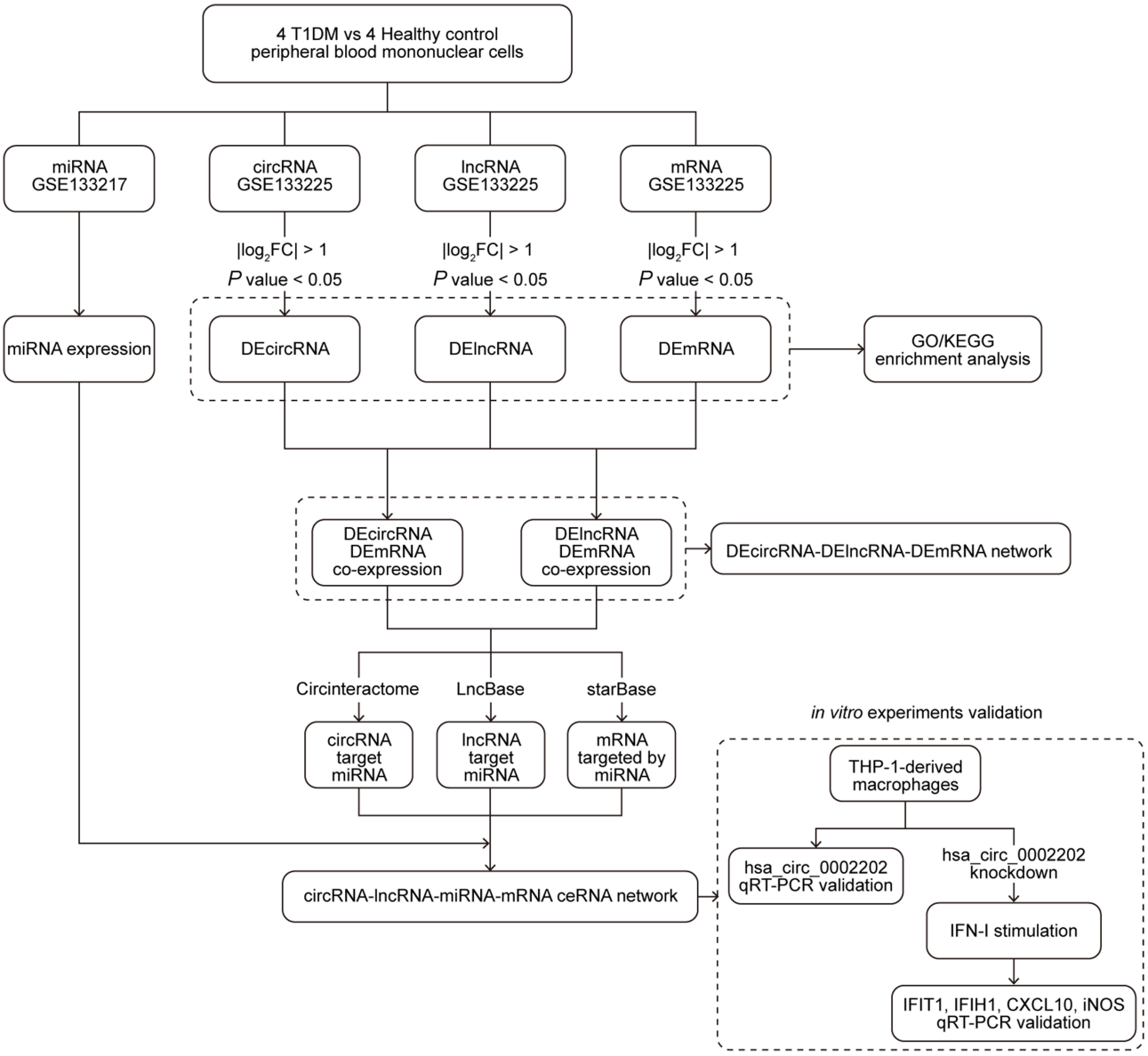

Figure 1 The analysis flow chart of this study.

conducted with the "clusterProfiler" package[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),[40] and KEGG analysis is used to interpret the potential functions and pathways.[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 mRNAs 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 lncRNA-miRNA interactions. starBase web tool (http://starbase.sysu.edu.cn/) was applied to predict the miRNA-mRNA interactions. Finally, a circRNA-lncRNA-miRNA-mRNA interaction network visualized by Cytoscape software[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_2. Then, according to a previous study,[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′-AGTACAACAATTCAGGTGATT-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® 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[43] and normFinder[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	GCCTTGCTGAAGTGTGGAGGAA
IFIT1 reverse	ATCCAGGCGATAGGCAGAGATC
IFIH1 forward	GACTCGGGAATTCGTGGAGG
IFIH1 reverse	CTCAAACGATGGAGAGGGCA
iNOS forward	GCTCTACACCTCCAATGTGACC
iNOS reverse	CTGCCGAGATTTGAGCCTCATG
CXCL10 forward	GGTGAGAAGAGATGTCTGAATCC
CXCL10 reverse	GTCCATCCTTGGAAGCACTGCA
hsa_circ_0002202 forward	GACAAAAGCATGGGGTGTGAG
hsa_circ_0002202 reverse	GCCTCTTCCCATCACCTGAAT
GAPDH forward	GTCTCCTCTGACTTCAACAGCG
GAPDH reverse	ACCACCCTGTTGCTGTAGCCAA
18S rRNA forward	ACACGGACAGGATTGACAGA
18S rRNA reverse	GGACATCTAAGGGCATCACA
β-actin forward	CACCATTGGCAATGAGCGGTTC
β-actin reverse	AGGTCTTTGCGGATGTCCACGT
β-tubulin forward	TGGACTCTGTTCGCTCAGGT
β-tubulin reverse	TGCCTCCTTCCGTACCACAT
U6 forward	CTCGCTTCGGCAGCACA
U6 reverse	AACGCTTCACGAATTTGCGT

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:0005902) (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:0004955), prostanoid receptor activity (GO:0004954), 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-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, 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

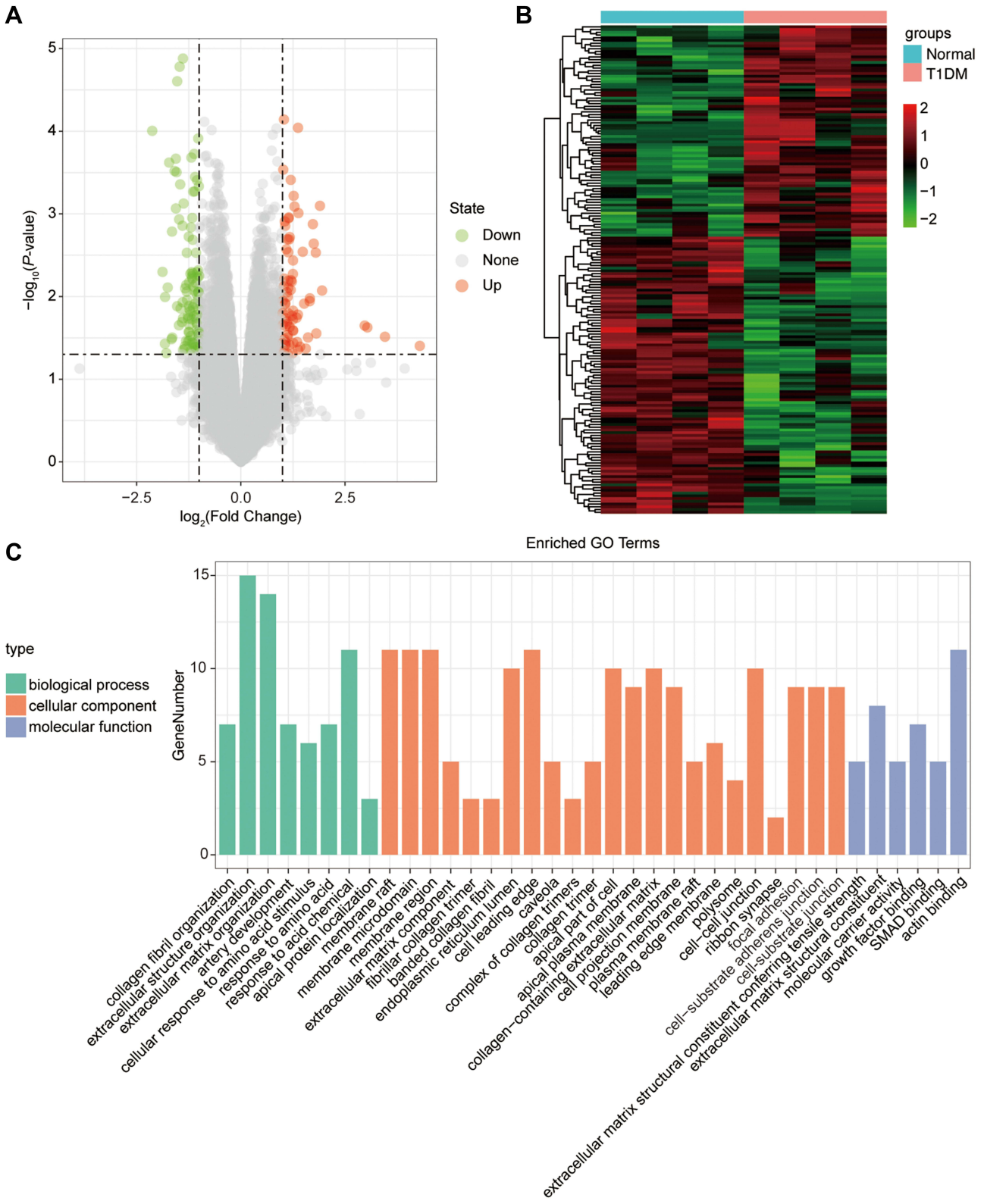

Figure 2 The differentially expressed circRNAs in T1DM and healthy patients. (**A**) Volcano plot of DEcircRNAs between normal and T1DM groups. Red and green indicate up- and downregulation, respectively. (**B**) Heatmap of DEcircRNAs between normal and T1DM groups. Red color represents increased expression, 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.

Table 2 Differentially Expressed circRNAs Between the Control Group and T1DM Group

circRNAs	Log2FoldChange	Regulation	P-value	P-adj
hsa_circ_0060875	−2.1258337	Down	9.90×10^{-5}	0.36011603
hsa_circ_0091120	−1.8790129	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	0.6986421
hsa_circ_0017702	−1.7544417	Down	0.00777686	0.6371225
hsa_circ_0089817	−1.7206724	Down	0.00023941	0.36707996
hsa_circ_0061761	−1.6617103	Down	0.03278591	0.6886992
hsa_circ_0043949	−1.6515359	Down	0.00163728	0.49940512
hsa_circ_0026805	−1.6448912	Down	0.03133761	0.6886992
hsa_circ_0066856	−1.5895376	Down	0.00030271	0.36707996
hsa_circ_0010600	−1.558822	Down	0.00021508	0.36707996
hsa_circ_0089863	−1.5576906	Down	0.00085911	0.45375667
hsa_circ_0012945	−1.5426338	Down	0.00031327	0.36707996
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}	0.27136735
hsa_circ_0070052	−1.4551817	Down	0.00043961	0.37883821
hsa_circ_0055707	−1.4461302	Down	0.01391048	0.6461669
hsa_circ_0018927	−1.4141948	Down	0.0203531	0.66888734
hsa_circ_0053289	−1.3992471	Down	0.00139236	0.49940512
hsa_circ_0055713	−1.3964991	Down	0.01169841	0.6461669
hsa_circ_0092322	−1.3886845	Down	1.32×10^{-5}	0.27136735
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	−1.3119179	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	−1.2544915	Down	0.02684532	0.6886992
hsa_circ_0072670	−1.24989	Down	0.00188517	0.52606124
hsa_circ_0078706	−1.2409986	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*)

Table 2 (Continued).

circRNAs	Log2FoldChange	Regulation	P-value	P-adj
hsa_circ_0008732	−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	0.0188451	0.66175152
hsa_circ_0007872	−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	0.00205924	0.52606124
hsa_circ_0086765	−1.1459122	Down	0.00525476	0.61994831
hsa_circ_0084641	−1.1433833	Down	0.01349551	0.6461669
hsa_circ_0015060	−1.1429878	Down	0.00053871	0.41025776
hsa_circ_0065173	−1.1388487	Down	0.00755684	0.6371225
hsa_circ_0043616	−1.1332645	Down	0.03696064	0.6896574
hsa_circ_0047903	−1.1276276	Down	0.01716979	0.65626057
hsa_circ_0018827	−1.1202055	Down	0.00018818	0.36707996
hsa_circ_0015069	−1.1175352	Down	0.04417262	0.69594076
hsa_circ_0032813	−1.1131832	Down	0.00855541	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	0.01225173	0.6461669
hsa_circ_0046840	−1.0988722	Down	0.00035777	0.36707996
hsa_circ_0028284	−1.0905105	Down	0.04120974	0.69432323
hsa_circ_0019432	−1.0752782	Down	0.00295458	0.52887377
hsa_circ_0047303	−1.0705012	Down	0.00689965	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	0.67318317
hsa_circ_0086805	−1.0531799	Down	0.01662828	0.65471981
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	0.00588311	0.62927103
hsa_circ_0033892	−1.0300829	Down	0.04042024	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	−1.0230977	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	1.00075362	Up	0.03650781	0.6896574
hsa_circ_0073355	1.00406779	Up	0.01584992	0.65471981
hsa_circ_0060973	1.00552219	Up	0.01129814	0.6461669
hsa_circ_0071490	1.00837299	Up	0.02198034	0.67318317
hsa_circ_0073332	1.01653192	Up	0.00029189	0.36707996
hsa_circ_0041267	1.02731163	Up	0.04826044	0.69864211
hsa_circ_0034557	1.02903097	Up	0.04566388	0.69594076
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	0.62927103
hsa_circ_0066752	1.05303312	Up	0.00123282	0.48639953
hsa_circ_0018918	1.05369965	Up	0.03867368	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_0084763	1.06852044	Up	0.0121094	0.6461669
hsa_circ_0079554	1.06923574	Up	0.02296689	0.67670006
hsa_circ_0003310	1.07580527	Up	0.03868275	0.6896574
hsa_circ_0072445	1.0780832	Up	0.01833869	0.6573827
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	0.6663805
hsa_circ_0011437	1.11571417	Up	0.00203065	0.52606124
hsa_circ_0038162	1.12089009	Up	0.0312031	0.6886992
hsa_circ_0006561	1.12140856	Up	0.02905904	0.6886992
hsa_circ_0019321	1.12534202	Up	0.01003317	0.6404092
hsa_circ_0066588	1.13259964	Up	0.00644124	0.6371225
hsa_circ_0068846	1.13350867	Up	0.04980974	0.69965823
hsa_circ_0048941	1.13392642	Up	0.00783921	0.6371225
hsa_circ_0013276	1.1353225	Up	0.01594875	0.65471981
hsa_circ_0084803	1.13561704	Up	0.00291642	0.52887377
hsa_circ_0009718	1.14501876	Up	0.00113062	0.47332912
hsa_circ_0052890	1.14899657	Up	0.00110269	0.47332912
hsa_circ_0052578	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_0077040	1.19660605	Up	0.00038828	0.36707996
hsa_circ_0064649	1.20323629	Up	0.00634396	0.63530743
hsa_circ_0057921	1.22298163	Up	0.00658344	0.6371225
hsa_circ_0010167	1.22782484	Up	0.01705561	0.65626057
hsa_circ_0002626	1.23796418	Up	0.04850693	0.69864211
hsa_circ_0004814	1.24697128	Up	0.01902014	0.66175152
hsa_circ_0073356	1.24865998	Up	0.0053345	0.61994831
hsa_circ_0045123	1.24884849	Up	0.02550036	0.68798091
hsa_circ_0069213	1.25118583	Up	0.00366065	0.58881715
hsa_circ_0079548	1.25190508	Up	0.01484117	0.6461669

(*Continued*)

Table 2 (Continued).

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	0.6896574
hsa_circ_0069324	1.26605445	Up	0.00060556	0.42191899
hsa_circ_0060335	1.28618107	Up	0.00081571	0.44105722
hsa_circ_0058206	1.33626161	Up	0.01802886	0.65626057
hsa_circ_0056882	1.34999287	Up	0.03545574	0.6886992
hsa_circ_0013437	1.36836499	Up	0.01654656	0.65471981
hsa_circ_0046700	1.36944609	Up	0.0439923	0.69594076
hsa_circ_0082549	1.37107512	Up	9.10×10^{-5}	0.36011603
hsa_circ_0057436	1.37990777	Up	0.00097797	0.47332912
hsa_circ_0048871	1.42092532	Up	0.04047976	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	0.01137625	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	1.74809879	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	1.89666917	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	3.03306764	Up	0.02362915	0.67886653
hsa_circ_0092236	3.45575278	Up	0.03065391	0.6886992
hsa_circ_0092221	4.29199121	Up	0.03950529	0.68996252

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.[45] lncRNA H2k2/miR-449a/b/Trim11 signaling pathway promotes mesangial cell proliferation in diabetic nephropathy.[46] Hsa_circ_010567/miR-141/TGF-β1 axis promotes myocardial fibrosis in diabetic mice.[47] 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

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	11	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	0.00744481
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	0.01385878
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	0.04570731
CC	GO:0005924	Cell-substrate adherens junction	9	0.04581649
CC	GO:0030055	Cell-substrate junction	9	0.04674156
MF	GO:0030020	Extracellular matrix structural constituent conferring tensile strength	5	0.00708066
MF	GO:0005201	Extracellular matrix structural constituent	8	0.00916654
MF	GO:0140104	Molecular carrier activity	5	0.00916654
MF	GO:0019838	Growth factor binding	7	0.01134742
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[48] or circRNA,[33] 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

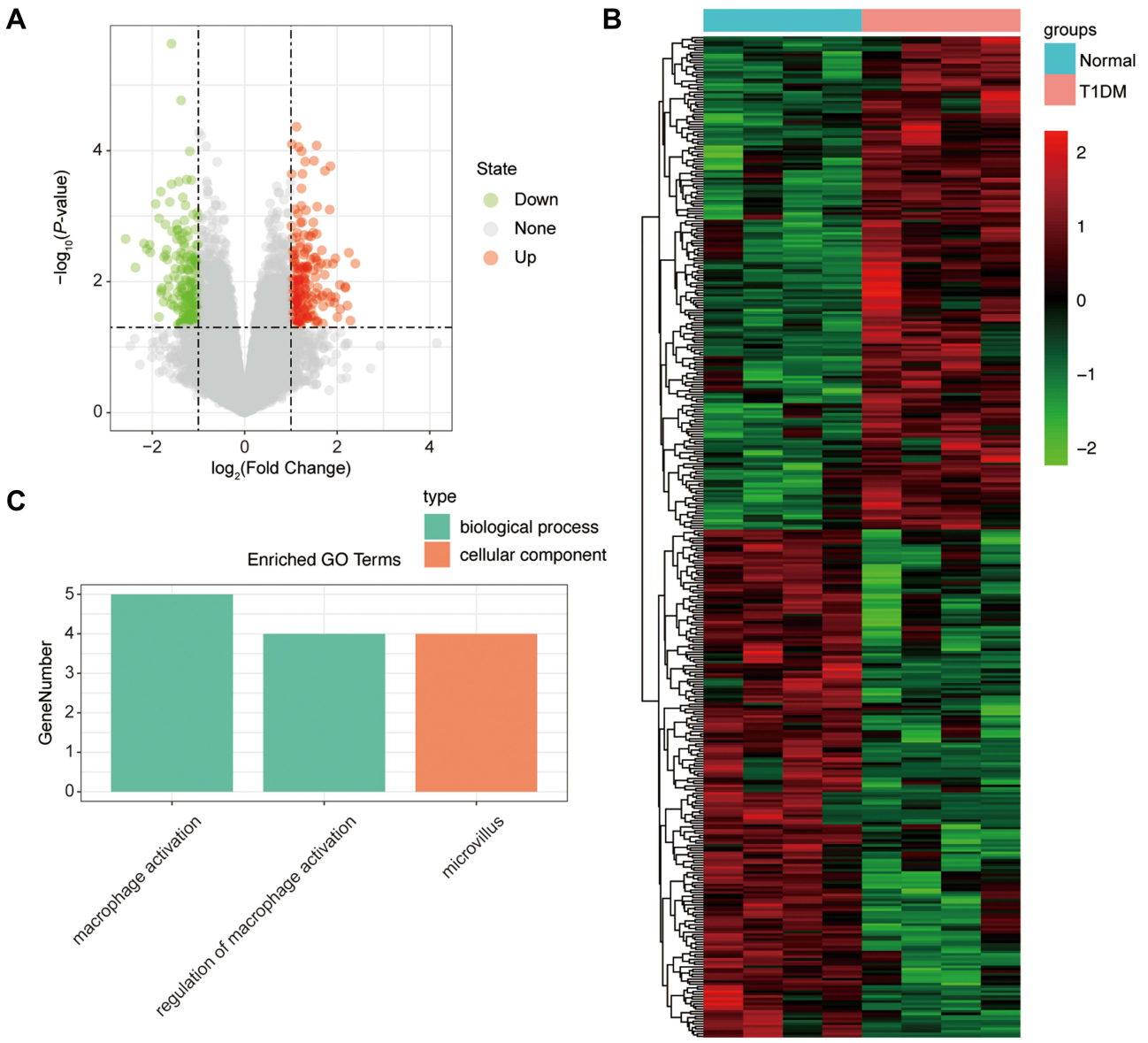

Figure 3 The differentially expressed lncRNAs in T1DM and healthy patients. (**A**) Volcano plot of DElncRNAs between normal and T1DM groups. Red and green indicate up- and downregulation, respectively. (**B**) Heatmap of DElncRNAs between normal and T1DM groups. Red color represents increased expression, 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.

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.[49] Liu et al found that circSAMD4A acts as an adipogenesis promoting factor.[50] 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,[26] we detected

Table 5 Differentially Expressed lncRNAs Between the Control Group and T1DM Group

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
lnc-MARC1-2:1	−2.571855	Down	0.002228	0.49624236
lnc-PSMG1-3:2	−2.3628597	Down	0.00610319	0.55695089
CCND2-AS1-201	−2.1767994	Down	0.00261656	0.51224337
lnc-ANGPTL2-7:1	−2.1177664	Down	0.00318539	0.53930742
AL356740.2–201	−2.0532982	Down	0.0027546	0.51224337
lnc-APBA2-1:3	−2.0384649	Down	0.00358789	0.54892347
lnc-SEL1L3-10:1	−1.9247783	Down	0.00065127	0.39679443
ENPP7P13	−1.8523605	Down	0.03454029	0.72695785
lnc-MBNL2-2:1	−1.8516299	Down	0.00108059	0.42609515
lnc-CTD-2523D13.1.1–2:3	−1.8151432	Down	0.00042329	0.33998788
LOC101929733	−1.805357	Down	0.01482033	0.65476375
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
lnc-CD5L-1:1	−1.7425319	Down	0.00420523	0.55695089
SEMA6A-AS1-206	−1.7140352	Down	0.00134151	0.4460612
LINC00299-203	−1.71106	Down	0.00391051	0.55546359
lnc-FRZB-2:2	−1.6847279	Down	0.00324333	0.53930742
GGNBP1	−1.6719447	Down	0.0166596	0.65620897
lnc-UNC5CL-7:1	−1.6687674	Down	0.00461045	0.55695089
lnc-MRPS5-13:1	−1.6546035	Down	0.00921325	0.6151086
lnc-C1orf64-1:1	−1.6395822	Down	0.01190126	0.63705043
AL136979.1–201	−1.6202871	Down	0.0006092	0.39679443
lnc-CNGB1-1:3	−1.5925938	Down	0.02212688	0.6889443
AL021937.6–201	−1.5827605	Down	0.00032605	0.33391458
lnc-RASGRP1-6:1	−1.5821617	Down	2.33×10^{-6}	0.05960188
lnc-ANO2-4:1	−1.5733225	Down	0.00170014	0.48365219
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	0.60770111
AC108935.1–201	−1.5001012	Down	0.00635053	0.55695089
lnc-TBC1D3C-4:1	−1.4786853	Down	0.00403532	0.55546359
lnc-LIPI-6:1	−1.4669252	Down	0.00132802	0.4460612
lnc-FCHSD2-4:1	−1.4647594	Down	0.00223289	0.49624236
AC104590.1–201	−1.458406	Down	0.00163683	0.47784335
lnc-NDFIP2-8:1	−1.4500676	Down	0.01442379	0.65361455
lnc-AL359878.1–1:1	−1.4473997	Down	0.04508299	0.74859413
lnc-NUP98-2:1	−1.4448238	Down	0.02667345	0.70331657
lnc-DTHD1-2:1	−1.4441469	Down	0.00161419	0.47784335
lnc-DCAF4L1-1:1	−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	0.49624236
lnc-IRF5-2:1	−1.4087918	Down	0.04752968	0.75874445
lnc-FXYD2-1:2	−1.4016591	Down	0.01605233	0.65476375
ENST00000434742	−1.3965605	Down	0.04266873	0.74199989
LINC00710-210	−1.3926583	Down	0.00459619	0.55695089
lnc-RUNX1T1-6:1	−1.390228	Down	0.04310897	0.74348205
lnc-REP15-2:1	−1.3887183	Down	0.01204392	0.63775317

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
lnc-GLCCI1-5:1	−1.3790449	Down	0.00360051	0.54892347
lnc-TDRD5-2:2	−1.3779141	Down	0.00653613	0.56344961
lnc-TIPARP-1:1	−1.3745656	Down	1.71×10^{-5}	0.219024
NONHSAT144810	−1.3733309	Down	0.04223393	0.74199989
lnc-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
NONHSAT078217	−1.3517092	Down	0.03830547	0.73920545
HSFY1P1	−1.3512769	Down	0.02395161	0.69616967
AL365295.1–203	−1.3483624	Down	0.00642502	0.55846139
lnc-ST8SIA4-9:1	−1.3434237	Down	0.04271071	0.74199989
LINC01461	−1.3413799	Down	0.01143714	0.63705043
lnc-GPR27-16:1	−1.3407603	Down	0.01468499	0.65476375
AC005772.1–201	−1.3381628	Down	0.00051768	0.37869313
MIR2117	−1.3345777	Down	0.00182095	0.49597572
lnc-GPR180-8:1	−1.3325294	Down	0.04785484	0.75909133
lnc-CDH19-1:1	−1.3297711	Down	0.00373595	0.55546359
lnc-MYLIP-1:1	−1.3230214	Down	0.03290443	0.7208645
lnc-AC006156.1–6:1	−1.3212148	Down	0.03163903	0.72031743
LINC00326-202	−1.3131651	Down	0.002781	0.51224337
lnc-THSD7A-5:1	−1.3104044	Down	0.01270662	0.63775317
AL513320.1–201	−1.3078099	Down	0.02483242	0.69822202
LOC100288570	−1.302538	Down	0.00116144	0.42609515
OR4F13P	−1.3002494	Down	0.00258605	0.51224337
SKAP1-AS1-201	−1.2965689	Down	0.0399885	0.74199989
lnc-ZC3H12B-8:1	−1.2960126	Down	0.00485753	0.55695089
lnc-DDX58-6:2	−1.2919894	Down	0.04664872	0.75453224
lnc-MRPL9-1:1	−1.2821415	Down	0.0193777	0.67753348
lnc-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
lnc-SERP2-13:1	−1.2711219	Down	0.03525604	0.72695785
lnc-NKD2-3:8	−1.2692144	Down	0.01741431	0.65667837
lnc-CSNK1A1-6:1	−1.2661357	Down	0.03246677	0.72031743
lnc-TMEM178-4:1	−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
lnc-SRY-12:1	−1.255766	Down	0.04179039	0.74199989
LOC101929541	−1.2543068	Down	0.00422143	0.55695089
lnc-IQCG-1:1	−1.2510293	Down	0.00960776	0.6151086
lnc-TRAF7-1:4	−1.250778	Down	0.02651159	0.7025969
AC068051.1–202	−1.250693	Down	0.01630728	0.65588218
lnc-WSB1-9:1	−1.2499003	Down	0.00027697	0.33391458
HIPK1-AS1-202	−1.247658	Down	0.00646044	0.55880591
lnc-ANKRD65-4:1	−1.2456674	Down	0.00167491	0.48182856
lnc-RASD1-2:1	−1.2336926	Down	0.03531618	0.72695785
lnc-PTPN12-1:1	−1.2251669	Down	0.00203611	0.49624236
lnc-ASAH2B-6:1	−1.2249331	Down	0.02282058	0.69285761
lnc-VSTM2B-7:1	−1.2187025	Down	0.00664315	0.56471029

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
AC009145.3–201	−1.2150544	Down	0.00669705	0.56471029
lnc-EXOC4-2:1	−1.2094249	Down	0.03638874	0.73000405
lnc-ASF1A-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
lnc-RP11-148O21.3.1–3:1	−1.1989594	Down	0.03101553	0.72031743
lnc-VCPIP1-2:1	−1.1940207	Down	0.01680361	0.65667837
lnc-MANEA-15:1	−1.1934022	Down	0.03073549	0.71864918
AP007216.1–201	−1.1933507	Down	0.03903039	0.74199989
lnc-BOC-1:1	−1.1894086	Down	0.03214827	0.72031743
lnc-ALCAM-16:1	−1.1864006	Down	0.00010229	0.23823842
AC243965.1–201	−1.1825172	Down	0.00992456	0.61994889
lnc-SNRPEP2-1:1	−1.1777925	Down	0.00505178	0.55695089
MIR8063	−1.1720035	Down	0.03554046	0.72695785
LINC01497	−1.1712102	Down	0.00396132	0.55546359
AP005202.1–201	−1.1711452	Down	0.02687222	0.70508418
lnc-CA5A-14:1	−1.170243	Down	0.01880508	0.66963349
TBC1D26-AS1-201	−1.1690859	Down	0.03794326	0.73763201
lnc-RHOB-6:4	−1.164896	Down	0.00952576	0.6151086
lnc-TMEM235-1:1	−1.1644461	Down	0.02080375	0.68520443
lnc-NKAIN3-1:1	−1.1639521	Down	0.01613077	0.65476375
lnc-TFAP2A-12:1	−1.1638797	Down	0.0458381	0.75250711
NONHSAT080748	−1.1637059	Down	0.04242998	0.74199989
lnc-WDR1-2:1	−1.1612431	Down	0.01413228	0.64612284
lnc-STYK1-2:1	−1.160814	Down	0.03332132	0.72302337
lnc-C2CD4A-8:3	−1.1589171	Down	0.03249489	0.72031743
lnc-RAB9A-4:1	−1.1570636	Down	0.04423563	0.74774931
lnc-GRIK4-2:1	−1.1570003	Down	0.01043825	0.62720663
AL356124.1–212	−1.1529537	Down	0.0059984	0.55695089
lnc-GRID1-10:2	−1.1509303	Down	0.00028173	0.33391458
lnc-DMRTA1-21:1	−1.1494581	Down	0.02080202	0.68520443
COPG2IT1	−1.1488501	Down	0.03280207	0.7208645
GUSBP1	−1.1442627	Down	0.03300713	0.7208645
lnc-AC016251.1–18:1	−1.1426114	Down	0.01124953	0.63705043
lnc-IGHMBP2-2:1	−1.1410125	Down	0.01522257	0.65476375
lnc-CLK1-5:1	−1.1408544	Down	0.00456639	0.55695089
lnc-DDIT4L-1:1	−1.139392	Down	0.0033263	0.54489032
lnc-ATP8A2-4:1	−1.1309851	Down	0.01285546	0.63775317
AC002550.1–201	−1.1258339	Down	0.03121112	0.72031743
lnc-BX255923.1–4:1	−1.1254471	Down	0.02958836	0.71263333
LRRC37A6P	−1.1246433	Down	0.01039373	0.62720663
lnc-THBD-3:1	−1.1181096	Down	0.01823629	0.66321547
SMIM2-IT1	−1.1152686	Down	0.04821159	0.75909133
lnc-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	0.55695089
lnc-HECA-8:3	−1.1007561	Down	0.01730192	0.65667837
lnc-CAMK2N2-1:1	−1.100534	Down	0.02254575	0.69130412

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
lnc-RET-2:1	−1.0994363	Down	0.02204275	0.6889443
AC006482.1–201	−1.0943276	Down	0.01606638	0.65476375
NONHSAT066757	−1.0893525	Down	0.02619728	0.7025969
lnc-PCIF1-1:1	−1.0831588	Down	0.03331068	0.72302337
lnc-RGS9-1:9	−1.0808278	Down	0.04328182	0.74348205
lnc-TMEM63B-3:1	−1.0806828	Down	0.03297302	0.7208645
AL354726.1–201	−1.0779947	Down	0.03804582	0.7382395
lnc-VPS45-5:1	−1.0767237	Down	0.03551093	0.72695785
MIR100HG-204	−1.0749286	Down	0.00478367	0.55695089
lnc-ERMN-3:1	−1.0724303	Down	0.01323341	0.63919136
lnc-POM121L12-9:1	−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
lnc-CCNJL-3:1	−1.0661945	Down	0.03740759	0.73503181
lnc-SLC4A3-7:4	−1.0657752	Down	0.00420941	0.55695089
AC096666.1–201	−1.0645687	Down	0.0475234	0.75874445
TRAPPC12-AS1-201	−1.0621034	Down	0.00527019	0.55695089
AC010973.1–201	−1.0620397	Down	0.01113385	0.63705043
lnc-PYGO1-3:1	−1.0617362	Down	0.00735041	0.57770209
NONHSAT106126	−1.0615194	Down	0.00454088	0.55695089
lnc-ZNF33A-7:1	−1.0611652	Down	0.02394318	0.69616967
AC021097.1–201	−1.0607721	Down	0.00678068	0.56733936
lnc-SNX11-9:1	−1.0565877	Down	0.04932529	0.75985275
LINC00092-202	−1.0542115	Down	0.00493655	0.55695089
LOC100130417	−1.0441384	Down	0.02061929	0.68461156
lnc-DACT1-2:1	−1.0422563	Down	0.00276522	0.51224337
lnc-CACNA1E-5:3	−1.0418233	Down	0.032085	0.72031743
lnc-KCNJ2-2:1	−1.0409158	Down	0.03770802	0.73763201
ZNF451-AS1-202	−1.0407145	Down	0.0199397	0.68003654
AC022509.1–203	−1.0393619	Down	0.04632896	0.75407344
AL162253.1–201	−1.039287	Down	0.04553105	0.75046636
LINC01339	−1.0376761	Down	0.01322858	0.63919136
RNU4-30P-201	−1.03405	Down	0.04484526	0.74859413
lnc-ZNF527-3:1	−1.0331657	Down	0.00495913	0.55695089
lnc-VSTM4-1:3	−1.0311378	Down	0.03884105	0.74199989
lnc-ORMDL2-3:1	−1.0308522	Down	0.03578571	0.7283161
lnc-AKIP1-5:1	−1.0271559	Down	0.02023333	0.68302181
AL359091.4–201	−1.0270896	Down	0.04632883	0.75407344
lnc-PPIAL4G-24:1	−1.0236308	Down	0.02813286	0.70952942
LOC100506679	−1.0230377	Down	0.00087856	0.41823037
lnc-TSSC1-12:1	−1.0215854	Down	0.00560415	0.55695089
LOC100505984	−1.0208834	Down	0.0255792	0.7025969
lnc-FAM50B-12:1	−1.0196309	Down	0.02412553	0.69616967
lnc-ALG9-1:1	−1.0176951	Down	0.00552229	0.55695089
AC096669.1–201	−1.0157852	Down	0.03891937	0.74199989
lnc-ZNF135-1:1	−1.0126176	Down	0.02399892	0.69616967
lnc-C2orf65-7:1	−1.0125274	Down	0.03958279	0.74199989
NONHSAT093043	−1.0122218	Down	0.0244619	0.69781796
lnc-MARCKS-2:1	−1.0108829	Down	0.01484675	0.65476375

(*Continued*)

Table 5 (Continued).

lncRNAs	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-HS3ST3A1-6:1	−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	0.65667837
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	0.04176408	0.74199989
NONHSAT103382	1.00610895	Up	0.01949203	0.67753348
lnc-ZNF729-1:1	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	0.04488089	0.74859413
lnc-SCARF1-1:1	1.0156664	Up	0.00981816	0.61762722
NONHSAT018354	1.01593666	Up	0.03530828	0.72695785
lnc-FMN2-5:1	1.01602171	Up	0.0002276	0.32373463
lnc-SGIP1-3:1	1.01645757	Up	0.01641438	0.65588218
LINC01640-201	1.01688724	Up	0.04089227	0.74199989
AC091906.1–201	1.01953621	Up	0.03271348	0.7208645
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	1.02955928	Up	0.0127837	0.63775317
lnc-VPS45-1:1	1.03014965	Up	0.02882574	0.71150768
lnc-ATP6AP2-5:1	1.03058486	Up	0.01059718	0.62720663
lnc-SSX1-3:1	1.03120136	Up	0.00345991	0.54892347
lnc-TMEM144-6:1	1.03146297	Up	0.00218147	0.49624236
AC064805.1–203	1.03207632	Up	0.01476632	0.65476375
AL049781.1–201	1.03367342	Up	0.03188715	0.72031743
lnc-CD38-5:1	1.03537123	Up	0.02413739	0.69616967
lnc-RDH10-3:1	1.0354704	Up	0.00905218	0.6151086
MIR527	1.03634444	Up	0.04629443	0.75407344
lnc-IL36B-3:1	1.04032276	Up	0.03473821	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	1.06395774	Up	0.02171233	0.6875777
lnc-FREM3-4:1	1.06877234	Up	0.03813847	0.7386227

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
lnc-ZAP70-2:44	1.0688365	Up	0.01504184	0.65476375
lnc-ZSCAN5A-1:1	1.06985443	Up	0.01950186	0.67753348
lnc-DDHD1-7:1	1.07032663	Up	0.00334132	0.54489032
TMEM18-DT-201	1.07452939	Up	0.00488947	0.55695089
ENST00000614227	1.07841048	Up	0.00384573	0.55546359
lnc-NADKD1-2:1	1.07972767	Up	0.02298006	0.69368951
lnc-WDR96-3:1	1.08166487	Up	0.02824276	0.70952942
AC106028.4–201	1.08382489	Up	0.04826811	0.75909133
lnc-LYSMD3-2:1	1.0840707	Up	0.01190799	0.63705043
RNU6-709P-201	1.08652258	Up	0.0044661	0.55695089
lnc-FAM75B-2:1	1.08830209	Up	0.02084896	0.68520443
lnc-CDYL-9:1	1.08948305	Up	0.00637373	0.55695089
lnc-PDE1C-2:3	1.09008387	Up	0.00078375	0.41823037
lnc-SRRM1-4:1	1.09019086	Up	0.01620667	0.65476375
AC012363.1–201	1.09404463	Up	0.04399763	0.74634378
lnc-RP1L1-3:3	1.09943997	Up	0.01034911	0.62720663
lnc-TBPL2-3:1	1.09976307	Up	0.02214589	0.6889443
AC091078.1–201	1.10348942	Up	0.01206545	0.63775317
AC079456.1–201	1.10454579	Up	0.00559852	0.55695089
lnc-ASPH-5:3	1.10750927	Up	0.02233274	0.69018461
lnc-EXTL3-1:3	1.11176621	Up	0.02864791	0.71004105
TMEM108-AS1-201	1.11243266	Up	0.04766525	0.75874445
LINC00463	1.1130875	Up	0.02148542	0.6875777
TYMSOS-202	1.11588444	Up	0.00210834	0.49624236
lnc-FAM19A3-7:1	1.11995024	Up	4.32×10^{-5}	0.23823842
AC011481.1–201	1.1228884	Up	0.02649529	0.7025969
ATRNL1	1.12368531	Up	0.01534705	0.65476375
SNHG14-221	1.12569191	Up	0.04719373	0.75708084
lnc-ACAD11-2:1	1.12954103	Up	0.01867463	0.66684299
AC127496.3–201	1.13361155	Up	0.00180459	0.49597572
lnc-FAM27B-9:1	1.13529595	Up	0.01792398	0.65667837
lnc-ANO6-2:1	1.14150763	Up	0.00932979	0.6151086
lnc-BAG4-4:1	1.14644342	Up	0.02936139	0.71263333
lnc-ABCA1-1:2	1.14734442	Up	0.00747609	0.58535254
lnc-GGPS1-7:1	1.14849917	Up	0.01982258	0.68003654
lnc-ITPRIP-7:1	1.14881355	Up	0.02032843	0.68302181
lnc-PCBP1-4:1	1.15063821	Up	0.00625079	0.55695089
lnc-PABPC3-3:2	1.15120963	Up	0.00091832	0.41823037
lnc-HERC4-1:1	1.15522135	Up	0.03708868	0.73471054
lnc-IQCH-7:1	1.1603186	Up	0.01001295	0.62174278
lnc-C16orf78-5:3	1.16644237	Up	8.81×10^{-5}	0.23823842
C1QTNF7-AS1-202	1.17053152	Up	0.00916598	0.6151086
lnc-VASH2-1:1	1.17220568	Up	0.04245329	0.74199989
LINC01255-204	1.17230984	Up	0.00953825	0.6151086
lnc-ATG3-2:1	1.17235799	Up	0.01125376	0.63705043
lnc-GLT1D1-5:1	1.17473163	Up	0.04455268	0.74859413
lnc-CR392000.1–2:1	1.17483834	Up	0.04007513	0.74199989
lnc-HMGB2-5:1	1.17590206	Up	0.02536006	0.69966978
lnc-CDY2A-13:1	1.18188326	Up	0.01485835	0.65476375

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
AC023355.1–202	1.1849183	Up	0.01732148	0.65667837
lnc-USP12-5:2	1.18622738	Up	0.04358103	0.74483576
LOC101929080	1.19054239	Up	0.01223231	0.63775317
lnc-KCNC2-5:1	1.19486915	Up	0.009252	0.6151086
lnc-KNTC1-4:1	1.19535911	Up	0.00297243	0.53593679
lnc-JAM3-8:1	1.19852384	Up	0.00257337	0.51224337
lnc-NKX6-1-10:1	1.20120674	Up	0.01409262	0.64546217
lnc-ARG2-1:2	1.20386745	Up	0.00126408	0.43152476
lnc-KALRN-4:1	1.20497602	Up	0.00582578	0.55695089
lnc-CORO2B-1:2	1.20602566	Up	0.00664972	0.56471029
lnc-URB2-1:3	1.20715033	Up	0.02185892	0.68799902
lnc-HS3ST3A1-5:2	1.21290644	Up	0.04894508	0.75985275
Z98885.3–201	1.21299164	Up	0.01621373	0.65476375
lnc-WDR64-2:2	1.21682833	Up	0.04578576	0.75240869
LOC101929452	1.2233498	Up	0.03206412	0.72031743
lnc-PAICS-4:1	1.22411726	Up	0.0006972	0.39679443
AL020994.1–201	1.2262244	Up	0.00037776	0.33998788
lnc-CNIH3-1:1	1.2316038	Up	0.00010236	0.23823842
PRNCR1	1.2406871	Up	0.00123666	0.43152476
AC024475.1–201	1.24543291	Up	0.02421639	0.69616967
lnc-DDX52-2:1	1.24950582	Up	0.00022629	0.32373463
lnc-SLFN12-6:1	1.24993787	Up	0.03623298	0.73000405
AC093297.1–201	1.26032356	Up	0.03683869	0.73355985
U1.18–201	1.26323937	Up	0.00602542	0.55695089
lnc-GTPBP5-3:1	1.26463283	Up	0.03100912	0.72031743
LINC02773-201	1.27552196	Up	0.00387626	0.55546359
lnc-FAM104A-4:2	1.2756097	Up	0.00884705	0.6151086
lnc-SYCP2-3:1	1.27585656	Up	0.01741856	0.65667837
NONHSAT106296	1.28232348	Up	0.02753193	0.70738927
lnc-TMEM123-3:2	1.28431214	Up	0.00636859	0.55695089
LOC102723833	1.28894382	Up	0.00193168	0.49624236
lnc-GPR149-4:1	1.29256774	Up	0.00893933	0.6151086
lnc-SLCO4C1-4:1	1.29343344	Up	0.02627738	0.7025969
AL359541.1–201	1.2959487	Up	0.009658	0.6151086
ATP2B1-AS1-201	1.29766918	Up	0.00356845	0.54892347
AP000879.1–202	1.29942575	Up	0.00578872	0.55695089
lnc-RP11-6L6.2.1–3:1	1.3032656	Up	0.01303033	0.63911018
LOC102546298	1.30753746	Up	0.00014704	0.27188326
lnc-ZCCHC9-2:5	1.30773357	Up	0.01041044	0.62720663
lnc-ITGB1-4:2	1.31033236	Up	0.00767846	0.59393265
lnc-RP11-257K9.7.1–3:1	1.31103839	Up	0.01633508	0.65588218
LINC02864-202	1.31194048	Up	0.01303027	0.63911018
LINC01855-201	1.32678547	Up	0.00081184	0.41823037
lnc-C8orf4-1:2	1.33018827	Up	0.00593828	0.55695089
lnc-RP11-150O12.3.1–1:4	1.34017651	Up	0.01509456	0.65476375
lnc-ZNF503-AS2-9:1	1.34488751	Up	0.03296829	0.7208645
AC120498.2–201	1.34578622	Up	0.00320335	0.53930742
lnc-HEATR4-5:1	1.3461323	Up	0.03623736	0.73000405
lnc-CNR1-1:2	1.35206876	Up	0.00627778	0.55695089

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
lnc-SMYD5-1:4	1.35280066	Up	0.00601195	0.55695089
lnc-NUPL1-1:1	1.35697674	Up	0.02392115	0.69616967
lnc-AKR1E2-5:1	1.35847468	Up	0.01769903	0.65667837
AC012314.2–201	1.35985353	Up	0.03496286	0.72695785
lnc-CNDP2-1:1	1.36188928	Up	0.00584868	0.55695089
lnc-CHGA-2:1	1.3642467	Up	0.02269448	0.69285761
MIR1307	1.36484241	Up	0.03613377	0.73000405
lnc-SRGN-3:1	1.37117291	Up	0.00300049	0.53721319
lnc-XRCC2-3:1	1.38735139	Up	0.00200603	0.49624236
LRRK2-DT-202	1.39577039	Up	0.01113659	0.63705043
AC113133.1–203	1.43171942	Up	0.00455193	0.55695089
lnc-CCL3-1:2	1.43199469	Up	0.02692513	0.70508418
lnc-RTKN2-5:1	1.43324395	Up	0.00204034	0.49624236
BX005019.1–201	1.43992263	Up	0.0338234	0.72437788
lnc-C14orf182-4:1	1.45445268	Up	0.01695345	0.65667837
AC034199.1–201	1.47353584	Up	0.0213565	0.6875777
lnc-LYZL1-10:1	1.48259417	Up	0.00124885	0.43152476
lnc-LRIG1-3:1	1.48289858	Up	0.00178858	0.49597572
AL391241.1–201	1.48399065	Up	0.03316116	0.72302337
lnc-MAP1LC3B2-4:3	1.49320191	Up	0.00670515	0.56471029
lnc-RAD51B-1:1	1.49785989	Up	0.00014303	0.27188326
MIR425	1.50669826	Up	0.0042996	0.55695089
lnc-SIM2-2:1	1.52947082	Up	0.04100787	0.74199989
PRMT5-AS1-206	1.53103618	Up	0.00853801	0.6151086
AC027018.1–202	1.53360865	Up	0.01496409	0.65476375
lnc-ARF6-5:1	1.5402516	Up	0.00426956	0.55695089
lnc-KCNK9-3:1	1.55537316	Up	8.35×10^{-5}	0.23823842
LOC102724484	1.55813648	Up	0.00484276	0.55695089
lnc-VAMP3-3:1	1.55906933	Up	0.01857284	0.66521456
lnc-MRPS18A-2:6	1.5595027	Up	0.00187188	0.49624236
lnc-TACR2-5:1	1.56018317	Up	0.03954105	0.74199989
lnc-APCDD1L-1:1	1.56781969	Up	0.00071636	0.3987193
lnc-RILP-1:5	1.57733865	Up	0.01232391	0.63775317
NONHSAT106835	1.58291652	Up	0.04113014	0.74199989
AC066595.1–201	1.59152878	Up	0.00607687	0.55695089
AP002505.2–201	1.65111587	Up	0.00528326	0.55695089
lnc-ROPN1B-8:1	1.66748053	Up	0.0033198	0.54489032
lnc-NLK-1:2	1.66793517	Up	0.01702869	0.65667837
lnc-SH3BGRL2-8:1	1.68256761	Up	0.01627335	0.65588218
LINC00862	1.69076057	Up	0.04360851	0.74483576
lnc-XK-2:1	1.69608599	Up	0.02384559	0.69616967
AL606468.1–201	1.72966979	Up	0.00784283	0.59809568
lnc-DRD3-2:1	1.73507434	Up	0.0002036	0.32373463
lnc-ASMT-7:1	1.77985488	Up	0.00534204	0.55695089
AC022001.3–201	1.78553082	Up	0.01479698	0.65476375
AC090643.2–201	1.83684053	Up	0.00079596	0.41823037
NONHSAT106837	1.84066898	Up	0.02058467	0.68445357
AC103993.1–202	1.85414231	Up	0.00017245	0.29435292

(*Continued*)

Table 5 (Continued).

lncRNAs	Log2FoldChange	Regulation	P-value	P-adj
lnc-CPXM2-2:2	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
lnc-C2orf62-1:1	1.96238874	Up	0.01728119	0.65667837
PELATON-201	2.00463147	Up	0.03488425	0.72695785
lnc-C5-1:1	2.0585191	Up	0.01120735	0.63705043
lnc-PON2-3:1	2.06777784	Up	0.02628724	0.7025969
lnc-IFNA2-2:1	2.17522445	Up	0.0119433	0.63705043
AL359258.1–201	2.17725336	Up	0.01246482	0.63775317
lnc-CEACAM6-1:1	2.22056145	Up	0.02321939	0.69449317
lnc-EVI2A-1:1	2.25337956	Up	0.00361694	0.54892347
lnc-CXCL3-1:1	2.28502109	Up	0.03936439	0.74199989
lnc-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:0005902	Microvillus	4	0.02267082

Abbreviations: BP, biological process; CC, cellular component.

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.[51] 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_0002207 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.[52] Increased expression of miR-326 was identified in PBMSCs[53] and peripheral blood lymphocytes[54] of patients with T1DM. Another study showed a decreased expression level of miR-326 in PBMCs of patients with T1DM.[55] 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.[56] miR-31-5p, miR-665, miR-326, miR-224 are associated with inflammatory bowel disease.[56–59] 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

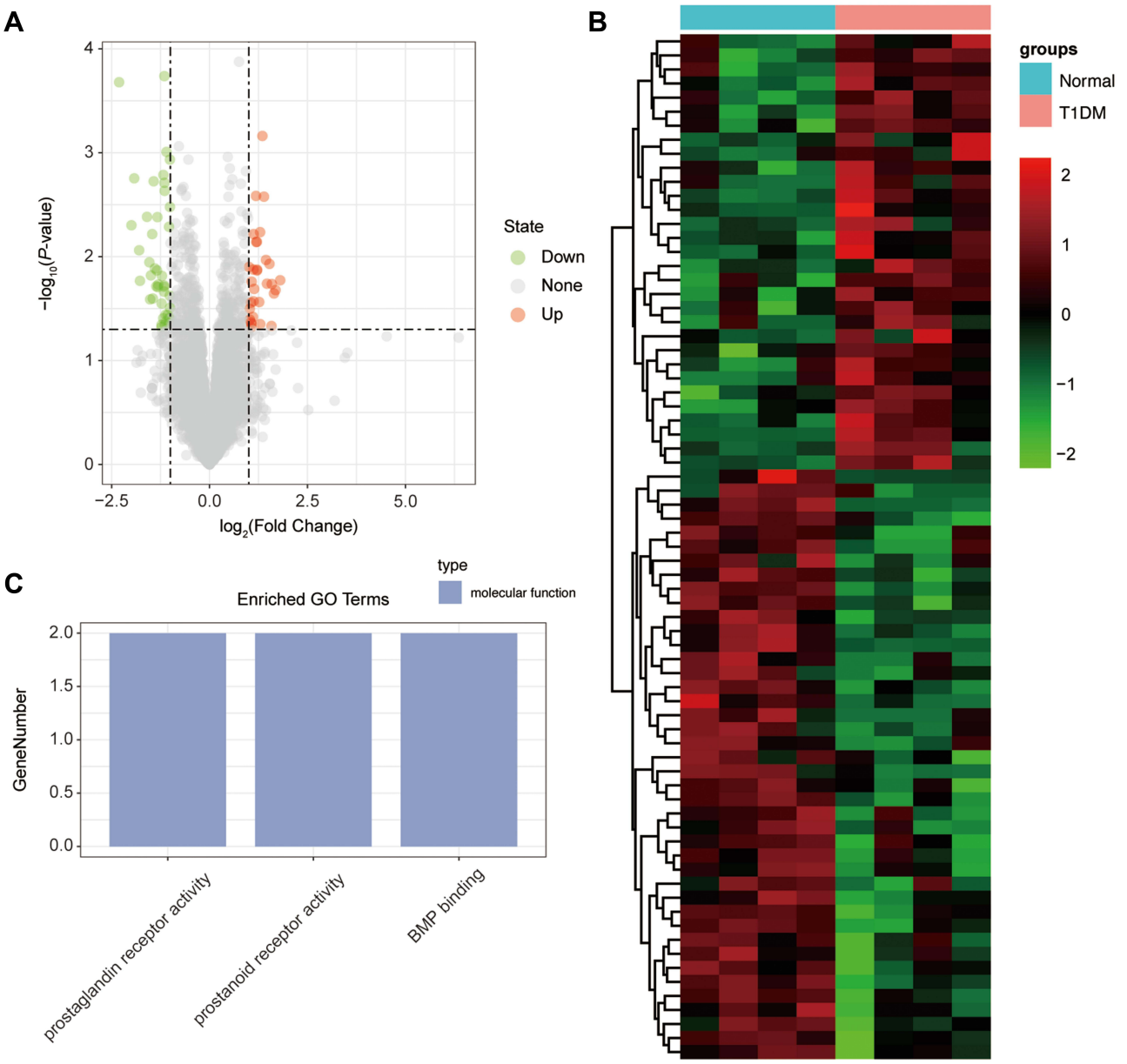

Figure 4 The differentially expressed mRNAs in T1DM and healthy patients. (**A**) Volcano plot of DEmRNAs between normal and T1DM groups. Red and green indicate up- and downregulation, respectively. (**B**) Heatmap of DEmRNAs between normal and T1DM groups. Red color represents increased expression, and green color represents decreased expression. The darker the color, the greater the difference in mRNA expression. (**C**) Enrichment analysis of the DEmRNAs in the category molecular function.

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.[60] 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.[61] 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.

Table 7 Differentially Expressed mRNAs Between the Control Group and T1DM Group

mRNAs	Log2FoldChange	Regulation	P-value	P-adj
RBFOX1	−2.3079121	Down	0.00020929	0.48868466
FAM132B	−1.9940805	Down	0.00498156	0.78986357
SLFNL1	−1.9223862	Down	0.00176092	0.71338425
CLDN22	−1.7965769	Down	0.00866828	0.8200064
GNAL	−1.7755788	Down	0.01707197	0.82671544
MUC15	−1.5965074	Down	0.00413517	0.78986357
CA8	−1.5357652	Down	0.01131812	0.82671544
PTGDR	−1.5165361	Down	0.02574051	0.82671544
TEX13A	−1.495935	Down	0.01513717	0.82671544
TAAR2	−1.4635903	Down	0.00606045	0.78986357
KIR3DL1	−1.4479969	Down	0.02527008	0.82671544
COL6A3	−1.4263206	Down	0.0018801	0.71338425
B4GALNT2	−1.3947065	Down	0.01298325	0.82671544
PARD3	−1.3582746	Down	0.01926125	0.82671544
SORBS1	−1.341606	Down	0.01356421	0.82671544
GPR32	−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	0.04530755	0.82671544
COL6A2	−1.2224407	Down	0.02822533	0.82671544
HSPB8	−1.2153355	Down	0.01531611	0.82671544
BFSP1	−1.1831939	Down	0.03922896	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	0.48868466
DHH	−1.1517769	Down	0.00194518	0.71338425
CRYM	−1.1448803	Down	0.00232428	0.71338425
SMKR1	−1.138156	Down	0.04519693	0.82671544
BPIFB3	−1.1194083	Down	0.03620019	0.82671544
FAM150B	−1.1105272	Down	0.04200652	0.82671544
TEX11	−1.0988657	Down	0.00098015	0.71338425
NPR3	−1.0702284	Down	0.03640359	0.82671544
ATP13A4	−1.0357916	Down	0.04369288	0.82671544
CAMK2N2	−1.0343627	Down	0.00515457	0.78986357
KIR2DL3	−1.0313509	Down	0.03893691	0.82671544
CACNA2D2	−1.0155401	Down	0.02373916	0.82671544
WDR76	−1.0120059	Down	0.00116238	0.71338425
GPR180	−1.0109237	Down	0.00332039	0.78986357
AMHR2	−1.0089921	Down	0.03106529	0.82671544
PCDHB15	1.00754421	Up	0.01257116	0.82671544
MARCKS	1.02701386	Up	0.03176063	0.82671544
DEFB123	1.02969089	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
OR2L13	1.07004067	Up	0.04427013	0.82671544

(*Continued*)

Table 7 (Continued).

mRNAs	Log2FoldChange	Regulation	P-value	P-adj
C17orf64	1.07345437	Up	0.01738992	0.82671544
SGK1	1.10667874	Up	0.03799544	0.82671544
COMP	1.11621286	Up	0.01328963	0.82671544
RASSF8	1.1211237	Up	0.0268822	0.82671544
SLC6A14	1.12250998	Up	0.00605879	0.78986357
RAPGEF5	1.13847388	Up	0.02042072	0.82671544
GREM2	1.18378203	Up	0.00260009	0.71338425
ARRDC3	1.18980995	Up	0.00721663	0.78986357
FILIP1L	1.20891948	Up	0.00719201	0.78986357
ADGRG4	1.20976755	Up	0.01358302	0.82671544
ASIC2	1.21384452	Up	0.01333649	0.82671544
MARCH1	1.26722335	Up	0.02731178	0.82671544
AGXT	1.28961174	Up	0.00580496	0.78986357
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	0.01831872	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	Gene Number	P-adj
MF	GO:0004955	Prostaglandin receptor activity	2	0.043054
MF	GO:0004954	Prostanoid receptor activity	2	0.043054
MF	GO:0036122	BMP binding	2	0.04305384

Abbreviation: MF, molecular function.

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.[62] Meanwhile, another study showed that SORBS1 might be a new susceptibility gene for diabetic nephropathy.[63] CACNA2D2 is the voltage-gated calcium channel auxiliary subunit alpha2delta2 gene that encodes a calcium channel protein,[64] and Huang et al identified CACNA2D2 as a diabetes-related atherogenesis gene.[65] Besides, GREM2 and HSPB8 are closely related to inflammatory response,[66,67] suggesting a regulatory role in the T1DM macrophages inflammation. These

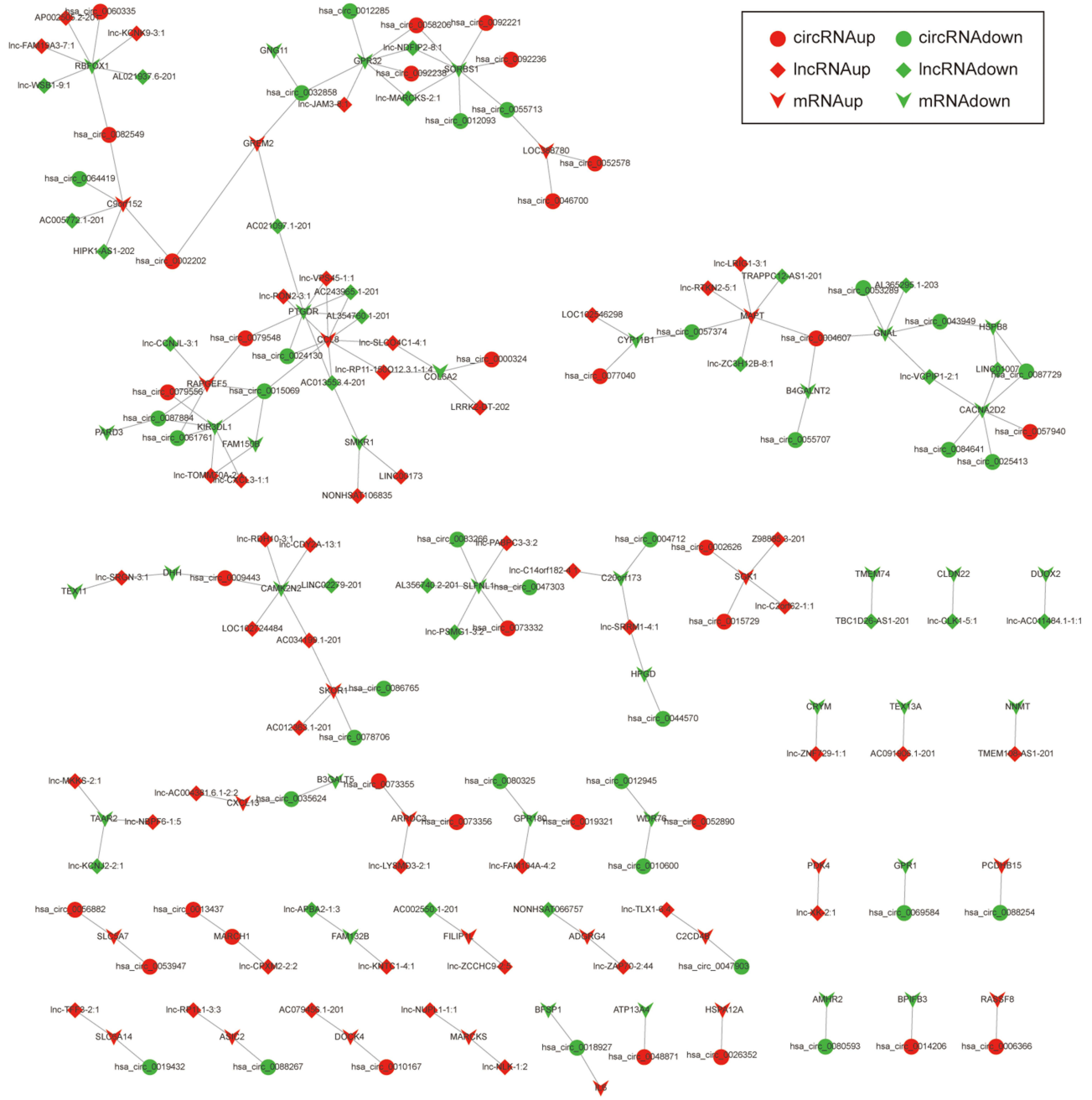

Figure 5 The circRNA-lncRNA-mRNA network. The round nodes represent DEcircRNAs, the rhombic nodes represent DElncRNAs, the v-type nodes represent DEmRNAs. The up or down-regulated genes are represented in red and green, respectively.

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 lncRNAs can also regulate gene expression by affecting transcription.[68,69] 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

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	0.65598378
miR-133a-3p	−0.3784617	Down	0.01526582	0.49284222
miR-431-5p	−0.376715	Down	0.26619136	0.82438552
miR-30a-5p	−0.3686175	Down	0.04189063	0.60118096
miR-23b-3p	−0.3650878	Down	0.06512818	0.65598378
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	0.34045223
miR-330-3p	−0.3418255	Down	0.04863712	0.61412501
miR-6085	−0.3367	Down	0.01118897	0.43937422
miR-196b-5p	−0.3352881	Down	0.05202185	0.63253996
miR-324-5p	−0.3283337	Down	0.05990781	0.64832335
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	0.34045223
miR-199a-3p	−0.2669967	Down	0.18245092	0.77350881
miR-28-5p	−0.2650704	Down	0.00020694	0.11527458
miR-128-3p	−0.2599197	Down	0.04105635	0.60118096
miR-301a-3p	−0.2587877	Down	0.1947074	0.77997491
miR-652-3p	−0.2571135	Down	0.014974	0.49284222
miR-1301-3p	−0.2557511	Down	0.01179643	0.43937422
miR-379-5p	−0.2531956	Down	0.355301	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*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-127-3p	−0.2446309	Down	0.33136688	0.85489649
miR-223-3p	−0.2440992	Down	0.01055265	0.43937422
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-7f-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}	0.08408842
miR-374c-5p	−0.2292803	Down	0.02737626	0.58146271
miR-152-3p	−0.2286181	Down	0.06717209	0.65890175
miR-497-5p	−0.2266935	Down	0.08775824	0.71090581
miR-195-5p	−0.2257144	Down	0.11867951	0.74226488
miR-744-5p	−0.2244425	Down	0.11526467	0.74226488
miR-543	−0.2168851	Down	0.13054129	0.74892227
miR-7-1-3p	−0.2147568	Down	0.00184957	0.32405862
miR-17-3p	−0.2126031	Down	0.07709504	0.68910078
miR-22-5p	−0.2119735	Down	0.00065497	0.15302397
miR-6073	−0.2022809	Down	0.47456765	0.8954764
miR-26a-5p	−0.2017921	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-136-5p	−0.1997377	Down	0.06492627	0.65598378
miR-376c-3p	−0.1996448	Down	0.64319632	0.95274614
miR-199a-5p	−0.1994898	Down	0.35912007	0.8588192
miR-340-5p	−0.198198	Down	0.28288034	0.83193599
miR-769-5p	−0.1956911	Down	0.22581488	0.79102241
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	−0.1823045	Down	0.36292288	0.8588192
miR-487a-3p	−0.1822157	Down	0.16729778	0.76915081
miR-411-5p	−0.1820523	Down	0.11624338	0.74226488
miR-33a-5p	−0.1803366	Down	0.1091139	0.74226488
miR-2355-5p	−0.1784709	Down	0.01806897	0.53734625
miR-182-5p	−0.1775695	Down	0.00022427	0.11527458
miR-421	−0.1771404	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*)

Table 9 (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	0.36854655
miR-18a-5p	−0.1601252	Down	0.30503491	0.83933588
miR-505-5p	−0.159129	Down	0.03015598	0.59616058
miR-146b-5p	−0.1575493	Down	0.29357044	0.83872374
miR-339-3p	−0.1564803	Down	0.09255755	0.72287071
miR-382-5p	−0.1556784	Down	0.57309052	0.93390911
miR-24-1-5p	−0.1555473	Down	0.0214993	0.53734625
let-7g-5p	−0.1552145	Down	0.0589026	0.64832335
miR-141-3p	−0.1552026	Down	0.2682486	0.82860446
miR-410-3p	−0.1546221	Down	0.67560231	0.95648223
miR-4484	−0.1524305	Down	0.15907323	0.75988515
miR-29c-3p	−0.1520516	Down	0.27357655	0.83107769
miR-143-3p	−0.1517947	Down	0.5724,9896	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	0.83108541
miR-1202	−0.1447347	Down	0.21813416	0.78840757
miR-340-3p	−0.143247	Down	0.33859524	0.85489649
miR-331-3p	−0.1428154	Down	0.14940403	0.75393664
miR-5196-5p	−0.1427908	Down	0.00386774	0.34045223
miR-20a-3p	−0.142275	Down	0.0577224	0.64832335
miR-628-5p	−0.1421981	Down	0.13722984	0.75376261
miR-4443	−0.1404353	Down	0.3747999	0.86499071
miR-381-3p	−0.1404195	Down	0.62104792	0.94829596
miR-628-3p	−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	0.09755372	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	0.14604441	0.75376261
miR-6763-5p	−0.1325476	Down	0.05511816	0.64056718
miR-200c-3p	−0.1319846	Down	0.1147884	0.74226488
miR-652-5p	−0.131862	Down	0.03226253	0.59871978
miR-103a-3p	−0.130681	Down	0.15260836	0.75393664
miR-548am-5p	−0.1286466	Down	0.14518387	0.75376261
miR-192-5p	−0.1269884	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	−0.1246398	Down	0.38653847	0.86961208
miR-130b-3p	−0.1231865	Down	0.2852138	0.83289761
miR-320d	−0.123168	Down	0.24893553	0.80715125
miR-4788	−0.1222474	Down	0.07291182	0.68406327
miR-484	−0.1219113	Down	0.12894549	0.74892227

(*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	−0.1199575	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	0.35828046
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	0.16316836	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	−0.0984553	Down	0.02308954	0.53734625
miR-6724-5p	−0.0973248	Down	0.05694408	0.64832335
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	0.55959148
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	0.59616058
miR-548L	−0.0889439	Down	0.01327019	0.46067162
miR-6856-3p	−0.088886	Down	0.01234784	0.44695703

(*Continued*)

Table 9 (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	0.53734625
miR-148a-5p	−0.0830521	Down	0.01814262	0.53734625
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	0.0990518	0.73085631
miR-618	−0.0814829	Down	0.01137484	0.43937422
miR-629-5p	−0.081454	Down	0.32855493	0.85489649
miR-6784-5p	−0.0814167	Down	0.03529383	0.59871978
miR-425-5p	−0.0813279	Down	0.23355464	0.80019585
miR-4261	−0.0812625	Down	0.16684807	0.76915081
miR-4482-3p	−0.0811715	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	0.53734625
let-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	0.53734625
miR-196a-5p	−0.0765723	Down	0.27611079	0.83108541
miR-1249-3p	−0.0757546	Down	0.2545288	0.81031406
miR-9-5p	−0.0751537	Down	0.12923434	0.74892227
miR-6516-5p	−0.0745078	Down	0.06014748	0.64832335
miR-4687-5p	−0.0740003	Down	0.30255863	0.83872374
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
let-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	0.0546774	0.64056718
miR-5692c	−0.0723209	Down	0.08824084	0.71090581

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-4688	−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	0.14424637	0.75376261
miR-515-5p	−0.069631	Down	0.03156651	0.59871978
miR-7156-5p	−0.0690574	Down	0.1545765	0.75393664
miR-6886-3p	−0.0685914	Down	0.12854264	0.74892227
miR-16-2-3p	−0.0684503	Down	0.21995732	0.78841048
miR-4731-3p	−0.0681986	Down	0.30047948	0.83872374
miR-548ax	−0.0680894	Down	0.14111828	0.75376261
miR-296-3p	−0.0678209	Down	0.10482914	0.74226488
miR-664a-5p	−0.0677982	Down	0.45251254	0.89093879
miR-655-5p	−0.0677311	Down	0.10801005	0.74226488
miR-4680-3p	−0.0675655	Down	0.21604469	0.7853205
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	0.14725315	0.75376261
miR-758-3p	−0.0665848	Down	0.62687523	0.9498341
miR-937-3p	−0.0665441	Down	0.05297921	0.63842356
miR-548av-3p	−0.066494	Down	0.08687757	0.70907074
miR-5572	−0.0661791	Down	0.05630095	0.64832335
miR-140-5p	−0.0660041	Down	0.45375538	0.89093879
miR-1227-5p	−0.0658486	Down	0.03691231	0.59871978
miR-4776-5p	−0.0657861	Down	0.03971689	0.59871978
miR-548ab	−0.0655982	Down	0.10855319	0.74226488
miR-15b-3p	−0.0655518	Down	0.07743768	0.68910078
miR-6796-3p	−0.0655189	Down	0.12426931	0.74454632
miR-1233-5p	−0.0654842	Down	0.15416195	0.75393664
miR-922	−0.0653003	Down	0.08895039	0.71411286
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	0.18856121	0.77997491
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	0.08215352	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	−0.0623133	Down	0.10094184	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	−0.0595461	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	0.75393664
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-5090	−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	0.29465932	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	0.67570774
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	0.93953261
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*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-1237-3p	−0.053556	Down	0.0995295	0.73085631
miR-6739-3p	−0.0534981	Down	0.21199749	0.78263372
miR-513a-3p	−0.0534758	Down	0.27013449	0.83107769
miR-3691-3p	−0.0526913	Down	0.08393675	0.70009532
miR-6764-5p	−0.0526382	Down	0.06180898	0.65102084
miR-1245b-5p	−0.052259	Down	0.18642439	0.77777707
miR-5194	−0.0519302	Down	0.31143873	0.8475125
miR-4520-2-3p	−0.0519039	Down	0.0572582	0.64832335
miR-152-5p	−0.0518119	Down	0.27837305	0.83108541
miR-4446-5p	−0.0517576	Down	0.11542673	0.74226488
miR-449c-5p	−0.0517263	Down	0.17444718	0.77062416
miR-4708-3p	−0.0517126	Down	0.08718535	0.70907074
miR-4659b-3p	−0.051703	Down	0.18474022	0.77578819
miR-7706	−0.051404	Down	0.03554956	0.59871978
miR-6837-3p	−0.0513624	Down	0.07988723	0.68910078
miR-6757-5p	−0.051295	Down	0.37187056	0.86489351
miR-4798-5p	−0.0512733	Down	0.16679352	0.76915081
miR-6832-3p	−0.0512067	Down	0.20749798	0.78263372
miR-30c-5p	−0.051185	Down	0.3283045	0.85489649
miR-1266-3p	−0.051152	Down	0.15251966	0.75393664
miR-1262	−0.0506055	Down	0.1481356	0.75376261
miR-885-5p	−0.0505099	Down	0.23316458	0.80004402
miR-3529-3p	−0.0503778	Down	0.29076307	0.83872374
miR-2052	−0.0503661	Down	0.24372971	0.80715125
miR-4743-5p	−0.0503648	Down	0.33589778	0.85489649
miR-125b-2-3p	−0.0502628	Down	0.1992263	0.77997491
miR-4275	−0.0501719	Down	0.23383155	0.80019585
miR-3166	−0.050155	Down	0.11485278	0.74226488
miR-4492	−0.0499947	Down	0.23805179	0.80380192
miR-6864-5p	−0.0499078	Down	0.21015153	0.78263372
miR-384	−0.049905	Down	0.19524287	0.77997491
miR-6885-3p	−0.0495386	Down	0.2725345	0.83107769
miR-4665-5p	−0.0494764	Down	0.1995748	0.77997491
miR-6865-5p	−0.0494428	Down	0.20017313	0.77997491
miR-3977	−0.0491608	Down	0.217245	0.78636571
miR-6873-3p	−0.0490828	Down	0.4649756	0.89396011
miR-3136-5p	−0.0490032	Down	0.1782882	0.77062416
miR-550b-3p	−0.0489921	Down	0.21365444	0.78441702
miR-1197	−0.0487257	Down	0.25155855	0.80715125
miR-4487	−0.048424	Down	0.16645497	0.76915081
miR-769-3p	−0.0484013	Down	0.31433383	0.84917098
miR-4519	−0.0483057	Down	0.07649724	0.68910078
miR-647	−0.0482847	Down	0.35163792	0.8588192
miR-6728-5p	−0.0481616	Down	0.39964052	0.87364718
miR-2114-5p	−0.0480611	Down	0.10413781	0.74226488
miR-488-3p	−0.0479121	Down	0.22846615	0.79102241
miR-4633-5p	−0.0477808	Down	0.14610901	0.75376261
miR-6794-3p	−0.0476669	Down	0.28649085	0.83289761
miR-4522	−0.0476432	Down	0.23913101	0.80380192

(*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	0.08455247	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	0.81031406
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	0.16855939	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	0.83381898
miR-6785-3p	−0.043203	Down	0.53395073	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

(*Continued*)

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	−0.0423211	Down	0.18015658	0.77062416
miR-651-5p	−0.0422148	Down	0.33409291	0.85489649
miR-6854-3p	−0.0421954	Down	0.37351408	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	0.33293924	0.85489649
miR-7106-3p	−0.0413412	Down	0.25137777	0.80715125
miR-5591-3p	−0.04123	Down	0.29994998	0.83872374
miR-7705	−0.041217	Down	0.0634476	0.65539395
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	−0.0406686	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	0.25219551	0.80715125
miR-21-5p	−0.0368457	Down	0.89594126	0.99898712
miR-4257	−0.0367867	Down	0.53676574	0.9213181
miR-3173-5p	−0.036755	Down	0.43342459	0.88898739
miR-6866-3p	−0.0365902	Down	0.260655	0.8189283
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	0.31939227	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	0.91147569
miR-106b-5p	−0.0359461	Down	0.61507233	0.94689808
let-7a-3p	−0.0357979	Down	0.56296401	0.92970327
miR-518f-5p	−0.0357722	Down	0.33145655	0.85489649
miR-4718	−0.0357336	Down	0.43521457	0.88941554
miR-2682-5p	−0.0357322	Down	0.15095123	0.75393664
miR-766-5p	−0.0357183	Down	0.31558575	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	0.36316867	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	−0.0345925	Down	0.20637386	0.78227259
miR-3144-3p	−0.0345136	Down	0.37885574	0.86499071
miR-4799-3p	−0.0344395	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	0.80715125
miR-4636	−0.0333881	Down	0.20375987	0.77997491
miR-200a-5p	−0.0333265	Down	0.3457056	0.8588192
miR-513c-3p	−0.0332212	Down	0.44118445	0.88952595
miR-5008-3p	−0.0331369	Down	0.29943133	0.83872374
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	0.31023739	0.84730085
miR-129-2-3p	−0.0328576	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	0.53862579	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	0.48200927	0.9030564
miR-208a-5p	−0.0322369	Down	0.41564505	0.8804535
miR-6892-3p	−0.0322175	Down	0.65570287	0.95321673
miR-5010-3p	−0.0321995	Down	0.49798778	0.91032268
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	0.8804535
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	0.86195734
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

(*Continued*)

Table 9 (Continued).

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	0.75393664
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	0.93953261
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	−0.0293344	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

(*Continued*)

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	0.48890952	0.90656383
miR-4511	−0.027387	Down	0.55883847	0.92752708
miR-4650-5p	−0.0272772	Down	0.6722039	0.95648223
miR-4726-3p	−0.0272611	Down	0.49220061	0.90695643
miR-3610	−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	0.52255245	0.91732227
miR-621	−0.0269064	Down	0.42966946	0.8869482
miR-4503	−0.0268456	Down	0.51622064	0.91376348
miR-19a-5p	−0.0268393	Down	0.41567275	0.8804535
miR-3939	−0.0267855	Down	0.4278704	0.88394447
miR-6834-3p	−0.0267572	Down	0.45270781	0.89093879
miR-3160-3p	−0.0267371	Down	0.34553725	0.8588192
miR-548j-3p	−0.026724	Down	0.39225869	0.87281803
miR-4264	−0.0267094	Down	0.36033208	0.8588192
miR-2115-5p	−0.0266976	Down	0.46939468	0.89396011
miR-6782-3p	−0.0266664	Down	0.50624103	0.912181
miR-4707-3p	−0.0266129	Down	0.6122267	0.94386479
miR-659-5p	−0.0266029	Down	0.51175645	0.91376348
miR-1273c	−0.0265915	Down	0.56371885	0.92988283
miR-4778-3p	−0.026464	Down	0.56324824	0.92970327
miR-548a-5p	−0.0263646	Down	0.54053286	0.9213181
miR-8076	−0.0263375	Down	0.39074351	0.87281803
miR-6774-3p	−0.0262921	Down	0.21570366	0.7853205
miR-187-3p	−0.0262687	Down	0.61864354	0.94829596
miR-6780b-3p	−0.0262058	Down	0.55359073	0.92384946
miR-4654	−0.0262048	Down	0.40631365	0.87475982
miR-4479	−0.0261019	Down	0.40303872	0.87475982
miR-548ao-5p	−0.0260327	Down	0.36119964	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-518a-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
NC1_00000197	−0.0257608	Down	0.53660801	0.9213181
miR-200b-5p	−0.0257468	Down	0.28862915	0.83439474
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	0.52153217	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

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-4468	−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-548ay-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	0.8588192
miR-934	−0.0248951	Down	0.36815835	0.86195734
miR-7112-5p	−0.0248867	Down	0.53293019	0.9213181
miR-8078	−0.0247883	Down	0.36500255	0.8588192
miR-214-5p	−0.0247315	Down	0.31406257	0.84917098
miR-6814-5p	−0.0247263	Down	0.48666242	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	0.57698708	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	0.85516921
miR-6728-3p	−0.0240234	Down	0.61921683	0.94829596
NC2_00092197	−0.0239201	Down	0.26857562	0.82861865
miR-1286	−0.0238976	Down	0.42361731	0.8823614
miR-548e-5p	−0.0238883	Down	0.48489172	0.90449982
miR-219a-1-3p	−0.0237329	Down	0.56052984	0.92768099
miR-641	−0.0237023	Down	0.67361652	0.95648223
miR-145-5p	−0.0236869	Down	0.9434724	0.99898712
miR-6744-5p	−0.0236591	Down	0.54886022	0.92261663
miR-4649-5p	−0.0236051	Down	0.61179602	0.94386479
miR-3171	−0.0235034	Down	0.67350194	0.95648223
miR-149-3p	−0.023432	Down	0.39448524	0.87310741
miR-4524b-5p	−0.0234286	Down	0.42410749	0.8823614
miR-1265	−0.0233405	Down	0.49287871	0.90695643
miR-7152-3p	−0.023304	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

(*Continued*)

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	0.88961123
miR-501-3p	−0.022561	Down	0.72779336	0.96963657
miR-3178	−0.0225061	Down	0.35728742	0.8588192
miR-511-3p	−0.0223247	Down	0.47990324	0.90289262
miR-4434	−0.0222334	Down	0.481052	0.9030564
miR-6777-3p	−0.022166	Down	0.63978023	0.95096807
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	0.87310741
miR-7109-5p	−0.0211595	Down	0.50943748	0.91230009
miR-196b-3p	−0.0210447	Down	0.55285141	0.92384946
miR-662	−0.0210389	Down	0.71800577	0.96505269
miR-5192	−0.020993	Down	0.46504184	0.89396011
miR-1266-5p	−0.0209397	Down	0.55339061	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-519d-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	0.85489649
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	−0.0195894	Down	0.64183749	0.95128163
miR-298	−0.0195803	Down	0.55851468	0.92752708
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	0.88952595
miR-589-3p	−0.0192968	Down	0.6412559	0.95096807
miR-6722-3p	−0.0192565	Down	0.43605587	0.88941554
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	0.92752708
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	0.96077402
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	−0.018482	Down	0.76305689	0.98140055
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	0.48413304	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

(*Continued*)

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	0.71123,168	0.96505269
miR-216b-3p	−0.0176221	Down	0.51523309	0.91376348
miR-3622a-3p	−0.0175364	Down	0.57580661	0.9339091 1
miR-3919	−0.0175071	Down	0.5510952	0.92349191
miR-4701-3p	−0.0174818	Down	0.44866694	0.88964976
miR-3131	−0.0174639	Down	0.52596692	0.91954761
miR-4760-5p	−0.0173869	Down	0.67234291	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	0.50461254	0.91199313
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	−0.0168628	Down	0.70862699	0.96360966
miR-4802-3p	−0.0168272	Down	0.57328301	0.9339091 1
miR-376a-2-5p	−0.0168259	Down	0.59327345	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	0.9339091 1
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	0.60967682	0.94386479
miR-4651	−0.0160382	Down	0.82761866	0.99438053
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	−0.015822	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	0.95510802
miR-206	−0.0153486	Down	0.55904258	0.92752708
miR-4452	−0.0153427	Down	0.58344668	0.93436563
miR-510-3p	−0.0153235	Down	0.66778315	0.95631006
miR-146b-3p	−0.0153142	Down	0.57687517	0.9339091
miR-4513	−0.0152798	Down	0.6014067	0.93953261
miR-7847-3p	−0.0152761	Down	0.77823881	0.985258
miR-6739-5p	−0.0152297	Down	0.77612631	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	0.93953261
miR-1236-5p	−0.0148479	Down	0.73719766	0.97354829
miR-655-3p	−0.0148337	Down	0.67655901	0.95648223
miR-6773-5p	−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	0.63864074	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-5582-3p	−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	0.99898712
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	0.99063213
miR-6068	−0.0137686	Down	0.82973935	0.99448905
miR-631	−0.0137437	Down	0.67728143	0.95648223
miR-6737-5p	−0.0137008	Down	0.74839715	0.97742837
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	0.9339091
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	0.9339091
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-548s	−0.0126651	Down	0.74107714	0.97402999
miR-4799-5p	−0.0126574	Down	0.70111791	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	0.6536841	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	0.8556283	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	0.66679721	0.95631006
miR-519e-5p	−0.0122324	Down	0.58087819	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	0.98667434
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

(*Continued*)

Table 9 (Continued).

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-548t-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	0.95631006
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-5p	−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	0.95853044
miR-3135a	−0.0105893	Down	0.69622559	0.96226104
miR-4295	−0.010552	Down	0.72600758	0.96826128
miR-7107-3p	−0.0105176	Down	0.84262259	0.99654281
miR-128-2-5p	−0.0105073	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	0.71051853	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	−0.009957	Down	0.64086171	0.95096807
miR-1251-3p	−0.0099478	Down	0.74176683	0.97411382
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	−0.0092731	Down	0.76802718	0.98237037
miR-498	−0.009158	Down	0.69256634	0.96106669
miR-219a-2-3p	−0.0091545	Down	0.82074845	0.99168948
miR-450b-3p	−0.0090465	Down	0.85244841	0.99898712
miR-615-3p	−0.0090186	Down	0.80687156	0.99064883
miR-657	−0.009012	Down	0.82272197	0.99252298
miR-5011-3p	−0.0089942	Down	0.70445092	0.96360966
miR-4792	−0.008984	Down	0.83702003	0.99654281
miR-3944-3p	−0.0089807	Down	0.81317265	0.99092163
miR-4769-3p	−0.0089698	Down	0.92653983	0.99898712
miR-6872-5p	−0.0089365	Down	0.66920104	0.95648223
miR-4727-3p	−0.008894	Down	0.78361029	0.98667434
miR-6876-5p	−0.0088936	Down	0.75998162	0.98140055
miR-205-5p	−0.0088756	Down	0.6575788	0.95321673
miR-494-5p	−0.0088591	Down	0.81959201	0.99127826
miR-2355-3p	−0.008706	Down	0.85986073	0.99898712
miR-4474-3p	−0.0086358	Down	0.7670933	0.98227692
miR-7852-3p	−0.008608	Down	0.73513737	0.97354829
miR-383-5p	−0.0085958	Down	0.85496752	0.99898712
miR-875-5p	−0.0085243	Down	0.8839679	0.99898712
miR-6822-5p	−0.0082844	Down	0.81901427	0.99127826
miR-5691	−0.0082025	Down	0.78963006	0.98667434
miR-7155-3p	−0.0081525	Down	0.79710014	0.98759926
miR-4448	−0.0081318	Down	0.71750381	0.96505269
miR-3182	−0.0080719	Down	0.7367675	0.97354829
miR-5680	−0.0080707	Down	0.8196367	0.99127826
miR-654-5p	−0.0080072	Down	0.87347525	0.99898712
miR-4794	−0.0079851	Down	0.81435699	0.99122915
miR-4772-5p	−0.0079826	Down	0.80753955	0.99064883
miR-100-5p	−0.0078341	Down	0.98391904	0.99898712
let-7g-3p	−0.0077228	Down	0.75985452	0.98140055
miR-4645-5p	−0.0076272	Down	0.82812993	0.99440018
miR-188-5p	−0.0076142	Down	0.87848853	0.99898712
miR-338-5p	−0.0076122	Down	0.81671067	0.99127826
miR-1256	−0.0076115	Down	0.84311541	0.99654281
miR-708-5p	−0.0075769	Down	0.80679807	0.99064883
miR-6789-5p	−0.0075666	Down	0.92606518	0.99898712
miR-6787-3p	−0.0075105	Down	0.89165272	0.99898712
miR-6815-5p	−0.0074763	Down	0.81614637	0.99127826
miR-718	−0.0074274	Down	0.83027884	0.99448905
miR-3622a-5p	−0.0073929	Down	0.83149808	0.99505896
miR-629-3p	−0.0073902	Down	0.90441834	0.99898712

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-4318	−0.0071434	Down	0.79009082	0.98667434
miR-1224-5p	−0.0071228	Down	0.89904345	0.99898712
miR-3681-5p	−0.0071212	Down	0.85999628	0.99898712
miR-5580-5p	−0.0070837	Down	0.87394584	0.99898712
miR-767-5p	−0.0070818	Down	0.78482358	0.98667434
miR-8067	−0.0070745	Down	0.78450315	0.98667434
miR-6751-5p	−0.0070414	Down	0.82126995	0.99185328
miR-6748-3p	−0.0069865	Down	0.77607548	0.985258
miR-374a-3p	−0.006964	Down	0.8671137	0.99898712
miR-1247-5p	−0.0069552	Down	0.79780852	0.98759926
miR-1206	−0.0069354	Down	0.88342507	0.99898712
miR-6716-3p	−0.0069342	Down	0.88604018	0.99898712
miR-7153-3p	−0.0068762	Down	0.80682369	0.99064883
miR-635	−0.0068419	Down	0.87010589	0.99898712
miR-616-5p	−0.0067948	Down	0.87844038	0.99898712
miR-548q	−0.0067864	Down	0.80815498	0.99064883
miR-6832-5p	−0.0067224	Down	0.85778301	0.99898712
miR-2682-3p	−0.0066297	Down	0.79941131	0.98820926
miR-412-5p	−0.00662	Down	0.89035774	0.99898712
miR-302f	−0.0066155	Down	0.88132151	0.99898712
miR-3064-3p	−0.0065595	Down	0.82587428	0.99340905
miR-34a-3p	−0.0063862	Down	0.87642148	0.99898712
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	0.99898712
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	0.99898712
miR-92a-2-5p	−0.0059985	Down	0.89337705	0.99898712
miR-3192-5p	−0.0059849	Down	0.85140192	0.99898712
miR-3616-5p	−0.0059161	Down	0.87556977	0.99898712
miR-216b-5p	−0.0059046	Down	0.78988169	0.98667434
miR-1273g-5p	−0.0058234	Down	0.84875466	0.99693761
miR-454-5p	−0.0056392	Down	0.87659395	0.99898712
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	0.99898712
miR-1185-5p	−0.0054925	Down	0.8750581	0.99898712
miR-6809-3p	−0.0054802	Down	0.90618848	0.99898712
miR-5695	−0.0054138	Down	0.84065578	0.99654281
miR-1976	−0.0053957	Down	0.89787741	0.99898712
miR-563	−0.0053882	Down	0.91226822	0.99898712
miR-6734-3p	−0.0053774	Down	0.87471748	0.99898712
miR-4319	−0.0053747	Down	0.86232995	0.99898712
miR-342-3p	−0.0052338	Down	0.97293249	0.99898712
miR-6895-5p	−0.005215	Down	0.8608465	0.99898712
miR-4723-5p	−0.0051688	Down	0.81224515	0.99064883
miR-4528	−0.0051614	Down	0.92980523	0.99898712
NC2_00079215	−0.0051563	Down	0.87570139	0.99898712

(*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	0.87183868	0.99898712
miR-920	−0.0047252	Down	0.86831937	0.99898712
miR-4705	−0.0047207	Down	0.87713185	0.99898712
miR-9500	−0.004718	Down	0.87680729	0.99898712
miR-5704	−0.0047001	Down	0.91499362	0.99898712
miR-5694	−0.0046743	Down	0.83419238	0.99622199
miR-4685-5p	−0.0046459	Down	0.88067889	0.99898712
miR-6504-5p	−0.0043974	Down	0.90204635	0.99898712
miR-3151-5p	−0.0043147	Down	0.8748898	0.99898712
miR-6722-5p	−0.0042257	Down	0.89460988	0.99898712
miR-603	−0.0041155	Down	0.8667461	0.99898712
miR-8052	−0.0040761	Down	0.91117923	0.99898712
miR-4287	−0.0040522	Down	0.89608593	0.99898712
miR-4320	−0.0040192	Down	0.89469173	0.99898712
miR-6838-3p	−0.0039418	Down	0.8910569	0.99898712
miR-4266	−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	0.89804142	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	0.91415349	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	0.90906861	0.99898712
miR-1263	−0.0034603	Down	0.91405859	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

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-3200-3p	−0.0032855	Down	0.92266612	0.99898712
miR-450a-1-3p	−0.0032779	Down	0.94125452	0.99898712
miR-30c-1-3p	−0.0031641	Down	0.93461856	0.99898712
miR-548w	−0.0031582	Down	0.92537786	0.99898712
miR-4690-3p	−0.0031051	Down	0.92408199	0.99898712
miR-6849-5p	−0.0030846	Down	0.91722387	0.99898712
miR-7113-3p	−0.0030742	Down	0.93227711	0.99898712
miR-606	−0.0030314	Down	0.91669444	0.99898712
miR-455-5p	−0.0030307	Down	0.94950521	0.99898712
miR-5197-5p	−0.0030231	Down	0.96329908	0.99898712
miR-6726-5p	−0.0030115	Down	0.89240213	0.99898712
miR-135b-3p	−0.0029845	Down	0.93259063	0.99898712
miR-4451	−0.0029258	Down	0.90566083	0.99898712
miR-5196-3p	−0.0028833	Down	0.9410239	0.99898712
miR-30a-3p	−0.0028798	Down	0.96173026	0.99898712
miR-7159-3p	−0.0028746	Down	0.93108389	0.99898712
miR-144-5p	−0.0028729	Down	0.98291237	0.99898712
miR-204-5p	−0.0027756	Down	0.96390565	0.99898712
miR-6729-5p	−0.0027536	Down	0.9342249	0.99898712
miR-524-3p	−0.0027175	Down	0.93463627	0.99898712
miR-4692	−0.0027174	Down	0.93330804	0.99898712
miR-4254	−0.0027026	Down	0.94607389	0.99898712
miR-197-3p	−0.0026814	Down	0.97446832	0.99898712
miR-6808-5p	−0.0026431	Down	0.94489125	0.99898712
miR-6795-5p	−0.0026283	Down	0.91449896	0.99898712
miR-4324	−0.00262	Down	0.9400151	0.99898712
miR-513b-3p	−0.0024873	Down	0.93432363	0.99898712
miR-193b-3p	−0.0024777	Down	0.98359496	0.99898712
miR-3664-3p	−0.0024542	Down	0.92943662	0.99898712
miR-6743-5p	−0.0024529	Down	0.9027108	0.99898712
miR-6507-5p	−0.0024365	Down	0.93017877	0.99898712
miR-5692b	−0.0024253	Down	0.90975261	0.99898712
miR-3158-5p	−0.0024079	Down	0.93792342	0.99898712
miR-758-5p	−0.002329	Down	0.95116671	0.99898712
miR-1283	−0.0023082	Down	0.95634844	0.99898712
miR-6510-3p	−0.0022771	Down	0.94891395	0.99898712
miR-3121-5p	−0.0022103	Down	0.97235279	0.99898712
miR-25-3p	−0.0021921	Down	0.97945036	0.99898712
miR-3681-3p	−0.0021322	Down	0.9550712	0.99898712
miR-6887-3p	−0.0020516	Down	0.95483442	0.99898712
miR-101-5p	−0.0020024	Down	0.96328694	0.99898712
miR-6799-5p	−0.0019956	Down	0.96608755	0.99898712
miR-219b-3p	−0.0019641	Down	0.95601519	0.99898712
miR-580-3p	−0.0019317	Down	0.94837611	0.99898712
miR-6792-3p	−0.0019166	Down	0.956652	0.99898712
NC1_00000215	−0.0018841	Down	0.96373938	0.99898712
miR-6811-5p	−0.0018232	Down	0.96188232	0.99898712
miR-4704-3p	−0.0017889	Down	0.96132284	0.99898712
miR-4309	−0.0017661	Down	0.95105748	0.99898712

(*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	−0.0009929	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	−0.00045	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-548bb-3p	4.80×10^{-5}	Up	0.99929046	1
miR-627-3p	4.86×10^{-5}	Up	0.99946876	1
miR-6718-5p	0.00012601	Up	0.99652509	0.99904195
miR-6790-5p	0.00014766	Up	0.9958867	0.99904195
miR-4666a-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*)

Table 9 (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	0.99092761	0.99904195
miR-3689a-5p	0.00038906	Up	0.98808154	0.99904195
miR-6827-3p	0.0004124	Up	0.99192316	0.99904195
miR-5089-5p	0.00043586	Up	0.99014203	0.99904195
miR-3146	0.00045422	Up	0.98491092	0.99898712
miR-4791	0.00046421	Up	0.98577094	0.99898712
miR-4670-3p	0.00049717	Up	0.98246602	0.99898712
miR-6129	0.00052485	Up	0.98770083	0.99904195
miR-4798-3p	0.00052915	Up	0.98085346	0.99898712
miR-7845-5p	0.00054149	Up	0.98878954	0.99904195
miR-587	0.00056284	Up	0.98476648	0.99898712
miR-4706	0.00057658	Up	0.98417593	0.99898712
miR-3650	0.00058852	Up	0.98065605	0.99898712
miR-4537	0.00060113	Up	0.98049055	0.99898712
miR-6735-3p	0.00062976	Up	0.98562082	0.99898712
miR-4749-5p	0.00064826	Up	0.98398478	0.99898712
miR-3185	0.00065819	Up	0.97570375	0.99898712
miR-891a-3p	0.00066649	Up	0.98470713	0.99898712
miR-3529-5p	0.00069812	Up	0.98705831	0.99904195
miR-520f-3p	0.00079577	Up	0.98055025	0.99898712
miR-5703	0.00079607	Up	0.97556576	0.99898712
miR-4535	0.00083155	Up	0.98315972	0.99898712
miR-4793-3p	0.00087755	Up	0.98068497	0.99898712
miR-3649	0.00090916	Up	0.96843892	0.99898712
miR-3655	0.0009646	Up	0.97337242	0.99898712
miR-6806-3p	0.00100569	Up	0.98161655	0.99898712
miR-1304-5p	0.00104513	Up	0.96964137	0.99898712
miR-3148	0.001135	Up	0.96629547	0.99898712
miR-1298-3p	0.00116617	Up	0.96906897	0.99898712
miR-378a-5p	0.00119067	Up	0.9950831	0.99904195
miR-7161-3p	0.00122334	Up	0.97003457	0.99898712
miR-23a-3p	0.00125302	Up	0.99132986	0.99904195
miR-6849-3p	0.00127333	Up	0.97699099	0.99898712
miR-3191-5p	0.00129186	Up	0.96125721	0.99898712
miR-4699-5p	0.00129705	Up	0.97103377	0.99898712
miR-3126-3p	0.00139265	Up	0.95926798	0.99898712
miR-3140-5p	0.00140044	Up	0.9636057	0.99898712
miR-6723-5p	0.00142556	Up	0.97534113	0.99898712
miR-573	0.00142671	Up	0.95512489	0.99898712
miR-4733-5p	0.00143716	Up	0.97172874	0.99898712
miR-92b-3p	0.00146746	Up	0.97672286	0.99898712
miR-1180-5p	0.00147286	Up	0.95840719	0.99898712
miR-4768-3p	0.00148174	Up	0.96684936	0.99898712
miR-6804-3p	0.00150994	Up	0.96312591	0.99898712
miR-5010-5p	0.00150997	Up	0.95909548	0.99898712
miR-5007-3p	0.00153164	Up	0.98261968	0.99898712

(*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	0.00178895	Up	0.9671217	0.99898712
miR-1282	0.00180239	Up	0.9642268	0.99898712
miR-5583-5p	0.00182263	Up	0.97743092	0.99898712
miR-4437	0.0018404	Up	0.95314944	0.99898712
miR-4431	0.00185753	Up	0.94002562	0.99898712
miR-548ap-3p	0.00191567	Up	0.96952875	0.99898712
miR-30b-3p	0.00192048	Up	0.96868055	0.99898712
miR-588	0.00194739	Up	0.95288558	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	0.94507478	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	0.96654653	0.99898712
miR-4677-5p	0.0022962	Up	0.94525282	0.99898712
miR-6847-3p	0.00230232	Up	0.96282302	0.99898712
miR-4684-5p	0.00237006	Up	0.94302918	0.99898712
miR-4769-5p	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-6829-3p	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	0.91664185	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	0.91996491	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*)

Table 9 (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	0.95072657	0.99898712
miR-548aw	0.00338056	Up	0.93884878	0.99898712
miR-1271-3p	0.0034496	Up	0.89829719	0.99898712
miR-5590-3p	0.00347784	Up	0.92848311	0.99898712
miR-6511a-5p	0.00354836	Up	0.89798915	0.99898712
miR-9-3p	0.00359347	Up	0.92054605	0.99898712
miR-511-5p	0.00361469	Up	0.9155092	0.99898712
miR-516a-3p	0.00364134	Up	0.91537755	0.99898712
miR-5186	0.00366302	Up	0.8725406	0.99898712
miR-885-3p	0.00369562	Up	0.85885838	0.99898712
miR-4456	0.00380003	Up	0.9123011	0.99898712
miR-8086	0.00380099	Up	0.88474931	0.99898712
miR-6816-5p	0.0038261	Up	0.92075975	0.99898712
miR-4274	0.00389749	Up	0.9244925	0.99898712
miR-3909	0.003979	Up	0.91039561	0.99898712
miR-3978	0.00405802	Up	0.91465819	0.99898712
miR-6743-3p	0.00407426	Up	0.88971427	0.99898712
miR-4732-5p	0.00428378	Up	0.86998959	0.99898712
miR-610	0.00430615	Up	0.87817427	0.99898712
miR-3157-5p	0.0043107	Up	0.87760033	0.99898712
miR-16-5p	0.00434127	Up	0.93567182	0.99898712
miR-379-3p	0.00441424	Up	0.90423587	0.99898712
miR-6796-5p	0.00443933	Up	0.87139356	0.99898712
miR-4450	0.00444525	Up	0.91178	0.99898712
miR-8059	0.00447583	Up	0.91263621	0.99898712
miR-6746-3p	0.00448799	Up	0.90899954	0.99898712
miR-4255	0.00458999	Up	0.84328656	0.99654281
miR-1183	0.0047103	Up	0.856079	0.99898712
miR-760	0.00477938	Up	0.92370615	0.99898712
miR-4495	0.00479005	Up	0.86428986	0.99898712
miR-7152-5p	0.00481184	Up	0.93769352	0.99898712
miR-8064	0.00496846	Up	0.88459861	0.99898712
miR-7-5p	0.00499621	Up	0.96784354	0.99898712
miR-6748-5p	0.00501023	Up	0.84754757	0.99654281
miR-4462	0.00504316	Up	0.9290548	0.99898712
miR-1908-5p	0.00506377	Up	0.84310963	0.99654281
miR-4306	0.00507078	Up	0.88556954	0.99898712
miR-217	0.00510601	Up	0.84588598	0.99654281
miR-4640-5p	0.00513123	Up	0.87451458	0.99898712
miR-3928-3p	0.00518066	Up	0.83609674	0.99654281
miR-520g-3p	0.00520766	Up	0.90908556	0.99898712
miR-6890-5p	0.00522115	Up	0.85094437	0.99898712
miR-1288-3p	0.00522151	Up	0.93793162	0.99898712
miR-548aq-5p	0.00523516	Up	0.88953513	0.99898712
miR-6078	0.00525155	Up	0.87577069	0.99898712

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-3915	0.00526613	Up	0.83166795	0.99505896
miR-6719-3p	0.00527162	Up	0.88460055	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-6839-3p	0.00532191	Up	0.87262952	0.99898712
miR-3927-5p	0.00548928	Up	0.86784757	0.99898712
miR-4643	0.00549469	Up	0.89871642	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	0.84415095	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	0.78579776	0.98667434
miR-4263	0.00647493	Up	0.82323114	0.99252298
miR-30c-2-3p	0.00658433	Up	0.78325746	0.98667434
miR-4253	0.00662912	Up	0.86666295	0.99898712
miR-8085	0.0066686	Up	0.80768958	0.99064883
miR-7161-5p	0.00667439	Up	0.83283078	0.9955233
miR-6763-3p	0.00667776	Up	0.87862251	0.99898712
miR-3127-3p	0.00671663	Up	0.8253678	0.99340905
miR-1179	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-3657	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*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-3153	0.0074168	Up	0.76947281	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-4441	0.00799964	Up	0.70676444	0.96360966
miR-211-3p	0.00803022	Up	0.87470817	0.99898712
miR-3174	0.00810481	Up	0.75961032	0.98140055
miR-6720-5p	0.00818865	Up	0.84626862	0.99654281
miR-4304	0.0082361	Up	0.79025258	0.98667434
miR-1264	0.00861208	Up	0.8411249	0.99654281
miR-3912-3p	0.00863814	Up	0.87433044	0.99898712
miR-4506	0.00870046	Up	0.90739398	0.99898712
miR-1284	0.008722	Up	0.79085029	0.98667434
miR-5681b	0.00876411	Up	0.8584131	0.99898712
miR-548aa	0.00890056	Up	0.84798854	0.99654281
miR-4269	0.00892899	Up	0.81451596	0.99122915
miR-7158-5p	0.00894845	Up	0.86729561	0.99898712
miR-452-5p	0.00895862	Up	0.85771099	0.99898712
miR-4490	0.00898673	Up	0.73250027	0.9725372
miR-656-5p	0.00904604	Up	0.74755094	0.97721563
miR-6506-5p	0.00904757	Up	0.67559786	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	0.98667434
miR-888-5p	0.00930898	Up	0.6728992	0.95648223
miR-4494	0.00934109	Up	0.65694105	0.95321673
miR-3689b-3p	0.00939617	Up	0.78293583	0.98667434
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	0.80087863	0.98907164
miR-596	0.0096344	Up	0.6972447	0.96239183
miR-6823-3p	0.0096698	Up	0.83033428	0.99448905
miR-3200-5p	0.00979753	Up	0.82584554	0.99340905
miR-6828-3p	0.00989754	Up	0.76984199	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	0.70048463	0.96268515
miR-4748	0.01013589	Up	0.79150405	0.98667434
miR-4742-3p	0.0101833	Up	0.77805094	0.985258

(*Continued*)

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	0.01022264	Up	0.72226246	0.96627512
miR-2681-5p	0.01028915	Up	0.71152528	0.96505269
miR-203a-5p	0.01029073	Up	0.74476166	0.97605174
miR-4536-5p	0.01032611	Up	0.79814929	0.98759926
miR-548aj-5p	0.01034554	Up	0.76659882	0.98213308
miR-3150a-3p	0.01034608	Up	0.72387137	0.96691758
miR-4433a-3p	0.01036148	Up	0.83417748	0.99622199
miR-450a-5p	0.01036798	Up	0.93799632	0.99898712
miR-5096	0.01038371	Up	0.71906775	0.96505269
miR-4762-5p	0.01039264	Up	0.77610745	0.985258
miR-6809-5p	0.01040392	Up	0.79202691	0.98667434
miR-3682-5p	0.01042188	Up	0.81098701	0.99064883
miR-1295b-3p	0.01043015	Up	0.71909568	0.96505269
miR-4444	0.01045387	Up	0.7631112	0.98140055
miR-888-3p	0.01047353	Up	0.76818709	0.98237037
miR-302d-3p	0.01049923	Up	0.80356561	0.99063213
miR-4520-3p	0.01052429	Up	0.61164525	0.94386479
miR-365b-5p	0.01054114	Up	0.79167801	0.98667434
miR-490-5p	0.01063911	Up	0.69008095	0.96036263
miR-4796-3p	0.01068572	Up	0.69512286	0.96185982
miR-6883-5p	0.01079249	Up	0.65690962	0.95321673
miR-6766-5p	0.01097063	Up	0.73980817	0.97402999
miR-5707	0.01098079	Up	0.7204253	0.96558066
miR-3187-5p	0.01105233	Up	0.61637057	0.94741169
miR-7846-3p	0.0110547	Up	0.76558774	0.98147681
miR-6777-5p	0.0111177	Up	0.65793259	0.95321673
miR-4258	0.01123609	Up	0.84001222	0.99654281
miR-4797-5p	0.01124647	Up	0.68924997	0.96036263
miR-181a-5p	0.01129006	Up	0.93201014	0.99898712
miR-4734	0.0113266	Up	0.68320782	0.95853044
miR-5682	0.01146077	Up	0.54685586	0.92261663
miR-5589-5p	0.01146606	Up	0.68330492	0.95853044
miR-1296-3p	0.01148509	Up	0.74748801	0.97721563
miR-489-3p	0.01149592	Up	0.76884233	0.98237037
miR-4496	0.01149734	Up	0.74960999	0.97742837
miR-7978	0.01150772	Up	0.78322993	0.98667434
miR-676-3p	0.01153637	Up	0.80272434	0.99063213
miR-4650-3p	0.01157133	Up	0.5971788	0.93868471
miR-216a-5p	0.0116056	Up	0.6784294	0.95648223
miR-5197-3p	0.01164863	Up	0.76952426	0.98237037
miR-3132	0.01168148	Up	0.75960371	0.98140055
miR-3150b-5p	0.011704	Up	0.78040012	0.98667434
miR-668-5p	0.01170815	Up	0.66036011	0.95397723
miR-5092	0.01171057	Up	0.65400126	0.95321673
miR-6834-5p	0.01173243	Up	0.63699015	0.95096807
miR-3179	0.01173464	Up	0.70553052	0.96360966
miR-582-3p	0.01180101	Up	0.65549123	0.95321673

(*Continued*)

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	0.95510802
miR-3149	0.01193411	Up	0.75330525	0.97975429
miR-4712-5p	0.01193425	Up	0.77741809	0.985258
miR-3130-3p	0.01198522	Up	0.72070737	0.96558066
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	0.99898712
miR-5008-5p	0.01210927	Up	0.67184466	0.95648223
miR-6769a-3p	0.01231759	Up	0.67377095	0.95648223
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	0.70448188	0.96360966
miR-6765-5p	0.01255238	Up	0.67419733	0.95648223
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	0.95065239
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	0.59548597	0.93868471
miR-3167	0.01333017	Up	0.63645436	0.95096807
miR-4710	0.01333306	Up	0.52798647	0.92119547
miR-4307	0.01336258	Up	0.70485276	0.96360966
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	0.93436563
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	0.95321673
miR-99b-3p	0.01433655	Up	0.54153182	0.92167998
miR-4644	0.01436547	Up	0.64547146	0.95321673
miR-1250-5p	0.01443761	Up	0.53908047	0.9213181
miR-372-3p	0.0144946	Up	0.58151827	0.93436563
miR-656-3p	0.01455139	Up	0.80755313	0.99064883
miR-4640-3p	0.01456831	Up	0.78150428	0.98667434
miR-105-3p	0.01458433	Up	0.55080673	0.92349191
miR-4498	0.01461732	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-6756-3p	0.0148236	Up	0.84494113	0.99654281
miR-6729-3p	0.01488382	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	0.96036263
miR-4744	0.01496713	Up	0.58205836	0.93436563
miR-1537-3p	0.01497413	Up	0.74459697	0.97605174
miR-5584-5p	0.015004	Up	0.6644876	0.95510802
miR-4778-5p	0.01507405	Up	0.70791484	0.96360966
miR-6852-3p	0.01514938	Up	0.63082411	0.95086097
miR-938	0.01520606	Up	0.65801777	0.95321673
miR-3177-5p	0.01524698	Up	0.51696969	0.91376348
miR-3199	0.0152907	Up	0.69019057	0.96036263
miR-4477a	0.01533614	Up	0.6204992	0.94829596
miR-1185-2-3p	0.01534462	Up	0.71296587	0.96505269
miR-6509-3p	0.01541891	Up	0.73653953	0.97354829
miR-6884-5p	0.01546598	Up	0.44533113	0.88952595
miR-4765	0.01550301	Up	0.49293956	0.90695643
miR-502-5p	0.01550968	Up	0.80976632	0.99064883
miR-5588-3p	0.0155201	Up	0.65535348	0.95321673
miR-3191-3p	0.01552654	Up	0.55550861	0.9264485
miR-4716-3p	0.01552688	Up	0.88286114	0.99898712
miR-4426	0.01555663	Up	0.60204571	0.93953261
miR-4311	0.01562945	Up	0.66332341	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-301b-5p	0.01621443	Up	0.61120826	0.94386479
miR-4642	0.01624775	Up	0.68349862	0.95853044
miR-6871-3p	0.01627526	Up	0.41542735	0.8804535
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	0.01667698	Up	0.87860394	0.99898712
miR-6740-3p	0.01668376	Up	0.71732029	0.96505269
miR-4727-5p	0.01668725	Up	0.59607151	0.93868471
miR-5004-3p	0.01670733	Up	0.5998042	0.93953261
miR-5684	0.01673479	Up	0.78501761	0.98667434
miR-5002-3p	0.01677134	Up	0.64641587	0.95321673
miR-1203	0.01680127	Up	0.66528781	0.95557578
miR-369-3p	0.01686971	Up	0.60979891	0.94386479
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	0.98830004
miR-3689a-3p	0.01718387	Up	0.49300838	0.90695643
miR-1909-5p	0.0172932	Up	0.65705658	0.95321673
miR-4750-3p	0.01735663	Up	0.74220642	0.97419331
miR-3675-3p	0.01737469	Up	0.80972313	0.99064883
miR-765	0.01737509	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	0.9498341
miR-139-3p	0.01757692	Up	0.86938452	0.99898712
miR-3194-3p	0.01763165	Up	0.50079992	0.91121111
miR-4679	0.01782269	Up	0.5908509	0.93675929
miR-27a-5p	0.01792569	Up	0.56305474	0.92970327
miR-1296-5p	0.01793662	Up	0.58790108	0.93675929
miR-4755-3p	0.01795334	Up	0.54032429	0.9213181
miR-671-5p	0.01798175	Up	0.91512111	0.99898712
miR-520e	0.01806457	Up	0.70204427	0.96268515
miR-670-3p	0.01811048	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	0.93675929
miR-148b-5p	0.01843913	Up	0.62829493	0.9498341
miR-153-3p	0.01844682	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	0.58123713	0.93436563
miR-939-3p	0.01900859	Up	0.6053071	0.94188142
miR-646	0.01904427	Up	0.50975211	0.91230009
miR-4724-5p	0.01904875	Up	0.46392595	0.89396011
miR-6731-3p	0.01906737	Up	0.72346229	0.96691758
miR-516b-5p	0.01910255	Up	0.48676275	0.90650744
miR-6779-3p	0.01916462	Up	0.62653619	0.9498341
miR-4482-5p	0.01920295	Up	0.54096071	0.9213181
miR-6823-5p	0.01922385	Up	0.46136863	0.89396011
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	0.89318606
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	0.70147127	0.96268515
miR-5698	0.01965235	Up	0.43976949	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-3664-5p	0.019903	Up	0.45946349	0.89396011
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	0.89396011
miR-6854-5p	0.02017661	Up	0.53693007	0.9213181
miR-520a-5p	0.02025704	Up	0.46924916	0.89396011
miR-6805-5p	0.02026553	Up	0.52305157	0.9175717
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	0.55122046	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*)

Table 9 (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	0.91687991
miR-548ba	0.02148162	Up	0.44559008	0.88952595
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	0.9303065
miR-6825-3p	0.02186425	Up	0.65344952	0.95321673
miR-556-5p	0.02187098	Up	0.63388765	0.95096807
miR-3190-3p	0.02201551	Up	0.50097307	0.91121111
miR-5693	0.02206122	Up	0.50386992	0.91147569
miR-499b-3p	0.02210218	Up	0.58323296	0.93436563
miR-5700	0.02218527	Up	0.58994637	0.93675929
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	0.02233079	Up	0.49202453	0.90695643
miR-380-5p	0.02237146	Up	0.51536985	0.91376348
miR-6742-3p	0.02237604	Up	0.58352406	0.93436563
miR-6833-5p	0.02243951	Up	0.50926238	0.91230009
miR-6871-5p	0.02248366	Up	0.42648147	0.88249386
miR-19b-2-5p	0.02252117	Up	0.64845823	0.95321673
miR-3671	0.0225583	Up	0.56831954	0.9303065
miR-4447	0.02263427	Up	0.43937869	0.88952595
miR-525-3p	0.02266101	Up	0.62137369	0.94829596
miR-6861-3p	0.02274475	Up	0.58950393	0.93675929
miR-1275	0.02289121	Up	0.91458073	0.99898712
miR-518e-5p	0.02294105	Up	0.45597788	0.89182889
miR-1287-3p	0.02310958	Up	0.45535913	0.891297
miR-3617-5p	0.02323344	Up	0.64968436	0.95321673
miR-6783-5p	0.0233775	Up	0.43556048	0.88941554
miR-7160-5p	0.02343496	Up	0.5065038	0.912181
miR-5579-5p	0.02344538	Up	0.55670065	0.92696334
miR-6760-3p	0.02347367	Up	0.73868143	0.97402999
miR-7154-3p	0.02348532	Up	0.45486744	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	0.67202426	0.95648223
miR-2467-5p	0.02382854	Up	0.48887473	0.90656383
miR-8054	0.02383556	Up	0.44148897	0.88952595
miR-4313	0.02387812	Up	0.69997027	0.96268515
miR-6761-5p	0.02391023	Up	0.46096324	0.89396011
miR-1272	0.02407068	Up	0.40836297	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	0.91032268
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	0.88952595
miR-20b-3p	0.02441946	Up	0.39889277	0.87364718
miR-4704-5p	0.02442544	Up	0.46980283	0.89396011
miR-504-5p	0.0244978	Up	0.4506903	0.88964976
miR-4746-5p	0.02467118	Up	0.35223335	0.8588192
miR-522-3p	0.02469827	Up	0.55698033	0.92696334
miR-4804-3p	0.024709	Up	0.36485338	0.8588192
miR-4461	0.0247,6583	Up	0.55726006	0.92696334
miR-138-5p	0.02479871	Up	0.48787964	0.90656383
miR-548f-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	0.88952595
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	0.40063252	0.87364718
miR-3159	0.02532184	Up	0.4205062	0.8823614
miR-4467	0.02533318	Up	0.37976904	0.86499071
miR-3168	0.02534439	Up	0.4408406	0.88952595
miR-6889-3p	0.02542975	Up	0.79127667	0.98667434
miR-3150b-3p	0.02552629	Up	0.42479341	0.8823614
miR-3614-3p	0.02580515	Up	0.3124631	0.8475125
miR-4724-3p	0.02587713	Up	0.55314262	0.92384946
miR-3679-3p	0.02591213	Up	0.71514096	0.96505269
miR-4694-3p	0.0260043	Up	0.29761764	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	0.51688833	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	0.39668404	0.87358867
miR-208b-5p	0.02643533	Up	0.53329665	0.9213181
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	0.88941554

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-6802-5p	0.02693858	Up	0.34140218	0.85516921
miR-4529-5p	0.02696507	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	0.0271424	Up	0.37609847	0.86499071
miR-6751-3p	0.02718007	Up	0.5677343	0.9303065
miR-642a-5p	0.02722384	Up	0.44317761	0.88952595
miR-6508-3p	0.02726898	Up	0.54595956	0.92261663
miR-620	0.02727251	Up	0.49055899	0.90695643
miR-1293	0.02763147	Up	0.35398018	0.8588192
let-7e-3p	0.02772595	Up	0.44949219	0.88964976
miR-4740-3p	0.02784092	Up	0.43135925	0.88759074
miR-548i	0.02787387	Up	0.49872931	0.91032268
miR-103a-2-5p	0.02787897	Up	0.51371703	0.91376348
miR-1273d	0.02792954	Up	0.26610662	0.82438552
miR-4747-5p	0.02795079	Up	0.31530614	0.84917098
miR-6749-3p	0.02808208	Up	0.34686008	0.8588192
miR-4421	0.02826019	Up	0.27677993	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	0.26192077	0.81989814
miR-1257	0.02865524	Up	0.3398032	0.85489649
miR-6509-5p	0.02865937	Up	0.38183201	0.86612247
miR-2909	0.02885471	Up	0.40484157	0.87475982
miR-202-5p	0.02889478	Up	0.54327852	0.9222099
miR-4786-3p	0.02906531	Up	0.4179162	0.88181004
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	0.8804535
miR-6836-3p	0.0293377	Up	0.53348401	0.9213181
miR-525-5p	0.02937872	Up	0.22645561	0.79102241
miR-1251-5p	0.02938206	Up	0.38217233	0.86612247
miR-1306-3p	0.02940317	Up	0.39910924	0.87364718
miR-1231	0.02946145	Up	0.23748454	0.80380192
miR-4302	0.02947784	Up	0.52691064	0.92057128
miR-485-5p	0.02948993	Up	0.37777711	0.86499071
miR-561-3p	0.02950935	Up	0.50098883	0.91121111
miR-892c-5p	0.02953377	Up	0.40024642	0.87364718
miR-7158-3p	0.02955477	Up	0.31285611	0.8475125
miR-3124-3p	0.02959642	Up	0.19296399	0.77997491
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	0.63334498	0.95096807
miR-3620-5p	0.02992468	Up	0.30788948	0.84538031
miR-3116	0.03005477	Up	0.25045141	0.80715125
miR-7973	0.03005652	Up	0.32648339	0.85489649
miR-5001-5p	0.0300737	Up	0.55332437	0.92384946

(*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	0.03055934	Up	0.28342391	0.83193599
miR-570-3p	0.0306498	Up	0.2948952	0.83872374
miR-653-3p	0.03065132	Up	0.39212471	0.87281803
miR-6076	0.03066423	Up	0.82,336,926	0.99252298
miR-1587	0.0306804	Up	0.68602982	0.96029228
miR-4717-3p	0.03073293	Up	0.218466	0.78840757
miR-548ap-5p	0.03080711	Up	0.44476972	0.88952595
miR-4445-5p	0.03089658	Up	0.272994	0.83107769
miR-6754-3p	0.03094721	Up	0.34121026	0.85516921
miR-586	0.03105401	Up	0.43070548	0.88759074
miR-943	0.03113862	Up	0.14257113	0.75376261
miR-3972	0.03114344	Up	0.29560155	0.83872374
miR-4419a	0.03130364	Up	0.36743134	0.86195734
miR-6859-3p	0.031345	Up	0.41109277	0.8793356
miR-302a-5p	0.03155607	Up	0.40519275	0.87475982
miR-548au-3p	0.03161619	Up	0.4213246	0.8823614
miR-4659a-3p	0.03161724	Up	0.4496733	0.88964976
miR-6820-3p	0.03164575	Up	0.534798	0.9213181
miR-203b-3p	0.0317454	Up	0.30313818	0.83872374
miR-6720-3p	0.03177041	Up	0.34314084	0.8578521
miR-645	0.03182286	Up	0.40658308	0.87475982
miR-514b-3p	0.03184083	Up	0.34095019	0.85516921
miR-759	0.0318701	Up	0.44743825	0.88952595
miR-5188	0.03190043	Up	0.36455651	0.8588192
miR-4717-5p	0.03219936	Up	0.3201688	0.85046325
miR-5702	0.03233689	Up	0.27668467	0.83108541
miR-548bb-5p	0.03234506	Up	0.17156305	0.77062416
miR-6771-5p	0.03246089	Up	0.23035881	0.79466058
miR-3672	0.03253566	Up	0.50166291	0.91147569
miR-466	0.03254509	Up	0.46426145	0.89396011
miR-4533	0.03257163	Up	0.24382571	0.80715125
miR-6760-5p	0.03259034	Up	0.83963668	0.99654281
miR-3155a	0.03263465	Up	0.24121568	0.80614344
miR-8057	0.0326443	Up	0.22658673	0.79102241
miR-4425	0.03265373	Up	0.16032466	0.76082142
miR-503-5p	0.03279131	Up	0.8542697	0.99898712
miR-874-3p	0.03282655	Up	0.84803079	0.99654281
miR-542-3p	0.03283932	Up	0.57655026	0.93390911
miR-3121-3p	0.03285515	Up	0.1695905	0.77062416
miR-1910-3p	0.03289378	Up	0.41332006	0.8804535
miR-552-3p	0.03299145	Up	0.31753409	0.84917098
miR-7843-3p	0.03299986	Up	0.36155796	0.8588192
miR-6792-5p	0.03301146	Up	0.29107891	0.83872374

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-5000-3p	0.03312279	Up	0.20177441	0.77997491
miR-1193	0.03318041	Up	0.11602809	0.74226488
miR-3942-3p	0.03318391	Up	0.49335607	0.90695643
miR-6845-5p	0.03321475	Up	0.46960894	0.89396011
miR-889-5p	0.03324309	Up	0.28522198	0.83289761
miR-1471	0.03333836	Up	0.31115147	0.8475125
miR-585-5p	0.03336345	Up	0.36213281	0.8588192
miR-6513-5p	0.03337839	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-6887-5p	0.03369513	Up	0.59653264	0.93868471
miR-4695-3p	0.03374892	Up	0.33789055	0.85489649
miR-487a-5p	0.03377349	Up	0.46369411	0.89396011
miR-4714-5p	0.03387409	Up	0.50397158	0.91147569
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	0.33771595	0.85489649
miR-6754-5p	0.03443972	Up	0.25391716	0.81031406
miR-3660	0.03456359	Up	0.21524655	0.7853205
miR-8073	0.03459958	Up	0.30226843	0.83872374
miR-3614-5p	0.03464852	Up	0.42573079	0.8823614
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	0.28417496	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	0.83439474
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-548at-5p	0.03573935	Up	0.30468684	0.83927672
miR-5571-3p	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	0.18990966	0.77997491
miR-1914-3p	0.03627463	Up	0.62987625	0.95065239
miR-6860	0.03627669	Up	0.14797885	0.75376261
miR-6750-5p	0.03627802	Up	0.2160179	0.7853205
miR-34b-3p	0.03637661	Up	0.40605985	0.87475982
miR-6886-5p	0.0365227	Up	0.27957753	0.83108541
miR-1245a	0.03668535	Up	0.43662861	0.88952595
miR-4720-5p	0.03681833	Up	0.13035282	0.74892227
miR-122-5p	0.03687171	Up	0.14472276	0.75376261
miR-1909-3p	0.03687721	Up	0.1819375	0.77344537
miR-1243	0.0369511	Up	0.34756238	0.8588192
miR-6848-5p	0.03696994	Up	0.27240881	0.83107769
miR-6736-5p	0.03706158	Up	0.32377062	0.85489649
miR-3679-5p	0.03734236	Up	0.73754807	0.97354829
miR-4285	0.03735561	Up	0.20814061	0.78263372
miR-561-5p	0.03752054	Up	0.29379641	0.83872374
miR-6882-3p	0.03761332	Up	0.15777935	0.75988515
miR-4474-5p	0.03763317	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	0.03806447	Up	0.28096822	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	0.77677007
miR-579-3p	0.0383978	Up	0.10369361	0.74226488
miR-6768-5p	0.03840136	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	0.3607905	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	0.20181095	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*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-1321	0.04002516	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	0.32836793	0.85489649
miR-6079	0.04060488	Up	0.25071618	0.80715125
miR-5699-5p	0.04066678	Up	0.26624124	0.82438552
miR-4272	0.04067212	Up	0.39660658	0.87358867
miR-548h-3p	0.0407351	Up	0.18575176	0.77677007
miR-6876-3p	0.04074924	Up	0.16606324	0.76915081
miR-892b	0.04078216	Up	0.30408928	0.83872374
miR-6807-5p	0.04078605	Up	0.53160743	0.9213181
miR-4518	0.04082069	Up	0.39033207	0.87281803
miR-100-3p	0.04085695	Up	0.45761716	0.89244441
miR-4327	0.04089764	Up	0.40025816	0.87364718
miR-6765-3p	0.04091817	Up	0.51555157	0.91376348
miR-380-3p	0.04097196	Up	0.35794546	0.8588192
miR-6846-3p	0.04101375	Up	0.27666692	0.83108541
miR-8081	0.04118224	Up	0.29757035	0.83872374
miR-4438	0.04125884	Up	0.14766533	0.75376261
miR-5591-5p	0.04127629	Up	0.13916892	0.75376261
miR-3621	0.04129921	Up	0.15845074	0.75988515
miR-3188	0.04129974	Up	0.18757745	0.77997491
miR-6818-5p	0.04132926	Up	0.20318418	0.77997491
miR-3926	0.04133196	Up	0.22292684	0.79102241
miR-556-3p	0.0413505	Up	0.54518596	0.92261663
miR-6506-3p	0.04136633	Up	0.18207566	0.77344537
miR-5705	0.04141633	Up	0.20989329	0.78263372
miR-3605-5p	0.04147755	Up	0.30032934	0.83872374
miR-92b-5p	0.04159862	Up	0.08293761	0.69839839
miR-5195-5p	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-5088-5p	0.04206638	Up	0.44931883	0.88964976
miR-630	0.04207906	Up	0.31704859	0.84917098
miR-19a-3p	0.04217759	Up	0.78509476	0.98667434
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	0.27726756	0.83108541
miR-193b-5p	0.04254371	Up	0.42377608	0.8823614
miR-3670	0.04282193	Up	0.11670866	0.74226488
miR-4453	0.04282594	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-6753-3p	0.04318932	Up	0.40952534	0.87779826
miR-4529-3p	0.04328269	Up	0.16597797	0.76915081

(*Continued*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-6733-5p	0.04335371	Up	0.20559661	0.78047751
miR-520f-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	0.04367162	Up	0.09379904	0.72555728
miR-1253	0.04375056	Up	0.1151096	0.74226488
miR-6781-3p	0.04381511	Up	0.07438659	0.68406327
miR-5589-3p	0.04405912	Up	0.2724389	0.83107769
miR-764	0.04417422	Up	0.11500808	0.74226488
miR-4262	0.04433845	Up	0.11386493	0.74226488
miR-6814-3p	0.04436611	Up	0.28593611	0.83289761
miR-939-5p	0.04444632	Up	0.61817978	0.94829596
miR-4648	0.04450342	Up	0.14541416	0.75376261
miR-5701	0.04456045	Up	0.73455339	0.97354829
miR-6818-3p	0.04464997	Up	0.21082098	0.78263372
miR-4777-5p	0.0448246	Up	0.23921914	0.80380192
miR-597-5p	0.04495088	Up	0.20999917	0.78263372
miR-4773	0.04495122	Up	0.17466302	0.77062416
miR-509-3-5p	0.04497037	Up	0.13341303	0.74892227
miR-1539	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	0.06957496	0.67187824
miR-548az-3p	0.04548397	Up	0.16890955	0.77062416
miR-7843-5p	0.04554652	Up	0.06781769	0.66270515
miR-4672	0.045715	Up	0.6358909	0.95096807
miR-4486	0.04580143	Up	0.22915805	0.79158088
miR-4725-3p	0.04588192	Up	0.09281998	0.72287071
miR-3176	0.04606993	Up	0.2120879	0.78263372
miR-6894-3p	0.04622563	Up	0.3885454	0.87210628
miR-3137	0.04657398	Up	0.36426293	0.8588192
miR-6893-3p	0.0466731	Up	0.32606651	0.85489649
miR-6780a-3p	0.04669084	Up	0.39101807	0.87281803
miR-5696	0.04708647	Up	0.28288192	0.83193599
miR-296-5p	0.04722118	Up	0.37763845	0.86499071
miR-6516-3p	0.04725137	Up	0.29769649	0.83872374
miR-3613-3p	0.04725775	Up	0.24707509	0.80715125
miR-8053	0.0473133	Up	0.20270231	0.77997491
miR-3152-5p	0.04732823	Up	0.19598155	0.77997491
miR-571	0.04734154	Up	0.84533752	0.99654281
miR-378b	0.04739432	Up	0.06860943	0.66790237
miR-499b-5p	0.04800234	Up	0.27973448	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	0.05004196	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-1827	0.04916334	Up	0.04790815	0.61412501
miR-4475	0.04922564	Up	0.24552818	0.80715125
miR-4538	0.04929697	Up	0.15188194	0.75393664
miR-4524a-3p	0.04946585	Up	0.16715218	0.76915081
miR-1297	0.04951592	Up	0.13022476	0.74892227
miR-545-5p	0.0495214	Up	0.21665067	0.7853205
miR-6848-3p	0.0496268	Up	0.25624536	0.81102287
miR-592	0.04984516	Up	0.24492201	0.80715125
miR-4762-3p	0.04991254	Up	0.19551925	0.77997491
miR-3157-3p	0.05023291	Up	0.06067089	0.64832335
miR-424-3p	0.05037082	Up	0.13197357	0.74892227
miR-3180-5p	0.05065927	Up	0.21258503	0.78263372
miR-4321	0.05096856	Up	0.12083398	0.74226488
miR-564	0.05101648	Up	0.67354792	0.95648223
miR-7155-5p	0.05113808	Up	0.06047598	0.64832335
miR-4460	0.05115466	Up	0.12549433	0.74465526
miR-4539	0.05115494	Up	0.0665464	0.65890175
miR-4793-5p	0.05132612	Up	0.2768576	0.83108541
miR-4521	0.05141996	Up	0.17417833	0.77062416
miR-3135b	0.05171743	Up	0.67625049	0.95648223
miR-6793-3p	0.05175787	Up	0.12086294	0.74226488
miR-3143	0.05205933	Up	0.22745616	0.79102241
miR-1273f	0.05237566	Up	0.3795035	0.86499071
miR-297	0.05241931	Up	0.12491919	0.74465526
miR-4675	0.05253927	Up	0.14239401	0.75376261
miR-4488	0.05266286	Up	0.176305	0.77062416
miR-4489	0.05272056	Up	0.1245739	0.74454632
miR-6757-3p	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	0.74358134	0.97549977
miR-378f	0.05332519	Up	0.33432056	0.85489649
miR-562	0.05334213	Up	0.20140266	0.77997491
miR-6732-3p	0.05336692	Up	0.2016338	0.77997491
miR-6879-3p	0.05340118	Up	0.22409885	0.79102241
miR-135b-5p	0.05351659	Up	0.20225766	0.77997491
miR-589-5p	0.05379551	Up	0.08919464	0.71411286
miR-548m	0.05393355	Up	0.35511374	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	0.11924634	0.74226488
miR-7111-5p	0.05581371	Up	0.04063447	0.60118096
miR-1469	0.05624999	Up	0.09534062	0.72924227
miR-3652	0.0564083	Up	0.2054363	0.78047751
miR-933	0.05650599	Up	0.12011652	0.74226488
miR-3117-3p	0.05656766	Up	0.12111369	0.74226488
miR-3190-5p	0.05684382	Up	0.22861872	0.79102241
miR-6761-3p	0.05710884	Up	0.16210545	0.76582906
miR-6835-3p	0.05736794	Up	0.27628877	0.83108541
miR-6080	0.05767708	Up	0.17847595	0.77062416
miR-4300	0.05768393	Up	0.05365624	0.63883244
miR-4429	0.0577899	Up	0.04674782	0.61412501
miR-1270	0.05788983	Up	0.01208124	0.44355407
miR-526b-5p	0.05789863	Up	0.08022807	0.68958576
miR-4639-5p	0.05791153	Up	0.14529474	0.75376261
miR-5588-5p	0.05792606	Up	0.03581121	0.59871978
miR-615-5p	0.05796346	Up	0.1150281	0.74226488
miR-1249-5p	0.05819312	Up	0.37560471	0.86499071
miR-1252-5p	0.05822212	Up	0.10268676	0.73922964
miR-150-3p	0.05825973	Up	0.25924851	0.81550632
miR-4790-5p	0.05830035	Up	0.10614619	0.74226488
miR-3678-5p	0.05866581	Up	0.30176797	0.83872374
miR-222-3p	0.05867964	Up	0.31819131	0.84917098
miR-4786-5p	0.0587769	Up	0.08817894	0.71090581
miR-6812-5p	0.05917651	Up	0.56525274	0.9303065
miR-3145-3p	0.05928081	Up	0.17130088	0.77062416
miR-601	0.05930908	Up	0.11511752	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	0.88952595
miR-3162-5p	0.05982246	Up	0.45070972	0.88964976
miR-664b-3p	0.05992559	Up	0.79741636	0.98759926
miR-3922-3p	0.0599527	Up	0.15889256	0.75988515
miR-4458	0.06005394	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-548al	0.06052741	Up	0.10733331	0.74226488
miR-301a-5p	0.06053351	Up	0.16686685	0.76915081
miR-566	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*)

Table 9 (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	0.06191006	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-6857-3p	0.06249059	Up	0.23882079	0.80380192
miR-6789-3p	0.0627565	Up	0.0762451	0.68910078
miR-520a-3p	0.06334441	Up	0.24890997	0.80715125
miR-7977	0.06345694	Up	0.74952299	0.97742837
miR-3622b-5p	0.06355498	Up	0.0461498	0.61412501
miR-1273h-3p	0.06364311	Up	0.0940119	0.72555728
miR-1305	0.06377145	Up	0.32183809	0.85270505
miR-8089	0.06424523	Up	0.17909857	0.77062416
miR-4663	0.06434253	Up	0.02836095	0.59258245
miR-4715-5p	0.06449671	Up	0.03872527	0.59871978
miR-6508-5p	0.06483137	Up	0.51403325	0.91376348
miR-3935	0.06495576	Up	0.33347485	0.85489649
miR-6867-3p	0.06507568	Up	0.04850407	0.61412501
miR-492	0.06516851	Up	0.04991087	0.62129395
miR-5094	0.06523354	Up	0.06079608	0.64832335
miR-6865-3p	0.06624252	Up	0.21168754	0.78263372
miR-4493	0.06642774	Up	0.0392186	0.59871978
miR-7114-3p	0.06671008	Up	0.13302163	0.74892227
miR-4288	0.06683348	Up	0.0299282	0.59616058
let-7i-3p	0.06709042	Up	0.30201312	0.83872374
miR-3975	0.06765074	Up	0.11109946	0.74226488
miR-3120-5p	0.0678456	Up	0.07987684	0.68910078
miR-7114-5p	0.06800749	Up	0.6569214	0.95321673
miR-548ah-5p	0.06819495	Up	0.07413876	0.68406327
miR-513c-5p	0.06843293	Up	0.40487621	0.87475982
let-7f-2-3p	0.06854085	Up	0.18035401	0.77062416
miR-4716-5p	0.06872344	Up	0.20833589	0.78263372
miR-4787-3p	0.06876198	Up	0.50943723	0.91230009
miR-600	0.06877777	Up	0.07989689	0.68910078
miR-7150	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*)

Table 9 (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	0.02312432	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	0.43792054	0.88952595
miR-455-3p	0.07223937	Up	0.12343738	0.74454632
miR-518d-3p	0.07256516	Up	0.18334791	0.77350881
miR-2861	0.07268732	Up	0.35615086	0.8588192
miR-648	0.07270619	Up	0.03799809	0.59871978
miR-515-3p	0.07293229	Up	0.08596047	0.70807179
miR-4329	0.07336799	Up	0.07363192	0.68406327
miR-4652-5p	0.07337191	Up	0.02576632	0.55959148
miR-935	0.0735817	Up	0.18143568	0.77328308
miR-4738-5p	0.07367585	Up	0.01998951	0.53734625
miR-6784-3p	0.07382632	Up	0.03657297	0.59871978
miR-500a-5p	0.07386426	Up	0.15142982	0.75393664
miR-2053	0.07413253	Up	0.1346475	0.75226974
miR-451b	0.07445664	Up	0.06375711	0.65542311
miR-6800-3p	0.07499934	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	0.21885155	0.78840757
miR-4753-3p	0.077048	Up	0.00651694	0.40231598
miR-4653-3p	0.07749411	Up	0.12336065	0.74454632
miR-550a-5p	0.07848802	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	0.74226488
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	0.99122915
miR-3195	0.08270457	Up	0.24420862	0.80715125
miR-548az-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*)

Table 9 (Continued).

miRNAs	Log2FoldChange	Regulation	P-value	P-adj
miR-542-5p	0.08526668	Up	0.46783284	0.89396011
miR-519e-3p	0.08567418	Up	0.11759491	0.74226488
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	0.09109285	0.72012996
miR-6738-3p	0.08676132	Up	0.07990351	0.68910078
miR-8061	0.08705854	Up	0.01130452	0.43937422
miR-7162-3p	0.08711663	Up	0.02294984	0.53734625
miR-6737-3p	0.08722144	Up	0.25604062	0.81102287
miR-6867-5p	0.08729181	Up	0.05940578	0.64832335
miR-1267	0.08783125	Up	0.01084837	0.43937422
miR-3591-3p	0.08842998	Up	0.00854575	0.40696367
miR-6515-5p	0.08897001	Up	0.04215507	0.60118096
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	0.08499877	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	0.84917098
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	0.78263372
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-3118	0.10852694	Up	0.0138673	0.46600109
miR-660-5p	0.10883293	Up	0.46688213	0.89396011
miR-663a	0.10974097	Up	0.28324328	0.83193599
miR-1238-5p	0.11034519	Up	0.01534139	0.49284222
miR-4665-3p	0.11195401	Up	0.49477477	0.90848159
miR-7704	0.11225656	Up	0.09124377	0.72012996
miR-4312	0.1126684	Up	0.06065803	0.64832335
miR-4466	0.1128636	Up	0.44582227	0.88952595
miR-3074-3p	0.1131561	Up	0.01597018	0.50670832
miR-6131	0.11373774	Up	0.11445403	0.74226488
miR-3941	0.1148302	Up	0.00122462	0.26227331
miR-4449	0.11599411	Up	0.33275425	0.85489649
miR-342-5p	0.11633261	Up	0.46550933	0.89396011
miR-548c-3p	0.11721243	Up	0.0425739	0.60118096
miR-638	0.11790044	Up	0.10193756	0.73589757
miR-937-5p	0.11821584	Up	0.16926304	0.77062416
miR-6769b-3p	0.1190295	Up	0.00061825	0.15302397
miR-483-3p	0.12066504	Up	0.06664188	0.65890175
miR-6752-3p	0.1209839	Up	0.11746481	0.74226488
miR-3164	0.12126773	Up	0.02485249	0.55568816
miR-425-3p	0.12135184	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	0.12797268	Up	0.05740226	0.64832335
miR-6797-3p	0.13035638	Up	0.16601533	0.76915081
miR-1181	0.13038863	Up	0.12071581	0.74226488
miR-6821-5p	0.13109406	Up	0.37417957	0.86499071
miR-1238-3p	0.13295731	Up	0.08977201	0.71650331
miR-6890-3p	0.13318201	Up	0.00293306	0.34045223
miR-1260a	0.13337208	Up	0.32936032	0.85489649
miR-8072	0.13401883	Up	0.00902604	0.40696367
miR-6880-3p	0.13423449	Up	0.01863114	0.53734625
miR-6734-5p	0.13476722	Up	0.02094573	0.53734625
miR-5580-3p	0.13672314	Up	0.05083706	0.62512553
miR-1304-3p	0.1371615	Up	0.00400137	0.34045223
miR-199b-5p	0.13739765	Up	0.5988803	0.93906184
miR-4465	0.13988188	Up	0.35513979	0.8588192
miR-4746-3p	0.14518648	Up	0.02208845	0.53734625
miR-6759-3p	0.14532219	Up	0.08313556	0.69839839
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	0.14780681	Up	0.1566901	0.75715578

(*Continued*)

Table 9 (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	0.85489649
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	0.15706346	Up	0.31237204	0.8475125
miR-6893-5p	0.15994903	Up	0.11245159	0.74226488
miR-33b-3p	0.16368374	Up	0.15801165	0.75988515
miR-34b-5p	0.16407042	Up	0.04167753	0.60118096
miR-513b-5p	0.16733719	Up	0.14386933	0.75376261
miR-3665	0.16739733	Up	0.40603336	0.87475982
miR-4785	0.16909089	Up	0.01306086	0.45981375
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	0.25114209	0.80715125
miR-1260b	0.17907235	Up	0.14017212	0.75376261
miR-3198	0.17929237	Up	0.02123337	0.53734625
miR-1290	0.18406083	Up	0.03967176	0.59871978
miR-4485-3p	0.1846673	Up	0.07340574	0.68406327
miR-6503-3p	0.18979698	Up	0.28804023	0.83439474
miR-582-5p	0.19045558	Up	0.62677845	0.9498341
miR-3940-5p	0.19057902	Up	0.08648205	0.70907074
miR-6879-5p	0.19101714	Up	0.02231673	0.53734625
miR-6125	0.19106394	Up	0.1196758	0.74226488
miR-3162-3p	0.19525376	Up	0.06057967	0.64832335
miR-4442	0.19537199	Up	0.02357392	0.54093726
miR-4669	0.19873977	Up	0.05792698	0.64832335
miR-8063	0.19905207	Up	0.33357986	0.85489649
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	0.13247253	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-362-5p	0.24215656	Up	0.28398808	0.83193599
miR-6767-5p	0.24557824	Up	0.00430298	0.34045223
miR-5006-5p	0.24665791	Up	0.10970319	0.74226488
miR-940	0.24920107	Up	0.1206625	0.74226488
miR-4512	0.24979984	Up	0.00061516	0.15302397
miR-5100	0.25235575	Up	0.34779581	0.8588192
miR-6740-5p	0.25563327	Up	0.00409229	0.34045223
miR-6088	0.25633403	Up	0.04560842	0.61412501
miR-3651	0.25657361	Up	0.09007374	0.71668583
miR-4428	0.26039231	Up	0.01098536	0.43937422
miR-619-5p	0.26233591	Up	0.02890641	0.59616058
miR-4299	0.26378168	Up	0.16313713	0.76802692
miR-1268a	0.26900448	Up	0.02969275	0.59616058
miR-4763-3p	0.27411287	Up	0.15236304	0.75393664
miR-4728-5p	0.27540238	Up	0.00902596	0.40696367
miR-1273g-3p	0.28401482	Up	0.00853108	0.40696367
miR-6780b-5p	0.28445951	Up	0.00201749	0.32405862
miR-193a-3p	0.29191057	Up	0.22860566	0.79102241
miR-4697-5p	0.29577233	Up	0.02066387	0.53734625
miR-338-3p	0.30407515	Up	0.33547234	0.85489649
miR-4713-3p	0.31190821	Up	0.00441411	0.34045223
miR-6127	0.31227553	Up	0.02937864	0.59616058
miR-3663-3p	0.32622686	Up	0.17739186	0.77062416
miR-197-5p	0.32730894	Up	0.01165849	0.43937422
miR-1225-5p	0.32794342	Up	0.04237249	0.60118096
miR-4667-5p	0.33094713	Up	0.11216581	0.74226488
miR-6089	0.33321123	Up	0.06419436	0.65598378
miR-642a-3p	0.33705253	Up	0.0354651	0.59871978
miR-3960	0.34205792	Up	0.21934296	0.78840757
miR-6087	0.34742973	Up	0.01824337	0.53734625
miR-4286	0.35393924	Up	0.15460101	0.75393664
miR-6875-5p	0.35408709	Up	0.00825659	0.40696367
miR-664b-5p	0.35527207	Up	0.00544933	0.36854655
miR-513a-5p	0.37891789	Up	0.00367033	0.34045223
miR-4459	0.38291314	Up	0.03613368	0.59871978
miR-424-5p	0.39379877	Up	0.17613337	0.77062416
miR-6090	0.40130574	Up	0.11481495	0.74226488
miR-365a-3p	0.40351876	Up	0.01344372	0.46067162
miR-1246	0.4191497	Up	0.0080711	0.40696367
miR-6785-5p	0.43652493	Up	0.02101025	0.53734625
miR-6869-5p	0.44434072	Up	0.00970313	0.42994906
miR-34a-5p	0.45746932	Up	0.20090282	0.77997491
miR-6132	0.46392014	Up	0.02511952	0.55568816
miR-451a	0.5157088	Up	0.15065058	0.75393664

(*Continued*)

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	0.65539395
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

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.

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

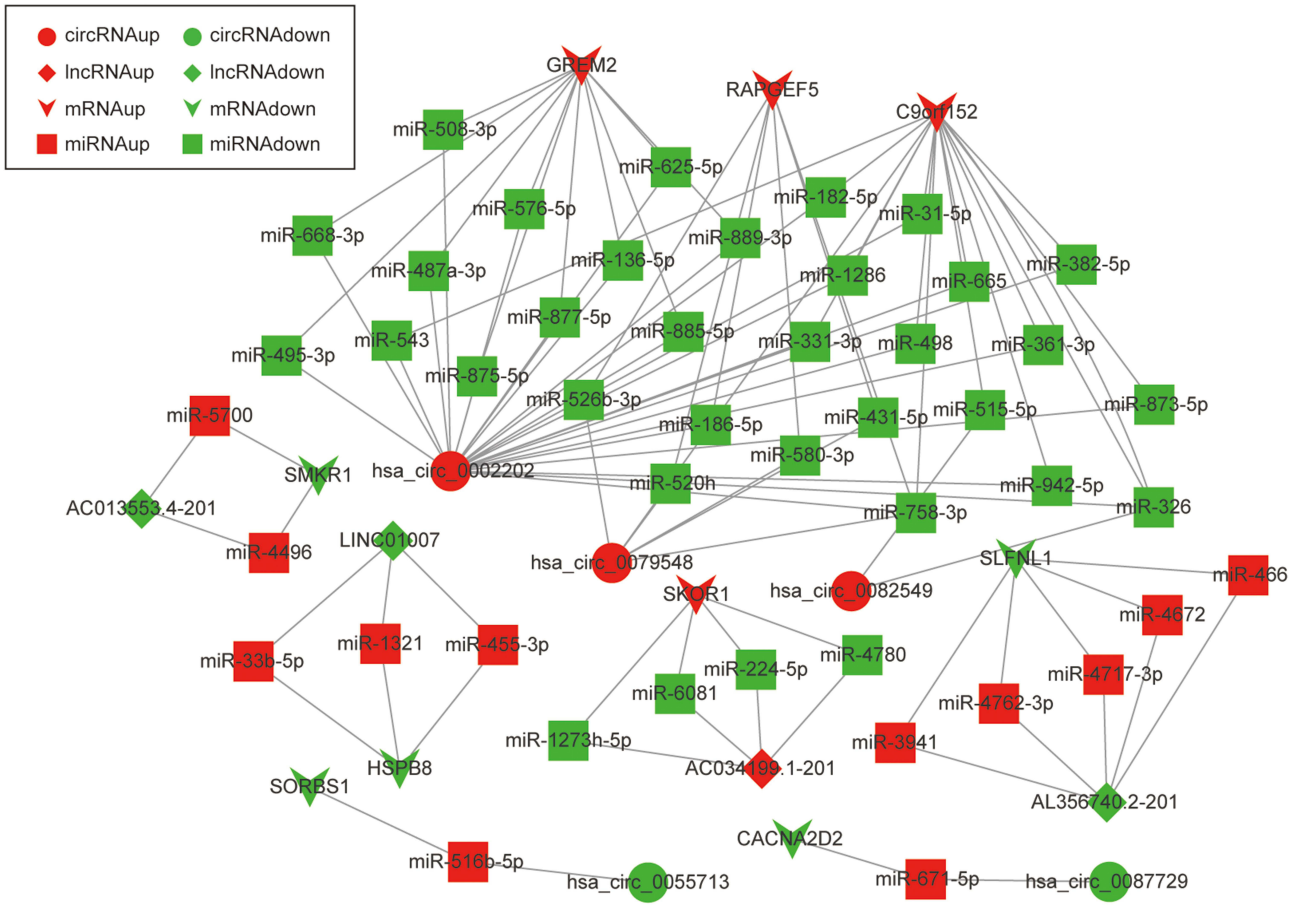

Figure 6 The circRNA-lncRNA-miRNA-mRNA network. The round nodes represent DEcircRNAs, the rhombic nodes represent DElncRNAs, the v-type nodes represent DEmRNAs, the square nodes represent DEmiRNAs. The up or down-regulated genes are represented in red and green, respectively.

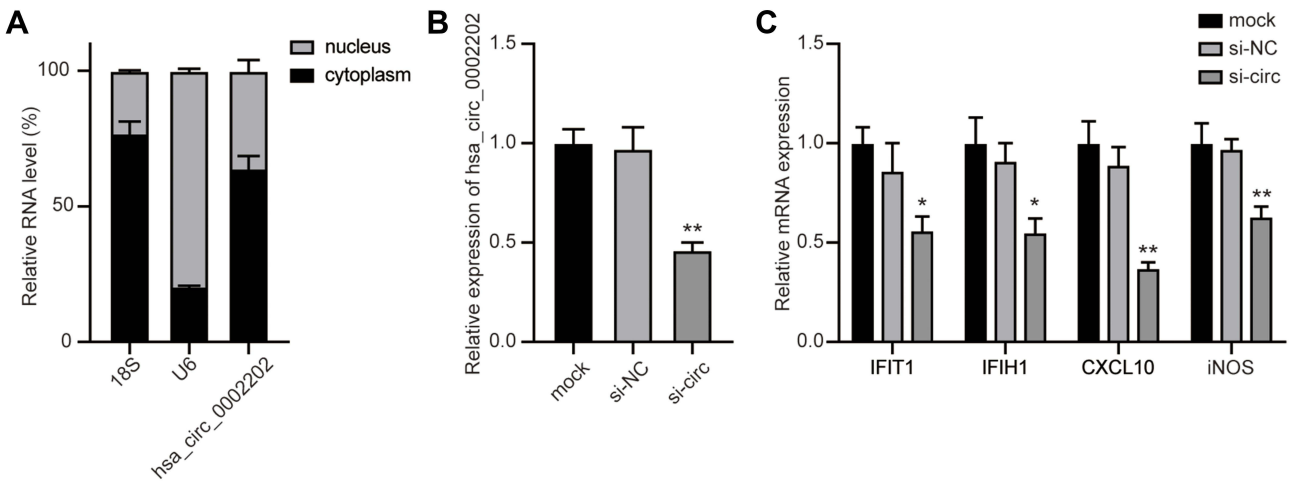

Figure 7 Inhibition of hsa_circ_0002202 suppressed IFN-I-induced inflammation. (**A**) Subcellular distribution of hsa_circ_0002202 in the nucleus and cytoplasm in THP-1-derived macrophages. (**B**) qRT-PCR detection of hsa_circ_0002202 expression after transfection with si-NC or si-circ. (**C**) qRT-PCR detection of IFIT1, IFIH1, CXCL10, and iNOS expression under IFN-I stimulation after treatment with hsa_circ_0002202 siRNA. Data are presented as the mean ± SD of three experiments and analyzed using one-way ANOVA with Tukey's post-test. *P<0.05, **P<0.01, compared with the si-NC group.

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 lncRNAs; 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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