

Research Article

Small RNA Sequencing Reveals Exosomal miRNAs Involved in the Treatment of Asthma by Scorpio and Centipede

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Received 25 September 2019; Accepted 3 December 2019; Published 16 January 2020

Academic Editor: Ernesto Picardi

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Asthma is a common respiratory disease with inflammation in the lungs. Exosomes and microRNAs (miRNAs) play crucial role in inflammation, whereas the role of exosomal miRNA in asthma remains unknown. Here, we aimed to identify the key exosomal miRNAs and their underlying mechanisms involved in scorpio and centipede (SC) treatment in asthma. Eighteen mice were randomly divided into three groups: control group, asthma group, and SC treatment group. Effect of SC was assessed by hematoxylin-eosin staining and real-time PCR. Exosomes from asthma and SC treatment groups were analyzed by small RNA-seq. Results revealed SC significantly alleviated the pathogenesis of asthma and suppressed the release of inflammatory cytokines. A total of 328 exosomal miRNAs were differentially expressed between the exosomes from asthma and SC-treated mice, including 118 up- and 210 downregulated in SC-treated mice. The altered exosomal miRNAs were primarily involved in the function of transcription, apoptotic process, and cell adhesion; and pathway of calcium, Wnt, and MAPK signaling. Real-time PCR verified exosomal miR-147 was downregulated, while miR-98-5p and miR-10a-5p were upregulated in SC-treated mice compared to asthma mice. Moreover, the target genes of miR-147-3p, miR-98-5p, and miR-10a-5p were mainly enriched in Wnt and MAPK inflammatory signaling. miR-10a-5p promoted the proliferation of mouse lung epithelial cells and downregulated the expression of Nfat5 and Map2k6. These data suggest SC-induced exosomal miRNAs might mediate the inflammatory signaling and might be involved in the SC treatment in asthma. The exosomal miRNAs might be promising candidates for the treatment of asthma.

1. Introduction

Asthma is one of the most common respiratory diseases, which affects more than 334 million people worldwide [1]. Characterized by reversible airway inflammation, airway obstruction, and airway hyperresponsiveness, asthma has the respiratory symptoms of wheeze, chest tightness, and cough [2]. The underlying mechanisms (endogenous) of asthma are complex and represents host-environment interactions that occur at different spatial scales. Genes associated with epithelial barrier dysfunction and immune responses make a major contribution to asthma [3]. Epithelial cells, dendritic cells, and idiopathic lymphocytes are involved in the pathogenesis of asthma, and infiltration of

eosinophils, basophils, and mast cells was occurred in airway smooth muscle and submucosal airway [4]. In patients with chronic asthma, persistent inflammation and smooth muscle hyperplasia can lead to thickening and narrowing of the airways, which triggers coughing, shortness of breath, and even difficulty breathing [5]. The recommended medications for adults and children include inhaled glucocorticoids and long-acting beta-2 agonists, while long-acting muscarinic antagonists, leukotriene receptor antagonists, or theophylline are considered as adjunctive therapies [3]. However, there are still limitations in the treatment of asthma with these drugs. Therefore, it is urgent to explore the pathogenesis of asthma and find new medical treatments.

Recently, large numbers of insects around the world have been identified as additional sources for novel and mechanically unique therapies. Insect Chinese medicine, such as scorpion, centipede, and earth dragon, is usually used in the treatment of refractory asthma, due to their functions of dredging collaterals, activating blood circulation and removing stasis. Scorpio and centipede (SC) showed significantly improve effects on airway inflammation and remodeling in asthmatic rats [6]. A previous study revealed that insects, including SC, produce hundreds of bioactive substances in the venom, which may be clinically useful [7]. In our previous study of 78 cases of refractory asthma, we found that treatment with SC could improve clinical symptoms and lung function and reduce airway inflammation, and no adverse reactions were found. However, the underlying mechanism of SC treatment in refractory asthma is still unknown.

Exosomes are a class of extracellular vesicles with diameters of 30 to 100 nm. As a new information carrier, exosomes carries proteins, messenger RNA (mRNA) and various noncoding RNAs, such as microRNAs (miRNAs), from donor cells to recipient cells [8]. They exist in biological fluids and play pivotal roles in multiple physiological and pathological processes [9]. Recently, the crucial role of exosomes in bronchial asthma has been discovered [10]. Bronchoalveolar lavage fluid (BALF) exosomes are involved in the cytokine and leukotriene production in allergic asthma [11]. Additionally, miRNAs have also been shown to function as potential biomarkers and therapeutic target for asthma [12]. The biological roles of exosomal miRNAs have attracted significant interest in the pulmonary field [13, 14]. Exosomal miRNAs from the BALF, such as let-7 and miRNA-200, can act as novel biomarkers for asthmatic patients [15]. However, the role of exosomal miRNAs in asthma is still largely unclear.

In the present study, we aimed to investigate the exosomal miRNAs involved in the SC treatment of refractory asthma. Effect of SC on asthma mice was assessed, and the exosomal miRNAs profiling in BALF of SC treated and control asthma mouse was investigated by small RNA sequencing. The results might provide a potential exosomal miRNAs involved in alleviating the symptoms associated with asthma.

2. Materials and Methods

2.1. Animals. SPF-grade male BALB/c mice (weight 20 ± 2 g) were obtained from J Shanghai Sipul-Bikai Laboratory Animal co., Ltd (Shanghai, China). Mice were housed in under nonpathogen conditions and in an environment of 22°C with 12 h light and 12 h dark cycle. The model was established after feeding for a week. The animal experiment in this study was approved via the animal care and ethical committee of Shanghai Municipal Hospital of Traditional Chinese Medicine.

2.2. Asthma Establishment and SC Treatment. A total of 18 mice were randomly divided into three groups: control

group, asthma group, and SC treatment group, with 6 mice in each group. Mice in asthma group and treatment group were sensitized on the 1st and 7th days, by intraperitoneal injection with 0.1 mL allergen drugs, including OVA (0.5 mg/mL) and aluminum hydroxide (2 mg/mL). The animal was motivated on day 15. Briefly, mice were placed in an airtight container filled with 2% OVA atomized fluid for 40 min once a day, for a total of 3 weeks. Mice in the control group were intraperitoneally injected with the same amount of normal saline on the 1st and 7th day. At the 15th day, they were placed in a container filled with normal saline atomizing fluid for 4 min, once a day for 3 weeks. From day 15, each group was given intragastric administration 1 h before each stimulation, once a day for 3 weeks. On days 15–36, control group and model group received 10 mL/kg normal saline, and SC treatment group received 0.625 g/kg SC solution. At the end of experiments, BALF of mice was collected and stored at -80°C . Mice were euthanized via CO_2 inhalation. The left lung of mice was partially immobilized and partially frozen.

2.3. Hematoxylin-Eosin (H&E) Staining. Lung tissues were fixed in 10% formalin and dehydrated with different concentrations of ethanol. Tissues were cut into 4–7 μm slices, placed in a 65°C constant temperature oven for 30 min, soaked in xylene I for 15 min, and then in xylene II for 15 min. The slices were soaked with 100% alcohol, 95% alcohol, 85% alcohol, and 75% alcohol for 5 min, respectively, and washed with running water for 10 min. Slices were stained with Hematoxylin aqueous solution for 5 min and eosin staining solution for 1–2 min. The slides were placed in xylene for 3 min, 2 times and sealed with neutral gum. Slides were analyzed by taking photos with a microscope (Nikon ECLIPSE Ni, Japan).

2.4. Exosome Extraction. Exosomes were obtained from BALF of asthma group and SC treatment group, using Exo-quick exosome precipitation kit (SBI System Biosciences, Inc.) based on the manufacturer's instruction. In brief, BALF was centrifuged at $3000 \times g$ for 15 min under 4°C, and then the supernatant was collected, and repeat the above centrifugation. The final supernatant was collected and transferred to a new tube, then added with 252 μL Exo-Quick Exosome Precipitation Solution, and incubated at 4°C for 1 h. Pelleted exosomes were obtained by centrifuging the above reaction at $1500 \times g$, for 30 min at 4°C. The isolated exosomes were resuspended using $1 \times$ Phosphate Buffered Saline (PBS).

2.5. Transmission Electron Microscopy (TEM). The extracted exosomes were dropped on the copper network for 1 min. The floating fluid at the edge was removed by a filter paper. Exosomes were washed using ultrapure water for three times. Phosphotungstic acid of 10 μL was added to the copper network and deposit for 1 min, and samples were desiccated at 20°C for 2 min. Exosomes were analyzed by a Transmission electron microscopy (NEC Electronics Corporation, JEM—1200EX).

2.6. Western Blot. Total protein of exosomes was isolated and the concentration was detected via a BCA assay kit (Pierce Biotechnology, Inc., Rockford, IL, USA). Equal protein from each group was loaded on 10% SDS-PAGE gel, and transferred to polyvinylidene fluoride membranes (Millipore, Bedford, MA, USA). Primary antibodies against CD63 (Santa Cruz, Santa Cruz, CA, USA; 1:100), and GAPDH (PB0141; 1:1000) was incubated with membranes at 4°C for overnight. Membranes were washed and incubated with goat antirabbit IgG-HRP secondary antibody for 2 h. Diaminobenzidine diaminobenzidine was used to stain the membranes. Enhanced chemiluminescence reagent (Thermo Fisher Scientific, Waltham, MA) was used to show the protein bands and the bands were observed by a Chemi-Doc MP system (Bio-Rad, Hercules, USA).

2.7. RNA Isolation, Small RNA Library Construction, and Sequencing. Three asthma mice and three SC treatment mice were involved in the RNA sequencing. Total RNA was isolated from BALF-derived exosomes via TRIzol (Invitrogen, Carlsbad, CA, USA). RNA concentration and integrity were measured by the NanoDrop 2000 spectrophotometer (NanoDrop Technologies, Inc., Wilmington, DE, USA). Illumina TruSeq RNA Sample Preparation Kit (Illumina, San Diego, CA, USA) was used to establish the small RNA libraries, followed by the manufacturer's recommendations. Briefly, 1 µg of total RNA was adapter-ligated with 120 nt adapter. RNA of target fragment size 135–170 nt was obtained by PAGE gel electrophoresis. Target RNA was collected with anhydrous ethanol and then reversely transcribed into cDNA and quantified with the Agilent Bioanalyzer 2100 system (Agilent Technologies, Santa Clara, CA, USA). All six libraries were sequenced on an Illumina HiSeq 2500 Genome Analyzer platform using pair-end mode, at Shanghai Yingbio biotechnology co. Ltd.

2.8. Data Processing. Raw reads were quality-controlled using FastQC (<http://www.bioinformatics.babraham.ac.uk/projects/fastqc/>). To identify known small noncoding RNAs, all clean reads were mapped to the miRBase database (<http://www.mirbase.org/>) using BWA. The reads that cannot be mapped to miRBase were then mapped to piRNA database to obtain piRNA. The transfer RNA-derived small RNAs (tsRNAs) were identified by mapping to tRNA database (<http://gtrnadb.ucsc.edu/>), tRFdb (<http://genome.bioch.virginia.edu/trfdb/>). Differential expressed miRNAs (DEmiRNAs) were identified by the EBSeq [16], and significant differences were defined as absolute log2 fold change >1 and false discovery rate (FDR) <0.05. Potential targets of DEmiRNAs were predicted by miRanda (Score ≥150 and Energy <−20) and RNAhybrid (Energy <−25), and the final target genes were obtained by intersection of these two algorithms. Function and pathway of target genes were analyzed by Gene Ontology (GO) and the Kyoto Encyclopedia of Genes and Genomes (KEGG) database, respectively. The significance level was assessed by Fisher test and the significant enrichment was obtained by P-value <0.05. GO includes three classes: biological process

(BP), cellular component (CC), and molecular function (MF).

2.9. Cell Culture. Mouse lung epithelial cells (TC-1 JHU-1) were purchased from Procell (Wuhan, China). TC-1 cells were incubated in Dulbecco-modified Eagle medium (DMEM; Life Technologies, Carlsbad, CA, USA) supplemented with 5% fetal bovine serum (FBS; Hyclone, Logan, UT, USA) and penicillin/streptomycin 100 IU/mL. Cells were cultured at 37°C, in a humidified atmosphere of 5% CO₂ and 95% air.

2.10. Cell Proliferation Assays. Cell proliferation was evaluated by CCK-8 assay. Cells were harvested after 48 h of miRNA mimics or inhibitor transfection and cultured in 96-well plates (Corning, NY, USA) with 2×10^4 cells/ml. CCK-8 solution (Beyotime, Shanghai, China) was added and the OD 450 was measured after culturing for 0, 24, 48, 72, or 96 h.

2.11. Validation of Exosomal miRNAs by Real-Time PCR. To identify key miRNAs associated with SC treatment in asthma, three exosomal miRNAs were selected for real-time PCR in six asthma mice and six SC-treated asthma mice, based on high their changed fold and abundance. RNA was isolated from BALF-derived exosomes of six asthma model mice and six SC treatment mice using TRIzol (Invitrogen, Carlsbad, CA, USA). Synthesis of cDNA was performed by specific reverse primer using High-Capacity cDNA Reverse Transcription Kit (Thermo Fisher, CA, USA). Real-time PCR was performed using SYBR Green Real-time PCR Master Mix (TOYOBO, No. QPK-201) and run on an ABI Q6 Real-time PCR System (Applied Biosystems Inc, USA). All reactions were performed in triplicate. The PCR process was as follows: one cycle of 95°C for 10 min, then 40 cycles of 95°C for 5 s, and annealing and extension at 55–58°C for 30 s. Data were analyzed using the $2^{-\Delta\Delta C_t}$ method. U6 was used as the reference genes, and primer sequences are shown in Table 1 of the Supplementary Materials.

2.12. Statistical Analysis. Statistical analysis and column diagram establishment were performed by GraphPad 7.0 (GraphPad Software, La Jolla, CA, USA). Data was presented as mean ± standard deviation (SD). Statistical comparisons between two groups were analyzed by unpaired *t*-test, and comparisons between three groups were analyzed by one-way ANOVA post Turkey test. The data were considered significant at *P*-values <0.05 (*) or highly significant at *P* <0.01 (**).

3. Results

3.1. SC Alleviates Pathogenesis and Inflammation in Asthma Mice. The pathogenesis of sham control mice, asthmatic mice, and SC-treated mice were analyzed by H&E staining of lung tissue. Compared with the control mice, the asthma mice showed inflammatory cells (including eosinophils, neutrophils, and lymphocytes) seriously infiltrated bronchial submucosa, bronchi, and perivascular (Figures 1(a) and

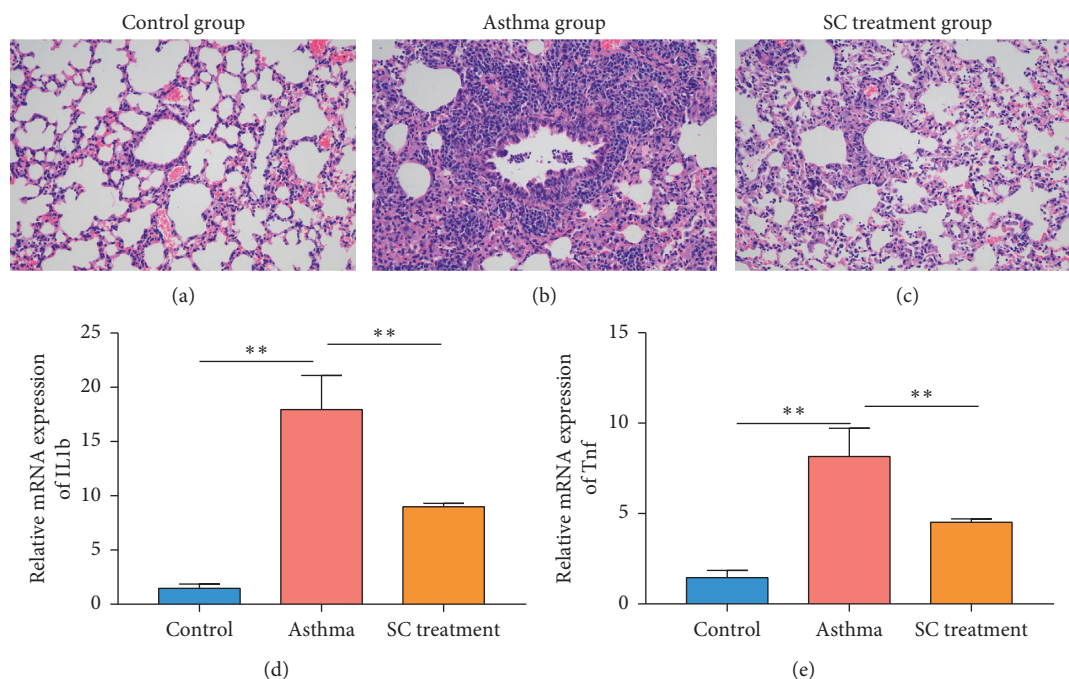


FIGURE 1: Scorpio and centipede (SC) improved pathology and inflammation of asthma in mice. (a–c) Histopathological analysis was performed by hematoxylin-eosin (H&E) staining. Enlargement factor is 200 (d and e). Expression of inflammatory factor was detected by real-time PCR. $n = 6$, two samples t -test, $**P < 0.01$.

1(b)). The asthma mice also displayed rupture of epithelial cell, thickening of bronchial wall and basement membrane, and irregular morphology. After SC treatment, the extent of inflammatory cell infiltration and inflammation in the lung tissues were decreased (Figure 1(c)), as compared to the asthma group. Additionally, we also detected the expression of inflammatory cytokines. The expression of IL1b and Tnf was significantly increased in the asthma group compared to that in the sham control group (Figures 1(d) and 1(e)). SC treatment significantly reduced the expression of IL1b and Tnf in lung tissues of asthma mice.

3.2. Characterization of the BALF-Derived Exosomes. To identify the purified exosomes, the BALF exosomes were observed by TEM which showed that exosomes were spherical particles with a complete membrane structure and with diameter of 100–150 nm (Figure 2(a)). Western blot showed that exosomes expressed the exosomal marker protein CD63 (Figure 2(b)). This result suggests the successful isolation of BALF exosomes from SC treatment and asthma model control.

3.3. Overview of the Small RNA Sequencing. A total of 263,659,786 raw reads were obtained from the six libraries, which generated 82,144,903 clean reads with an average of 82,144,903 clean reads per library (Table S1). An average of 13,690,817 reads per library were mapped to the miRbase, with mapped rate from 0.374% to 0.412 for each library (Table S2). Approximately 4407874 reads were uniquely mapped per library, with an average uniquely mapped rate of 0.32. Additionally, reads distribution showed that 2 peaks

appeared at 21–23 nt and 30–33 nt, respectively, in BALF exosomes (Figure 2(c)). Principle component analysis (PCA) revealed that the principal component of miRNAs in BALF derived exosomes can significantly discriminate asthma group and SC treatment group (Figure 2(d)). To focus on the highly represented miRNAs in exosomes, the miRNAs that have counts greater than 10 in at least one sample were considered as expressed miRNAs. As a result, 828 and 817 miRNAs were identified in the exosomes from asthma mouse and SC-treated asthma mouse, respectively (Figure 2(e)). Among the expressed miRNAs, 701 (74.1%) were shared in both groups, while 117 (12.4%) and 128 (13.5%) miRNAs were uniquely expressed in asthma and SC-treated asthma mice, respectively.

3.4. Differentially Expressed miRNAs in Exosomes. To identify exosomal miRNAs associated with the SC treatment in asthma, differentially expressed miRNAs (DEmiRNAs) between asthma and SC-treated asthma mice were analyzed. A total of 328 DEmiRNAs were identified between the exosomes from asthma and SC-treated asthma mice, including 118 up- and 210 downregulated miRNAs in the exosomes from SC-treated asthma mice compared to that from asthma mice (Figure 3(a)). Heat map showed the expression of DEmiRNAs was clustered into two clusters, including asthma group and SC-treated asthma group, respectively (Figure 3(b)).

3.5. Function and Pathway Analysis of Differentially Expressed miRNAs in Exosomes. To uncover the functions and mechanisms of the DEmiRNAs carried by exosomes, target

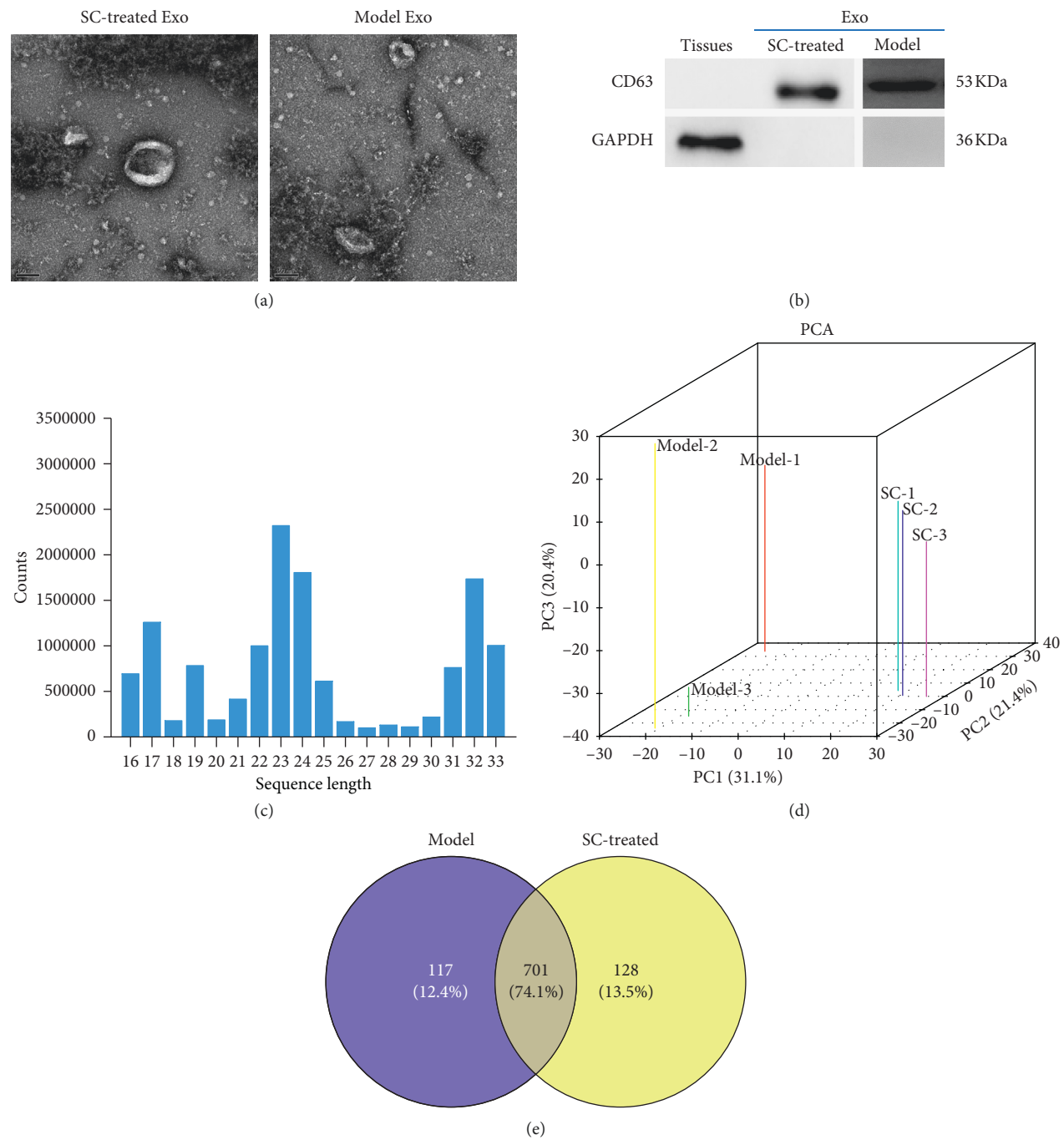


FIGURE 2: Exosomal identification and small RNA sequencing data. (a) Exosomes were analyzed by transmission electron microscopy (scale bar, 100 nm). (b) Western blot was used to measure the expression of exosomal marker in lung tissues and exosomes from bronchoalveolar lavage fluid of mice. (c) Length distribution of exosomal microRNAs (miRNAs). (d) Principal component analysis (PCA) of exosomal miRNAs from asthma group and SC treatment group. (e) Venn diagram analysis of common and unique exosomal miRNAs in the asthma group and SC treatment group. Model represents asthma group and SC represents SC treatment group.

genes of the DEMiRNAs were predicted, and GO and KEGG enrichment was performed for target genes. A total of 141,421 genes were predictably targeted by the DEMiRNAs (Figure 4(a)). GO analysis showed that DEMiRNAs were mainly associated with the function of transcription, apoptotic process, cell adhesion, transport, and cell proliferation

(Figure 4(b)). KEGG enrichment showed the targeted genes of DEMiRNAs were primarily involved in the pathway of metabolic pathways, calcium signaling pathway, Rap1 signaling pathway, Wnt signaling pathway, MAPK signaling pathway, cGMP-PKG signaling pathway, Ras signaling pathway, and FoxO signaling pathway (Figure 4(c)).

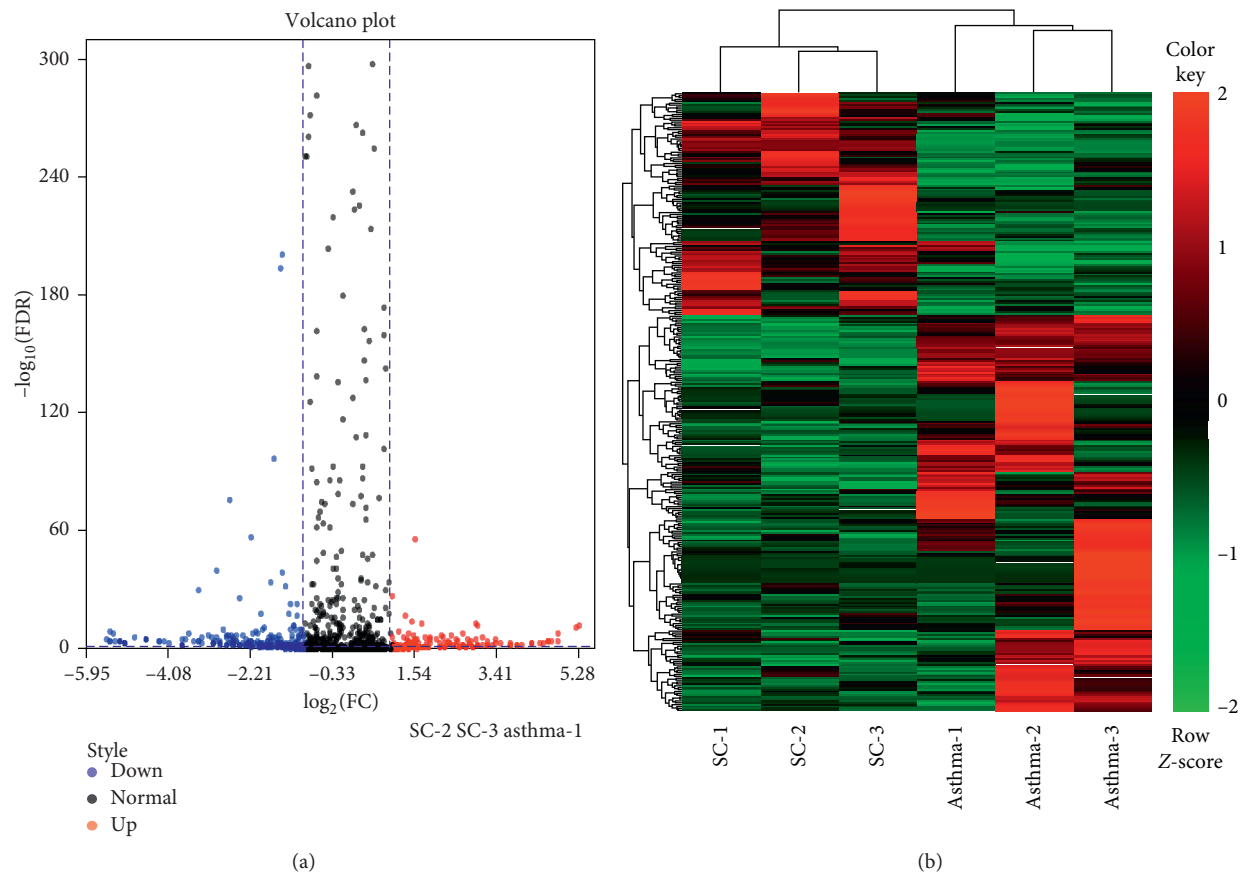


FIGURE 3: Analysis of differentially expressed miRNAs in exosomes between asthma group and SC treatment group. (a) Volcano plot analysis of differentially expressed miRNAs in bronchoalveolar lavage fluid- (BALF-) derived exosomes between the asthma group and SC treatment group. The blue point represents a downregulated exosomal miRNA and the red point represents an upregulated exosomal miRNA in the SC treatment group compared to the asthma group. (b) Heat map analysis differentially expressed miRNAs in BALF-derived exosomes between asthma group and SC treatment group. Green represents low expression level, red represents high expression level.

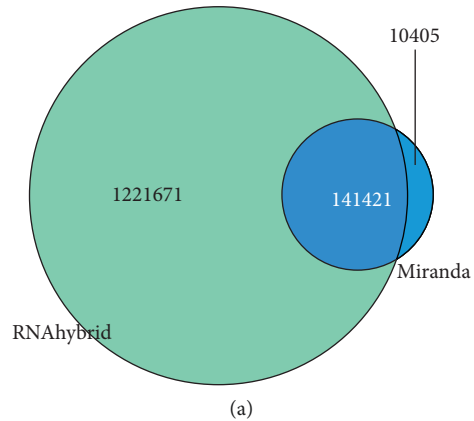


FIGURE 4: Continued.

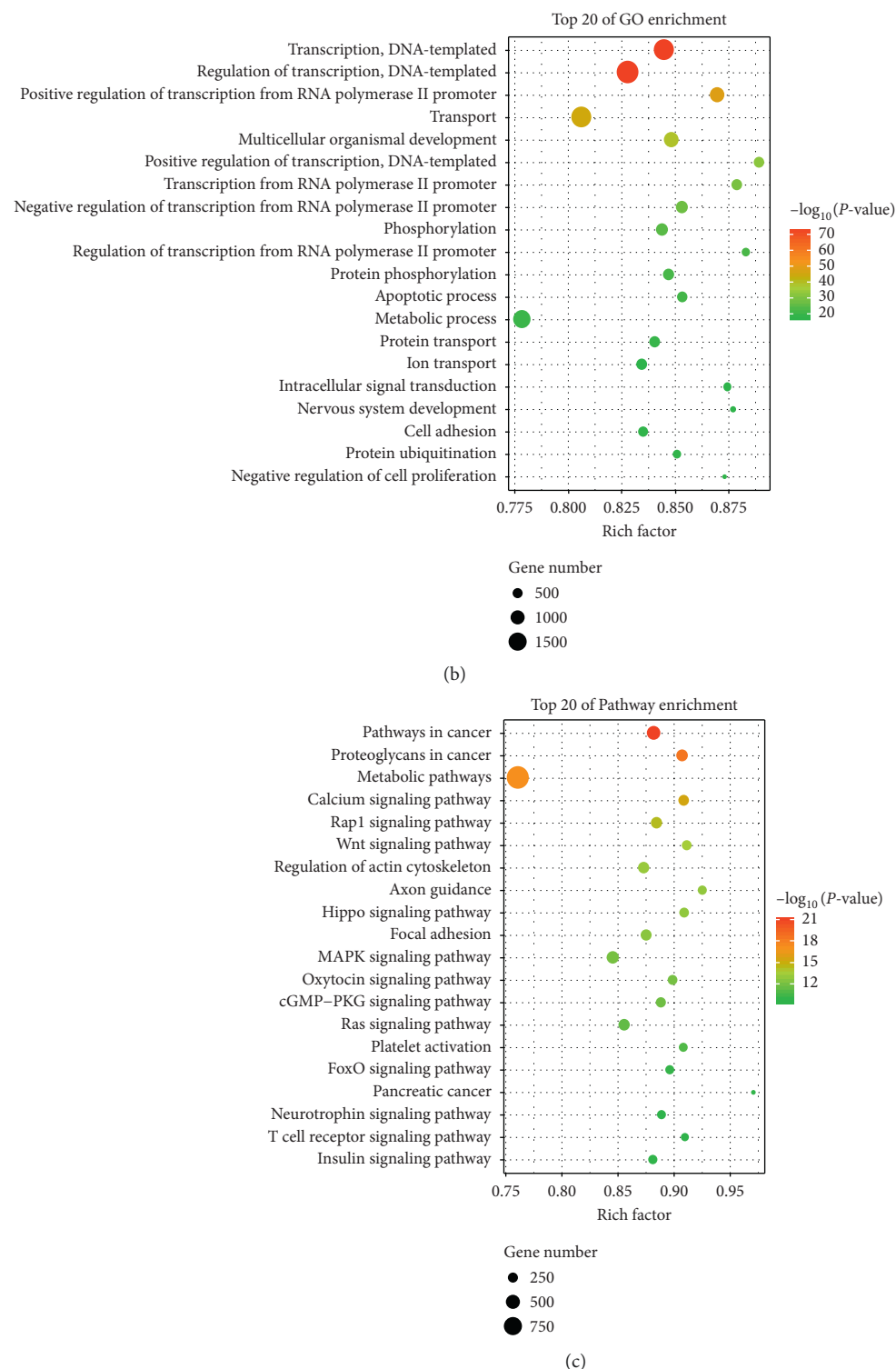


FIGURE 4: Function and pathway analysis of target genes of different exosomal miRNAs. (a) Target gene analysis of differentially expressed miRNAs. Number represents the target gene numbers of differentially expressed miRNAs using RNAhybrid and Miranda. (b) Gene Ontology (GO) analysis for target genes of differentially expressed miRNAs in BALF-derived exosomes between asthma group and SC treatment group. (c) Kyoto Encyclopedia of Genes and Genomes (KEGG) for target genes of differentially expressed miRNAs in BALF-derived exosomes between the asthma group and SC treatment group. The circle size represents the number of enriched genes and the color represents P value.

3.6. Validation of Differentially Expressed miRNAs from BALF Exosomes. To identify key exosomal miRNAs involved in SC treatment of asthma, three candidate miRNAs (mmu-miR-147-3p, mmu-miR-98-5p, and mmu-miR-10a-5p) were selected for real-time PCR in BALF exosomes, based on their high changed fold and abundance. In accordant with the RNA sequencing results, real-time PCR indicated that mmu-miR-147-3p was downregulated, while mmu-miR-98-5p and mmu-miR-10a-5p were upregulated in the BALF exosomes from the SC-treated mice compared to that from the asthma mice (Figures 5(a) and 5(b)).

3.7. Target Gene and Pathway Analysis of Differently Exosomal miRNAs. Using Miranda and RNAhybrid, we found 68, 77, and 151 genes were targeted by mmu-miR-147-3p, mmu-miR-98-5p, and mmu-miR-10a-5p, respectively (Table S3). The target genes of the three miRNAs that were significantly enriched in the KEGG terms were used for network construction (Figure 5(c)). Importantly, the target genes *cerberus 1* (*Cer1*), *nuclear factor of activated T cells 5* (*Nfat5*), *NKD inhibitor of WNT signaling pathway 1* (*Nkd1*), *presenilin 1* (*Psen1*), and *protein kinase C alpha* (*Prkca*) were enriched in the Wnt signaling pathway; *CRK like proto-oncogene* (*Crkl*), *microtubule associated protein tau* (*Mapt*), *protein kinase C alpha* (*Prkca*), *fibroblast growth factor 5* (*Fgf5*), and *mitogen-activated protein kinase kinase 6* (*Map2k6*) were enriched in MAPK signaling pathway.

3.8. mmu-miR-10a-5p Promotes Cell Proliferation of Mouse Lung Epithelial Cells. To investigate the function and mechanism of candidate miRNAs, mmu-miR-10a-5p was selected for further study, due to its high significant. Expression of miR-10a-5p was successfully increased in the mouse lung epithelial cells transfected with miR-10a-5p mimics, while decreased in the cells transfected with miR-10a-5p inhibitor, compared to the control (Figure 6(a)). CCK-8 assays showed miR-10a-5p mimics significantly promoted the proliferation of mouse lung epithelial cells, while miR-10a-5p inhibitor inhibited the proliferation of mouse lung epithelial cells (Figure 6(b)). Moreover, the predicted target genes, including *Nfat5* and *Map2k6*, were significantly decreased by miR-10a-5p mimics (Figure 6(c)), while miR-10a-5p inhibitor remarkably upregulated the expression of *Nfat5*, *Mapt*, and *Map2k6*.

4. Discussion

Asthma is a common airway disease, which is characterized by chronic inflammatory and affects approximately 7.5 percent of adults [17]. SC are two antiinflammatory Chinese medicines, which are gradually used in the therapy of refractory asthma in China. Scorpion improves collagen-induced arthritis by reducing inflammatory response, via downregulating *Tnf* and *IL-1b* in rats [18]. Moreover, SC displays significantly attenuating effects on airway inflammation and remodeling in

asthmatic rats [6]. Additionally, the effective components of centipede mainly include protein, peptide, carbohydrate, fatty acid, amino acid, trace, and elements. Extraction of *Scolopendra subspinipes mutilans* can inhibit inflammatory and neuropathic pain in sciatic nerve crush injury rats [19]. Centipede extraction showed the suppressed effects on inflammation and may partly via inhibition of the *NF-κB* signaling pathway [20]. The acid protein of centipede has a significant inhibitory effect on the apoptosis of cardiomyocytes induced by angiotensin, while the polypeptide of centipede has good analgesic activity. Although the active ingredient of scorpion is unclear, a polypeptide extracted from scorpion venom suppresses angiogenesis and angiogenesis-dependent tumor growth [21]. In the present study, SC alleviated pathological characteristics of asthma mice, such as reducing the infiltration of inflammatory cells in lung tissues. Furthermore, SC decreased the expression of inflammatory factors, including *Tnf* and *IL-1b* in lung tissues of asthma mice. These evidences revealed that SC might be an effective drug to treat asthma, while more research is needed to investigate the specific active ingredients of SC in the treatment of asthma.

Exosomes and miRNAs have been shown to modulate multiple genes and signaling pathways in inflammatory responses [22, 23]. Increasing evidence demonstrates that miRNAs play a crucial role in asthma, and several asthma-related miRNAs have been identified [24], whereas the role of exosomal miRNAs in asthma, especially their functions in the asthma treatment, remains unclear. Levänen et al. showed that 24 exosomal miRNAs are differentially expressed between BLAF of asthmatics and healthy volunteers [15]. In bronchial asthma mice, epithelial cells-derived exosomes can inhibit the generation of inflammation-induced exosomes [25], indicating that exosomes may be useful for asthma treatment. In the present study, we found 328 exosomal miRNAs altered between the asthma and SC-treated mice. Real-time PCR verified that exosomal mmu-miR-147-3p was downregulated and mmu-miR-98-5p and mmu-miR-10a-5p were upregulated after SC treatment. miR-147 has been shown to be induced by toll-like receptor and modulates inflammatory responses in mice macrophages [26]. miR-147 also reduces the production of inflammatory proteins induced by TLR2, TLR3, and TLR4-mediation [27]. miRNA-98 has been implicated to be involved in asthma by modulating peripheral B cells which is an important immune regulatory cell, via interfering the expression of thrombospondin 1 [28]. miR-10a mediates airway hyperresponsiveness by suppresses cell proliferation of airway smooth muscle, via targeting *BDNF* in asthmatic rats [29]. These evidences indicate exosomal miR-147, miR-98-5p, and miR-10a might be involved in the SC-treated process.

To investigate the mechanism of exosomal miRNAs in the treatment of asthma by SC, we analyzed the target genes and signaling pathway of differentially expressed miRNAs. We found the target genes of miR-147, miR-98-5p, and miR-10a were enriched in the pathway of Wnt and MAPK

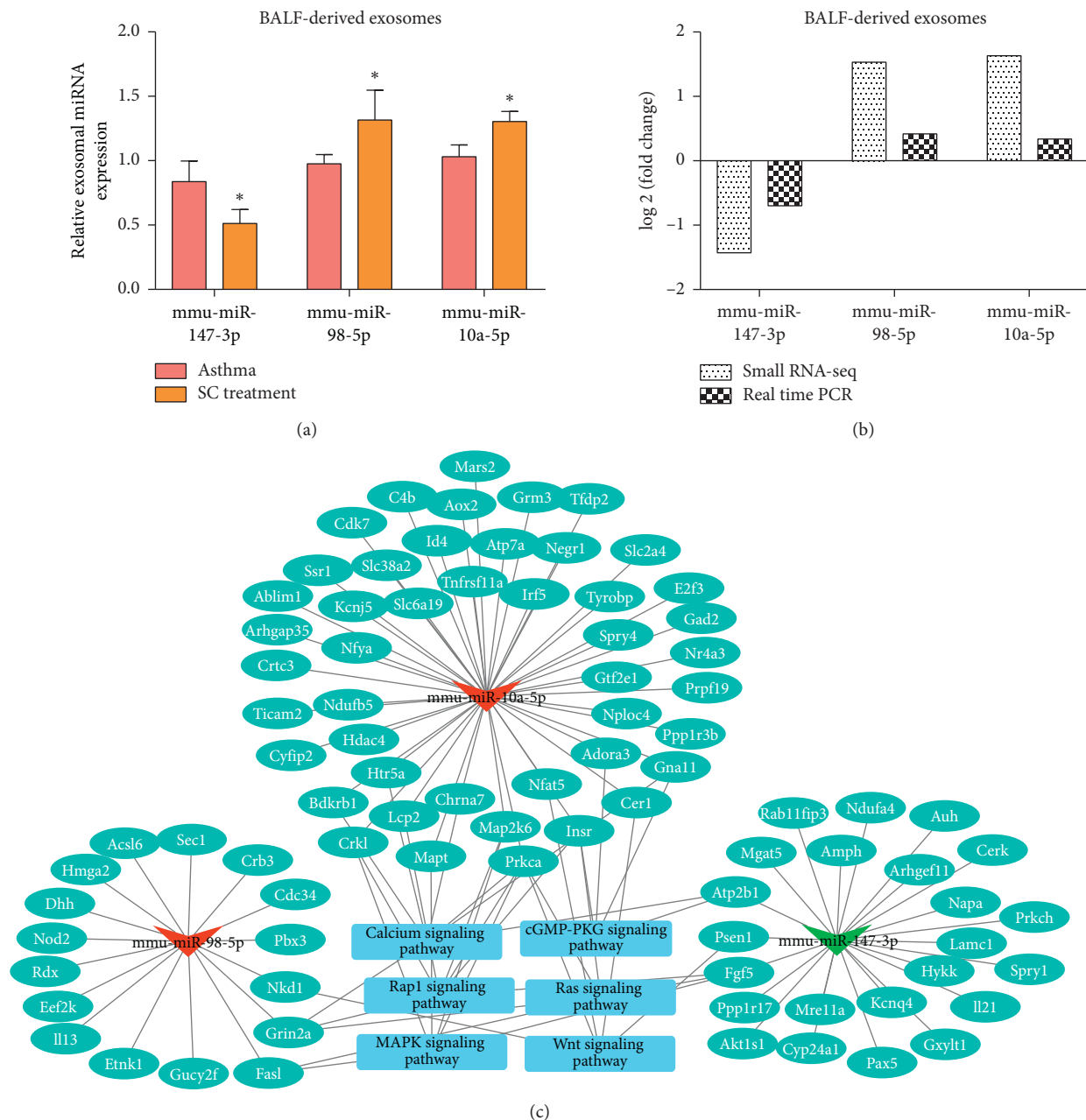


FIGURE 5: Expression and target gene analysis of the key exosomal miRNAs. (a) Candidate exosomal miRNAs were verified by real time PCR. $n = 6$, two samples t -test, $*P < 0.05$. (b) Change tendency comparison between the results of real-time PCR and small RNA-seq. Fold change: the fold change in SC treatment group compared to the asthma group. (c) Network analysis of miRNA-mRNA-pathway. Triangles, circles, and boxes represent miRNA, mRNA, and pathway, respectively. Red represents upregulated and green represents downregulated in SC treatment group compared to the asthma group.

signaling pathway. Recent findings showed canonical and noncanonical Wnt pathways play important roles in regulation of inflammatory responses, especially in asthma [30]. Furthermore, Wnt pathways are associated with airway remodeling, cell growth of smooth muscle, and metaplasia of goblet cell [31]. Suppression of Wnt antagonist significantly improves house dust mite-induced asthma, by impairing Th2 cell cytokine secretion and leukocyte infiltration [32]. Additionally, MAPK pathway also has important effect on inflammatory responses and is involved in asthma.

Inhibition of p38 MAPK might improve the corticosteroid insensitivity via modulating the release of IL-1 β and IL-8 in patients with severe asthma [33]. Ginkgolide B acts as an anti-inflammatory drug for asthma by inhibiting the kinase/ MAPK pathway and regulating extracellular T-helper 2 cytokines in asthma mouse [34]. JAX2 improves bronchial asthma suppressing the MAPK/NF- κ B inflammatory signaling pathway [35]. The present study showed that SC-induced exosomal miR-147, miR-98-5p, and miR-10a can target Wnt and MAPK pathways, suggesting exosomal

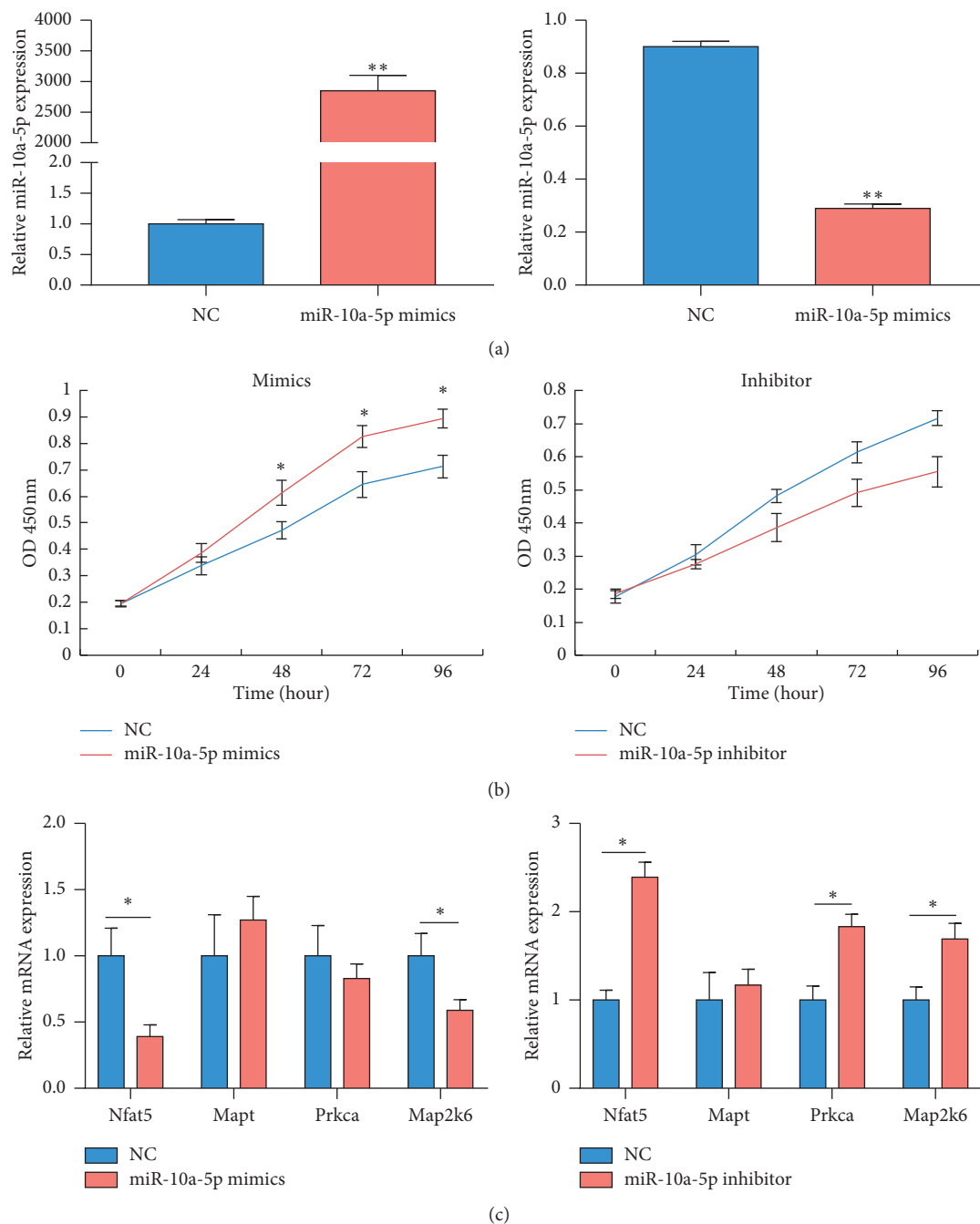


FIGURE 6: Functional and target gene validation of mmu-miR-10a-5p. (a) The transfection effect of mmu-miR-10a-5p mimics and inhibitor in mouse lung epithelial cells was verified by real-time PCR. (b) The effect of mmu-miR-10a-5p on proliferation of mouse lung epithelial cells was verified by CCK-8 assays. (c) The target gene expression of mmu-miR-10a-5p was verified by real-time PCR. $n = 3$, two samples t -test, * $P < 0.05$, ** $P < 0.01$.

miR-147, miR-98-5p, and miR-10a might mediate inflammatory pathways during the SC treatment in asthma.

In conclusion, SC can reduce the inflammatory infiltration in the lung tissues of asthma and suppress the release of inflammatory cytokines, including IL1b and Tnf. Furthermore, 328 exosomal miRNAs were differentially expressed between the asthma and SC-treated mice. SC-induced alteration of exosomal miR-147, miR-98-5p, and miR-10a-5p was verified by real-time PCR, and these

miRNAs were mainly involved in the Wnt and MAPK signaling pathways. These data might provide some novel molecular targets for the treatment of asthma.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval

The animal experiment in this study was approved by the animal care and ethical committee of Shanghai Municipal Hospital of Traditional Chinese Medicine.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

KS conceived and designed the study. BT, YWG, HF, and YWQ performed the experiments. BT and HF performed the analysis of microarrays results. BT wrote the paper. BT and YWG reviewed and edited the manuscript. All authors read and approved the manuscript.

Acknowledgments

The authors would like to thank all participants involved in this study.

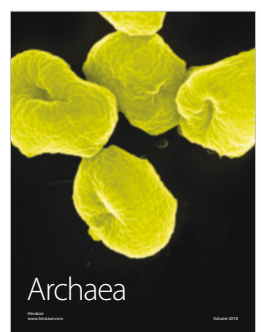
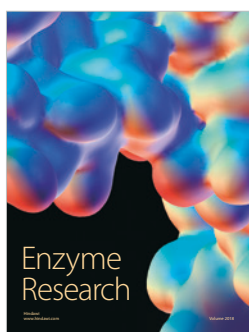
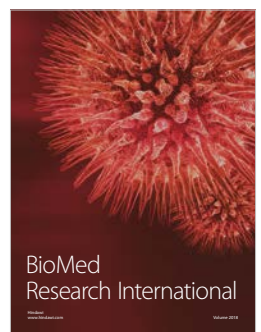
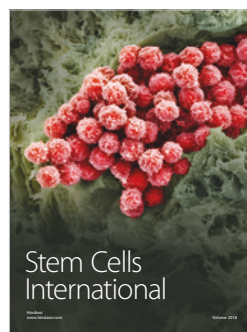
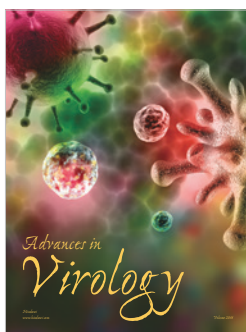
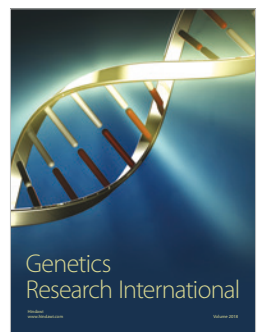
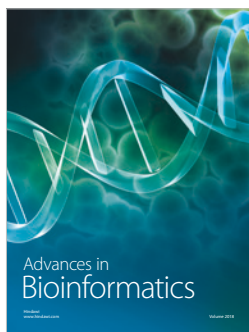
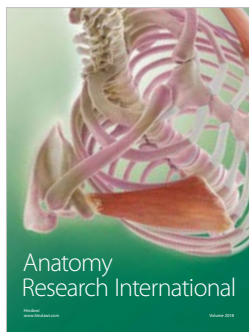
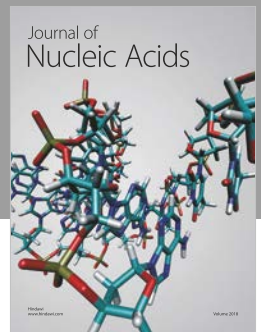
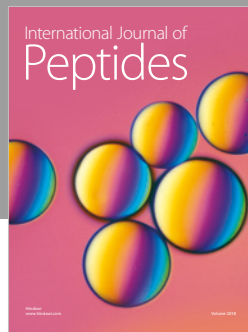
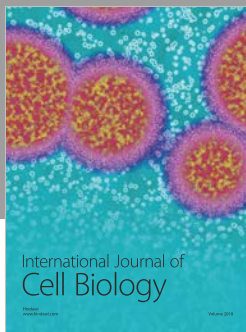
Supplementary Materials

Table S1: statistics of the small RNA-seq data. Table S2: statistics of the mapped reads. Table S3: target gene analysis for miR-147, miR-98-5p, and miR-10a. (*Supplementary Materials*)

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Supporting information:

Table S1 Statistics of the small RNA-seq data.

SampleName	TotalReads_Before	TotalBase_Before	TotalReads_After	TotalBase_After	ReadsFilter	BaseFilter%	GC%_Before	GC%_After
xiaochuan1-1	21005788	3150831317	5949406	139237445	0.2832269851	0.04419070	52	51
xiaochuan1-2	49999154	7499789222	13814335	332209556	0.2762913752	0.04429585	53	51
xiaochuan1-3	52447205	7866989228	14274545	343213067	0.2721697941	0.04362699	53	51
zhiliao3-1	48740485	7310991322	16547800	397513284	0.3395083169	0.05437200	55	50
zhiliao3-2	43724012	6558527069	14912751	355214848	0.3410654776	0.05416076	53	50
zhiliao3-3	47743142	7161391922	16646066	396053480	0.3486587871	0.05530398	55	50
	263659786	39548520080	82144903	1963441680	1.8609207340	0.2959503	321	303 0
xiaochuan1-1	21005788	3150831317	5949406	139237445	0.2832269851	0.04419070	52	51
xiaochuan1-2	49999154	7499789222	13814335	332209556	0.2762913752	0.04429585	53	51
xiaochuan1-3	52447205	7866989228	14274545	343213067	0.2721697940	0.04362699	53	51

3					1			
					0.05437200			
zhiliao3-1	48740485	7310991322	16547800	397513284	0.3395083169	55	50	
					0.05416076			
zhiliao3-2	43724012	6558527069	14912751	355214848	0.3410654776	53	50	
					0.05530398			
zhiliao3-3	47743142	7161391922	16646066	396053480	0.3486587871	55	50	
								#DIV/0
	43943297.67	6591420013	13690817.17	327240280	0.3101534560.04932505	53.5	50.5	!

Table S2 Statistics of the mapped reads.

#Item	xiaochuan1-1.miRNA	xiaochuan1-2.miRNA	xiaochuan1-3.miRNA	zhiliao3-1.miRNA	zhiliao3-2.miRNA	zhiliao3-3.miRNA
All	5949406	13814335	14274545	16547800	14912751	16646066
UnMapped	3530944	8592926	8935702	9847559	8773099	9817506
Mapped	2418462	5221409	5338843	6700241	6139652	6828560
MappedRate	0.407	0.378	0.374	0.405	0.412	0.41
UniqueMapped	2022768	4388023	4479734	5316953	4862081	5377685
UniqueMappedRate	0.34	0.318	0.314	0.321	0.326	0.323
RepeatMapped	395694	833386	859109	1383288	1277571	1450875
AllBase	139240287	332215819	343219844	397520703	355221681	396060770
UnMappedBase	87062153	219660031	228194796	252506021	222441146	248474344
MappedBase	52178134	112555788	115025048	145014682	132780535	147586426
UniqueMappedBase	43538937	94340535	96230413	114868897	104936553	116049333
RepeatMappedBase	8639197	18215253	18794635	30145785	27843982	31537093

Table S3 Target gene analysis for miR-147, miR-98-5p and miR-10a.

QueryID	SubjectID	OverlapInfo	Energy_Miranda	Score_Miranda	StartSubject_Miranda	EndSubject_Miranda	Energy_RNAhybrid	P-Value_RNAhybrid	StartSubject_RNAhybrid	EndSubject_RNAhybrid	AccessionID	Symbol	GeneType	Location	Strand	KeggID	Description
mmu-miR-147-3p	Pax5	Miranda_RNAhybrid	-23.77	157	2248	2269	-29.1	0.528892	2248	2270	NM_008782.2	Pax5	mRNA	chr4:44531506-44710440	-	mmu:18507	Paired box protein Pax-5
mmu-miR-147-3p	Kcnq4	Miranda_RNAhybrid	-25.16	157	847	867	-30.3	0.11836	850	868	NM_001081142.1	Kcnq4	mRNA	chr4:120696134-120747491	-	mmu:60613	Potassium voltage-gated channel subfamily KQT member 4
mmu-miR-147-3p	Kpnab6	Miranda_RNAhybrid	-22.47	155	88	109	-29.3	0.407137	79	110	NM_008468.4	Kpnab6	mRNA	chr4:129643985-129662500	-	mmu:16650	Importin subunit alpha-7
mmu-miR-147	Eif4g3	Miranda_RNAhybrid	-21.84	155	476	494	-25.4	0.426623	478	495	NM_172703.3	Eif4g3	mRNA	chr4:137993013-1382064	+	mmu:230861	Eukaryotic translation initiation

-3p		brid												47			factor 4 gamma 3
mmu -miR -147 -3p	Sh2 d5	Miran da_R NAhy brid	-25. 13	167	1481	1502	-27.3	0.380 039	1483	1503	NM_ 0010 9963 1.1	Sh2 d5	m RN A	chr4:138 250411- 1382609 68	+	mmu :230 863	SH2 domain-con taining protein 5
mmu -miR -147 -3p	Nduf a4	Miran da_R NAhy brid	-26. 74	165	40	60	-29.6	0.003 384	42	60	NM_ 0108 86.2	Nduf a4	m RN A	chr6:119 00373-1 1907446	-	mmu :179 92	Cytochrome c oxidase subunit NDUFA4
mmu -miR -147 -3p	Ppp 1r17	Miran da_R NAhy brid	-20. 27	159	1110	1131	-29.6	0.091 765	1002	1032	NM_ 0111 53.3	Ppp 1r17	m RN A	chr6:560 17515-5 6032688	+	mmu :190 51	Protein phosphatas e 1 regulatory subunit 17
mmu -miR -147 -3p	Fbxl 14	Miran da_R NAhy brid	-24	153	38	64	-26.9	0.633 167	40	65	NM_ 1339 40.3	Fbxl 14	m RN A	chr6:119 479668- 1194838 86	+	mmu :101 358	F-box/LRR-r epeat protein 14
mmu -miR -147 -3p	Hus 1	Miran da_R NAhy brid	-21. 61	163	70	91	-26.7	0.765 537	64	92	NM_ 0083 16.4	Hus 1	m RN A	chr11:89 93137-9 011191	-	mmu :155 74	Checkpoint protein HUS1
mmu -miR -147	lba5 7	Miran da_R NAhy	-21. 74	154	2651	2672	-27.5	0.547 648	2647	2673	NM_ 1831 10.1	lba5 7	m RN A	chr11:59 155369- 5916374	-	mmu :216 792	Putative transferase CAF17

-3p		brid												5			homolog, mitochondri al
mmu -miR -147 -3p	Zzef 1	Miran da_R NAhy brid	-25. 65	162	569	589	-30.8	0.139 223	570	590	NM_ 0010 4553 6.2	Zzef 1	m RN A	chr11:72 796226- 7292712 0	+	mmu :195 018	Zinc finger ZZ-type and EF-hand domain-con taining protein 1
mmu -miR -147 -3p	Enth d2	Miran da_R NAhy brid	-28. 81	173	289	309	-30	0.064 411	291	310	NM_ 1831 37.2	Enth d2	m RN A	chr11:12 0090522 -120098 695	-	mmu :787 77	AP-4 complex accessory subunit tepsin
mmu -miR -147 -3p	Tspy l4	Miran da_R NAhy brid	-22. 7	156	2251	2273	-28	0.430 284	2241	2273	NM_ 0302 03.2	Tspy l4	m RN A	chr10:34 297421- 3430132 0	+	mmu :724 80	Putative uncharacteri zed protein
mmu -miR -147 -3p	Ncln	Miran da_R NAhy brid	-23. 38	150	135	155	-26.2	0.370 782	138	156	NM_ 1340 09.3	Ncln	m RN A	chr10:81 486455- 8149669 1	-	mmu :103 425	Nicalin
mmu -miR -147 -3p	Atp2 b1	Miran da_R NAhy brid	-21. 69	152	91	112	-25.8	0.849 202	87	113	NM_ 0264 82.2	Atp2 b1	mi sc RN A	chr10:98 914359- 9902329 5	+	mmu :679 72	Plasma membrane calcium-tra nsporting

																	ATPase 1
mmu -miR -147 -3p	Cerk	Miran da_R NAhy brid	-22. 74	150	548	570	-28.1	0.398 344	551	570	NM_ 1454 75.4	Cerk	m RN A	chr15:86 139129- 8618633 6	-	mmu :223 753	Ceramide kinase
mmu -miR -147 -3p	Gxylt 1	Miran da_R NAhy brid	-20. 04	151	2629	2650	-26.8	0.856 991	2619	2651	NM_ 0010 3327 5.4	Gxylt 1	m RN A	chr15:93 239735- 9327533 6	-	mmu :223 827	Glucoside xylosyltransf erase 1
mmu -miR -147 -3p	Zdh hc2	Miran da_R NAhy brid	-22. 95	154	1538	1555	-28.6	0.280 816	1538	1555	NM_ 1783 95.3	Zdh hc2	m RN A	chr8:404 23002-4 0489592	+	mmu :705 46	Palmitoyltra nsferase ZDHHC2
mmu -miR -147 -3p	Sug p2	Miran da_R NAhy brid	-26. 61	155	45	68	-32	0.163 392	45	68	NM_ 1727 55.3	Sug p2	m RN A	chr8:702 34549-7 0263105	+	mmu :234 373	SURP and G-patch domain-con taining protein 2
mmu -miR -147 -3p	Foxl 1	Miran da_R NAhy brid	-29. 84	153	225	250	-33.9	0.022 396	225	251	NM_ 0080 24.2	Foxl 1	m RN A	chr8:121 127685- 1211306 44	+	mmu :142 41	Forkhead box protein L1
mmu -miR -147	Slc7 a5	Miran da_R NAhy	-23. 22	155	396	418	-31.4	0.080 776	393	418	NM_ 0114 04.3	Slc7 a5	m RN A	chr8:121 881146- 1219076	-	mmu :205 39	Putative uncharacteri zed protein

-3p		brid												86			
mmu -miR -147 -3p	Tnik	Miran da_R NAhy brid	-22. 89	151	2866	2884	-28.5	0.675 151	2867	2885	NM_ 0269 10.1	Tnik	m RN A	chr3:282 63214-2 8670585	+	mmu :665 113	Tnik protein
mmu -miR -147 -3p	Il21	Miran da_R NAhy brid	-24. 91	150	1373	1398	-27.9	0.440 249	1373	1398	NM_ 0217 82.3	Il21	m RN A	chr3:372 22759-3 7232636	-	mmu :605 05	Interleukin- 21
mmu -miR -147 -3p	Spry 1	Miran da_R NAhy brid	-23. 29	150	471	494	-27.9	0.177 262	465	495	NM_ 0118 96.2	Spry 1	m RN A	chr3:376 39947-3 7644599	+	mmu :240 63	Sprouty1
mmu -miR -147 -3p	Arhg ef11	Miran da_R NAhy brid	-23. 38	158	441	463	-28.9	0.097 504	445	463	NM_ 0010 0391 2.1	Arhg ef11	m RN A	chr3:876 17548-8 7738034	+	mmu :213 498	Protein Arhgef11
mmu -miR -147 -3p	Fam 19a3	Miran da_R NAhy brid	-22. 21	157	539	561	-31.7	0.139 952	532	562	NM_ 1832 24.3	Fam 19a3	m RN A	chr3:104 767405- 1047746 78	-	mmu :329 731	Protein FAM19A3
mmu -miR -147 -3p	Amp h	Miran da_R NAhy brid	-21. 01	154	2937	2959	-27.1	0.748 858	2953	2977	NM_ 1750 07.2	Amp h	m RN A	chr13:18 948351- 1915091 9	+	mmu :218 038	Amphiphysi n

mmu -miR -147 -3p	Auh	Miran da_R NAhy brid	-24. 72	166	246	268	-31.5	0.099 566	243	269	NM_ 0167 09.2	Auh	m RN A	chr13:52 907020- 5292970 5	-	mmu :119 92	Methylgluta conyl-CoA hydratase, mitochondri al
mmu -miR -147 -3p	2010 111l 01Ri k	Miran da_R NAhy brid	-25. 41	159	3813	3832	-29.7	0.357 533	3814	3832	NM_ 0280 79.2	2010 111l 01Ri k	m RN A	chr13:62 964893- 6330287 7	+	mmu :720 61	2010111l01 Rik protein
mmu -miR -147 -3p	Mre 11a	Miran da_R NAhy brid	-24. 64	162	2873	2893	-29.7	0.311 972	2873	2893	NM_ 0187 36.2	Mre 11a	m RN A	chr9:147 90642-1 4837125	+	mmu :175 35	Double-str and break repair protein MRE11A
mmu -miR -147 -3p	Al59 3442	Miran da_R NAhy brid	-23. 17	153	349	368	-28.6	0.557 957	2650	2668	NM_ 1789 06.5	Al59 3442	m RN A	chr9:526 73032-5 2679780	-	mmu :330 941	Uncharacteri zed protein C11orf87 homolog
mmu -miR -147 -3p	Hykk	Miran da_R NAhy brid	-20. 39	150	1242	1267	-26.5	0.764 182	663	682	NM_ 1773 51.4	Hykk	m RN A	chr9:549 17290-5 4949924	+	mmu :235 386	Hydroxylysi ne kinase
mmu -miR -147 -3p	Myo 1e	Miran da_R NAhy brid	-21. 22	162	848	869	-26.3	0.412 346	847	869	NM_ 1810 72.3	Myo 1e	m RN A	chr9:702 60427-7 0399766	+	mmu :716 02	Unconventi onal myosin-le

mmu -miR -147 -3p	Myo 5a	Miran da_R NAhy brid	-23. 31	167	2240	2261	-29.3	0.530 25	2239	2262	NM_ 0108 64.2	Myo 5a	m RN A	chr9:750 71015-7 5223688	+	mmu :179 18	Unconventi onal myosin-Va
mmu -miR -147 -3p	Ctds pl	Miran da_R NAhy brid	-23. 79	157	1877	1898	-30.5	0.233 688	1883	1899	NM_ 1337 10.3	Ctds pl	m RN A	chr9:118 929872- 1190441 19	+	mmu :692 74	CTD small phosphatas e-like protein
mmu -miR -147 -3p	Kdm 2a	Miran da_R NAhy brid	-23. 89	168	2168	2192	-30	0.239 515	2171	2192	NM_ 0010 0198 4.2	Kdm 2a	m RN A	chr19:43 16144-4 397077	-	mmu :225 876	Lysine-speci fic demethylas e 2A
mmu -miR -147 -3p	9130 011E 15Ri k	Miran da_R NAhy brid	-28. 92	162	1181	1201	-34.6	0.014 148	1180	1201	NM_ 1982 96.2	9130 011E 15Ri k	m RN A	chr19:45 817364- 4599857 0	-	mmu :716 17	UPF0668 protein C10orf76 homolog
mmu -miR -147 -3p	Nap a	Miran da_R NAhy brid	-20. 2	151	1081	1100	-25.8	0.532 808	1065	1100	NM_ 0258 98.3	Nap a	m RN A	chr7:160 98456-1 6113867	+	mmu :108 124	Putative uncharacteri zed protein
mmu -miR -147 -3p	Tme m14 5	Miran da_R NAhy brid	-28. 01	154	288	310	-29	0.091 361	290	311	NM_ 1833 11.2	Tme m14 5	m RN A	chr7:253 05995-2 5316196	+	mmu :330 485	Transmemb rane protein 145
mmu -miR	Ctu1	Miran da_R	-22. 81	164	323	344	-26.8	0.301 23	309	345	NM_ 1455	Ctu1	m RN	chr7:436 71976-4	+	mmu :233	Cytoplasmic tRNA

-147 -3p		NAhy brid									82.1		A	3678300		189	2-thiolation protein 1
mmu -miR -147 -3p	Akt1 s1	Miran da_R NAhy brid	-20. 14	160	139	161	-29.1	0.057 305	135	161	NM_ 0262 70.4	Akt1 s1	m RN A	chr7:448 50007-4 4855421	+	mmu :676 05	Proline-rich AKT1 substrate 1
mmu -miR -147 -3p	Spcs 2	Miran da_R NAhy brid	-21. 78	151	1938	1963	-27.5	0.430 499	1936	1963	NM_ 0256 68.3	Spcs 2	m RN A	chr7:998 37569-9 9858883	-	mmu :666 24	Signal peptidase complex subunit 2
mmu -miR -147 -3p	Stra db	Miran da_R NAhy brid	-20. 24	154	229	250	-25.6	0.286 19	217	251	NM_ 1731 55.1	Stra db	mi sc RN A	chr1:589 73527-5 8995126	+	mmu :227 154	STE20-relat ed kinase adapter protein beta
mmu -miR -147 -3p	Mga t5	Miran da_R NAhy brid	-21. 75	157	2819	2844	-27	0.852 337	2818	2844	NM_ 1451 28.3	Mga t5	m RN A	chr1:127 204973- 1274883 34	+	mmu :107 895	Mannoside acetylglucos aminyltransf erase 5
mmu -miR -147 -3p	Lam c1	Miran da_R NAhy brid	-24. 11	154	2307	2331	-28.3	0.384 614	2308	2331	NM_ 0106 83.2	Lam c1	m RN A	chr1:153 218922- 1533327 86	-	mmu :226 519	Laminin subunit gamma-1
mmu -miR -147 -3p	Tmp rss1 1f	Miran da_R NAhy brid	-25. 76	161	1268	1287	-31.3	0.117 673	1269	1288	NM_ 1787 30.3	Tmp rss1 1f	m RN A	chr5:865 21226-8 6632424	-	mmu :243 083	Transmemb rane protease serine 11F

mmu -miR -147 -3p	Fgf5	Miran da_R NAhy brid	-27. 49	152	801	820	-31.7	0.051 013	800	821	NM_ 0102 03.5	Fgf5	m RN A	chr5:982 54184-9 8277033	+	mmu :141 76	Fibroblast growth factor 5
mmu -miR -147 -3p	Lrrc8 b	Miran da_R NAhy brid	-23. 35	152	2960	2981	-29.1	0.432 036	2959	2982	NM_ 0010 3355 0.2	Lrrc8 b	m RN A	chr5:105 415775- 1054861 89	+	mmu :433 926	Volume-reg ulated anion channel subunit LRRC8B
mmu -miR -147 -3p	Rnft 2	Miran da_R NAhy brid	-21. 65	151	1231	1251	-27.2	0.581 524	1234	1251	NM_ 1729 98.3	Rnft 2	m RN A	chr5:118 190734- 1182451 11	-	mmu :269 695	RING finger and transmembr ane domain-con taining protein 2
mmu -miR -147 -3p	Ttyh 3	Miran da_R NAhy brid	-26. 94	154	80	104	-31.4	0.139 434	80	105	NM_ 1752 74.4	Ttyh 3	m RN A	chr5:140 620577- 1406490 31	-	mmu :783 39	Protein tweety homolog 3
mmu -miR -147 -3p	Pax9	Miran da_R NAhy brid	-21. 05	151	240	262	-31	0.159 477	230	263	NM_ 0110 41.2	Pax9	m RN A	chr12:56 694844- 5671282 4	+	mmu :185 11	Paired box protein Pax-9
mmu -miR	Prkc h	Miran da_R	-25. 43	155	842	866	-31.3	0.041 711	841	867	NM_ 0088	Prkc h	m RN	chr12:73 584796-	+	mmu :187	Protein kinase C eta

-147 -3p		NAhy brid									56.3		A	7377818 5		55	type
mmu -miR -147 -3p	Gph b5	Miran da_R NAhy brid	-22. 7	150	125	150	-27.9	0.189 245	125	151	NM_ 1756 44.3	Gph b5	m RN A	chr12:75 411720- 7541581 7	-	mmu :217 674	Glycoprotei n hormone beta 5
mmu -miR -147 -3p	Psen 1	Miran da_R NAhy brid	-24. 25	153	1260	1283	-31.3	0.219 413	1260	1283	NM_ 0089 43.2	Psen 1	m RN A	chr12:83 688145- 8373844 6	+	mmu :191 64	Presenilin-1
mmu -miR -147 -3p	Ddx 24	Miran da_R NAhy brid	-26. 01	155	98	121	-30	0.005 71	97	122	NM_ 0204 94.3	Ddx 24	m RN A	chr12:10 3407976 -103425 867	-	mmu :272 25	ATP-depen dent RNA helicase DDX24
mmu -miR -147 -3p	Zfp1 74	Miran da_R NAhy brid	-20. 58	151	2070	2088	-26.2	0.859 431	2315	2334	NM_ 0010 8121 7.1	Zfp1 74	m RN A	chr16:38 47190-3 872051	+	mmu :385 674	Protein Zfp174
mmu -miR -147 -3p	Ercc 4	Miran da_R NAhy brid	-22. 13	168	1964	1985	-27.6	0.631 792	1964	1986	NM_ 0157 69.2	Ercc 4	mi sc RN A	chr16:13 109689- 1314936 7	+	mmu :505 05	DNA repair endonucleas e XPF
mmu -miR -147 -3p	Nrip 1	Miran da_R NAhy brid	-20. 79	159	1084	1106	-26.2	0.838 916	1085	1107	NM_ 1734 40.2	Nrip 1	m RN A	chr16:76 287403- 7632480 8	-	mmu :268 903	Nuclear receptor-int eracting protein 1

mmu -miR -147 -3p	LOC 1081 6830 8	Miran da_R NAhy brid	-21. 75	160	1196	1217	-30.5	0.102 116	1527	1559							
mmu -miR -147 -3p	Rab 11fip 3	Miran da_R NAhy brid	-21. 71	159	1711	1733	-27.6	0.345 672	1709	1734	NM_ 1531 40.2	Rab 11fip 3	mi sc RN A	chr17:26 024378- 2606955 0	-	mmu :215 445	Rab11 family-inter acting protein 3
mmu -miR -147 -3p	Ankr d12	Miran da_R NAhy brid	-24. 28	158	412	435	-28.3	0.588 237	2827	2848	NM_ 0010 2557 2.1	Ankr d12	m RN A	chr17:65 965703- 6603155 1	-	mmu :106 585	Protein Ankrd12
mmu -miR -147 -3p	Nacc 2	Miran da_R NAhy brid	-21. 34	153	2231	2253	-26.9	0.795 461	2224	2253	NM_ 0264 95.3	Nacc 2	m RN A	chr2:260 55536-2 6092396	-	mmu :679 91	Nucleus accumbens- associated protein 2
mmu -miR -147 -3p	Lrrc8 a	Miran da_R NAhy brid	-26. 4	154	14	37	-32.9	0.035 024	11	38	NM_ 1777 25.4	Lrrc8 a	m RN A	chr2:302 37769-3 0263790	+	mmu :241 296	Volume-reg ulated anion channel subunit LRRC8A
mmu -miR -147 -3p	Rims 4	Miran da_R NAhy brid	-29. 66	163	977	1001	-34	0.071 921	978	1002	NM_ 1830 23.1	Rims 4	m RN A	chr2:163 863881- 1639186 83	-	mmu :241 770	Rims4 protein

mmu -miR -147 -3p	Cyp 24a1	Miran da_R NAhy brid	-20. 57	155	720	742	-28	0.236 355	720	743	NM_ 0099 96.3	Cyp 24a1	m RN A	chr2:170 482957- 1704971 45	-	mmu :130 81	Putative uncharacteri zed protein
mmu -miR -147 -3p	Tnfai p8	Miran da_R NAhy brid	-20. 07	151	1723	1742	-29.4	0.249 543	1976	1995	NM_ 1341 31.2	Tnfai p8	m RN A	chr18:49 979427- 5009322 9	+	mmu :106 869	Tumor necrosis factor alpha-induc ed protein 8
mmu -miR -147 -3p	LOC 1081 6839 5	Miran da_R NAhy brid	-26. 02	168	1057	1078	-28.6	0.194 703	1057	1079							
mmu -miR -98- 5p	Pap pa	Miran da_R NAhy brid	-22. 79	165	4255	4280	-26.8	0.792 268	4254	4281	NM_ 0213 62.1	Pap pa	m RN A	chr4:651 24174-6 5357509	+	mmu :184 91	Pappalysin- 1
mmu -miR -98- 5p	Acot 11	Miran da_R NAhy brid	-21. 14	166	3677	3701	-28.9	0.330 034	3676	3702	NM_ 0255 90.4	Acot 11	m RN A	chr4:106 744561- 1067998 31	-	mmu :329 910	Acyl-coenzy me A thioesterase 11
mmu -miR -98- 5p	Svop l	Miran da_R NAhy brid	-22. 02	162	866	888	-25.2	0.559 112	868	889	NM_ 1772 00.4	Svop l	m RN A	chr6:379 84752-3 8047012	-	mmu :320 590	Putative transporter SVOPL

mmu -miR -98- 5p	Tet3	Miran da_R NAhy brid	-20. 26	154	2689	2713	-27.5	0.680 474	3546	3570	NM_ 1831 38.2	Tet3	m RN A	chr6:833 62373-8 3457242	-	mmu :194 388	Methylcytosi ne dioxygenase TET3
mmu -miR -98- 5p	Gm5 878	Miran da_R NAhy brid	-20. 88	164	875	896	-27.6	0.531 513	400	430	NM_ 0010 3490 2.2	Gm5 878	m RN A	chr6:851 11416-8 5126094	-	mmu :545 861	Protein Gm5878
mmu -miR -98- 5p	Etnk 1	Miran da_R NAhy brid	-22. 63	155	3428	3451	-29	0.413 679	3429	3452	NM_ 0292 50.2	Etnk 1	m RN A	chr6:143 167230- 1432085 46	+	mmu :753 20	Putative uncharacteri zed protein
mmu -miR -98- 5p	Gm4 0814	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.127 641	99	122							
mmu -miR -98- 5p	Sow aha	Miran da_R NAhy brid	-21. 89	171	569	591	-25.6	0.515 767	565	592	NM_ 1831 73.2	Sow aha	m RN A	chr11:53 476578- 5348019 5	-	mmu :237 761	Ankrd43 protein
mmu -miR -98- 5p	Il13	Miran da_R NAhy brid	-21. 41	165	434	456	-26.9	0.122 299	421	457	NM_ 0083 55.3	Il13	m RN A	chr11:53 631323- 5363470 2	-	mmu :161 63	Interleukin- 13
mmu -miR 6	Acsl 6	Miran da_R	-20. 85	155	390	413	-25.1	0.871 055	380	414	NM_ 1448	Acsl 6	m RN	chr11:54 315297-	+	mmu :216	Long-chain acyl-CoA

-98-5p		NAhybrid									23.4		A	54364126		739	synthetase
mmu-miR-98-5p	Fnip1	Miranda_RNAhybrid	-24.37	176	1159	1180	-25.9	0.652079	1160	1181	NM_173753.4	Fnip1	mRNA	chr11:54438145-54516884	+	mmu:216742	Folliculin-interacting protein 1
mmu-miR-98-5p	Jmjd4	Miranda_RNAhybrid	-24.38	165	316	338	-27.1	0.495957	316	339	NM_178659.6	Jmjd4	mRNA	chr11:59450045-59458567	+	mmu:194952	JmjC domain-containing protein 4
mmu-miR-98-5p	LOC108167918	Miranda_RNAhybrid	-22.73	165	100	122	-28.4	0.136124	99	122							
mmu-miR-98-5p	Igf2bp1	Miranda_RNAhybrid	-25.12	172	4122	4143	-28.7	0.534799	4121	4144	NM_009951.4	Igf2bp1	mRNA	chr11:95957163-96005944	-	mmu:140486	Insulin-like growth factor 2 mRNA-binding protein 1
mmu-miR-98-5p	LOC108167806	Miranda_RNAhybrid	-22.73	165	100	122	-28.4	0.122471	99	122							
mmu-miR	LOC1081	Miranda_R	-22.73	165	157	179	-28.4	0.075538	156	179							

-98-5p	67809	NAhybrid															
mmu-miR-98-5p	Fam207a	Miranda_RNAhybrid	-21.35	150	1411	1434	-26.4	0.39134	1409	1435	NM_133998.3	Fam207a	mRNA	chr10:77486661-77516924	-	mmu:108707	Protein FAM207A
mmu-miR-98-5p	Cdc34	Miranda_RNAhybrid	-23.23	158	54	75	-25.9	0.065382	59	76	NM_177613.2	Cdc34	mRNA	chr10:79682203-79688398	+	mmu:216150	Ubiquitin-conjugating enzyme E2 R1
mmu-miR-98-5p	Fgd6	Miranda_RNAhybrid	-22.32	161	507	528	-25.2	0.854535	494	529	NM_053072.3	Fgd6	mRNA	chr10:94036001-94145339	+	mmu:13998	Fgd6 protein
mmu-miR-98-5p	Hmga2	Miranda_RNAhybrid	-21.83	164	8	28	-25.3	0.79013	8	29	NM_010441.2	Hmga2	mRNA	chr10:120361275-120476935	-	mmu:15364	High mobility group protein HMGI-C
mmu-miR-98-5p	Kcnv1	Miranda_RNAhybrid	-21.23	164	3031	3055	-25.3	0.997449	3029	3055	NM_026200.3	Kcnv1	mRNA	chr15:45096086-45116490	-	mmu:67498	Potassium voltage-gated channel subfamily V member 1
mmu-miR	Pced1b	Miranda_R	-22.63	165	226	247	-26.5	0.040552	225	247	NM_1722	Pced1b	mRNA	chr15:97247412-	+	mmu:239	PC-esterase domain-con

-98-5p		NAhybrid									93.4		A	97385693		647	taining protein 1B
mmu-miR-98-5p	Dhh	Miranda_RNAhybrid	-20.03	170	2059	2079	-25.1	0.796653	2058	2079	NM_007857.4	Dhh	mRNA	chr15:98893027-98895957	-	mmu:13363	Desert hedgehog protein
mmu-miR-98-5p	Letmd1	Miranda_RNAhybrid	-21.81	164	1064	1086	-25.6	0.418249	1063	1086	NM_134093.2	Letmd1	mRNA	chr15:100469018-100479164	+	mmu:68614	LETM1 domain-containing protein 1
mmu-miR-98-5p	Cbx5	Miranda_RNAhybrid	-20.44	159	6659	6681	-28.2	0.700872	1036	1067	NM_007626.3	Cbx5	mRNA	chr15:103191678-103215362	-	mmu:12419	Chromobox protein homolog 5
mmu-miR-98-5p	Hsh2d	Miranda_RNAhybrid	-20.39	167	138	161	-25.4	0.028911	137	161	NM_197944.1	Hsh2d	mRNA	chr8:72189668-72200958	+	mmu:209488	Hematopoietic SH2 domain-containing protein
mmu-miR-98-5p	Nkd1	Miranda_RNAhybrid	-21.62	158	359	382	-27	0.481183	363	382	NM_027280.3	Nkd1	mRNA	chr8:88521344-88594887	+	mmu:93960	Protein naked cuticle homolog 1
mmu-miR-98-5p	Nod2	Miranda_RNAhybrid	-20.27	169	1362	1385	-25.2	0.536581	1361	1385	NM_145857.2	Nod2	mRNA	chr8:88647314-88684464	+	mmu:257632	CARD15 short isoform

5p		brid															
mmu -miR -98- 5p	Elmo 3	Miran da_R NAhy brid	-22. 82	170	204	225	-30.3	0.022 372	200	225	NM_ 1727 60.3	Elmo 3	m RN A	chr8:105 305601- 1053106 23	+	mmu :234 683	Elmo3 protein
mmu -miR -98- 5p	Clcn 5	Miran da_R NAhy brid	-24	171	4145	4167	-25.5	0.939 365	4145	4168	NM_ 0166 91.4	Clcn 5	m RN A	chrX:715 5160-72 76896	-	mmu :127 28	Chloride channel protein
mmu -miR -98- 5p	Gucy 2f	Miran da_R NAhy brid	-21. 92	157	3453	3477	-25.7	0.937 759	3451	3477	NM_ 0010 0757 6.2	Gucy 2f	m RN A	chrX:142 083290- 1421972 76	-	mmu :245 650	Retinal guanylyl cyclase 2
mmu -miR -98- 5p	Klf8	Miran da_R NAhy brid	-23. 61	176	1479	1500	-26.5	0.788 871	1478	1500	NM_ 1737 80.4	Klf8	m RN A	chrX:153 237422- 1533978 86	+	mmu :245 671	Krueppel-lik e factor 8
mmu -miR -98- 5p	Gja8	Miran da_R NAhy brid	-21. 23	167	3346	3368	-27.3	0.697 721	142	167	NM_ 0081 23.3	Gja8	m RN A	chr3:969 13566-9 6926051	-	mmu :146 16	Gap junction alpha-8 protein
mmu -miR -98- 5p	Cyb 561 d1	Miran da_R NAhy brid	-21. 93	168	1205	1226	-26.2	0.701 613	1210	1227	NM_ 0280 61.1	Cyb 561 d1	m RN A	chr3:108 195771- 1082021 26	-	mmu :720 23	Cytochrome b561 domain-con taining

																	protein 1
mmu -miR -98- 5p	LOC 1081 6806 7	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.036 702	99	122							
mmu -miR -98- 5p	Gm4 1035	Miran da_R NAhy brid	-22. 73	165	157	179	-28.4	0.129 486	156	179							
mmu -miR -98- 5p	Vst m5	Miran da_R NAhy brid	-20. 65	164	395	415	-25.1	0.568 259	387	416	NM_ 0269 55.2	Vst m5	mi sc RN A	chr9:152 38923-1 5259421	+	mmu :691 37	V-set and transmembr ane domain-con taining protein 5
mmu -miR -98- 5p	Rnf2 14	Miran da_R NAhy brid	-21. 44	162	5388	5411	-25.8	0.963 327	5388	5411	NM_ 1787 09.4	Rnf2 14	m RN A	chr9:458 56769-4 5906435	-	mmu :235 315	RING finger protein 214
mmu -miR -98- 5p	Rdx	Miran da_R NAhy brid	-20. 6	167	962	983	-25.6	0.636 68	951	984	NM_ 0090 41.3	Rdx	m RN A	chr9:520 47150-5 2088738	+	mmu :196 84	Radixin
mmu -miR	1700 017B	Miran da_R	-21. 81	159	263	286	-25.3	0.301 013	267	287	NM_ 0288	1700 017B	m RN	chr9:572 53117-5	-	mmu :742	Uncharacteri zed protein

-98-5p	05Rik	NAhybrid									20.2	05Rik	A	7262410		11	C15orf39 homolog
mmu-miR-98-5p	Tmod2	Miranda_RNAhybrid	-23.37	163	5792	5816	-27	0.874412	5791	5817	NM_016711.3	Tmod2	mRNA	chr9:75565621-75610330	-	mmu:50876	Tropomodulin-2
mmu-miR-98-5p	Prr23a3	Miranda_RNAhybrid	-21.67	170	235	257	-25.4	0.279247	240	257							
mmu-miR-98-5p	Tusc2	Miranda_RNAhybrid	-21.85	159	473	497	-26.3	0.28811	472	498	NM_019742.4	Tusc2	mRNA	chr9:107563255-107566108	+	mmu:80385	Tumor suppressor candidate 2
mmu-miR-98-5p	Vps13a	Miranda_RNAhybrid	-21.03	166	880	900	-25.7	0.732931	870	901	NM_173028.4	Vps13a	mRNA	chr19:16615366-16780933	-	mmu:271564	Putative uncharacterized protein Vps13a 5' variant II
mmu-miR-98-5p	Tmem2	Miranda_RNAhybrid	-20.63	162	1545	1566	-26.7	0.4109	1542	1567	NM_031997.4	Tmem2	mRNA	chr19:21778340-21858360	+	mmu:83921	Transmembrane protein 2
mmu-miR-98-5p	Kcnk6	Miranda_RNAhybrid	-21.54	159	2885	2904	-25.2	0.818737	2888	2905	NM_00103352	Kcnk6	mRNA	chr7:29221928-29232522	-	mmu:52150	Kcnk6 protein

5p		brid									5.3						
mmu -miR -98- 5p	LOC 1081 6741 5	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.087 87	99	122							
mmu -miR -98- 5p	Sec1	Miran da_R NAhy brid	-20. 17	159	496	518	-25.2	0.281 737	419	438	NM_ 0199 34.2	Sec1	m RN A	chr7:456 77686-4 5684247	-	mmu :565 46	Galactoside 2-alpha-L-f ucosyltransf erase 3
mmu -miR -98- 5p	E030 018B 13Ri k	Miran da_R NAhy brid	-22. 9	160	916	934	-29.3	0.054 191	915	935	NM_ 0012 5631 1.1	E030 018B 13Ri k	m RN A	chr7:639 19164-6 3921029	+	mmu :381 994	Protein E030018B13 Rik
mmu -miR -98- 5p	LOC 1081 6743 4	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.136 124	99	122							
mmu -miR -98- 5p	Clpb	Miran da_R NAhy brid	-22. 19	165	908	929	-26.5	0.594 319	912	930	NM_ 0091 91.3	Clpb	m RN A	chr7:101 721982- 1017907 21	+	mmu :204 80	Caseinolytic peptidase B protein homolog
mmu -miR -98- 5p	Eef2 k	Miran da_R NAhy brid	-22. 66	169	623	645	-25.3	0.866 593	624	645	NM_ 0079 08.4	Eef2 k	m RN A	chr7:120 842829- 1209072 17	+	mmu :136 31	Eukaryotic elongation factor 2 kinase

mmu -miR -98- 5p	Mrpl 15	Miran da_R NAhy brid	-20. 02	153	1090	1111	-26	0.714 289	2452	2478	NM_ 0253 00.4	Mrpl 15	mi sc RN A	chr1:477 3198-47 85726	-	mmu :273 95	Mitochondri al ribosomal protein L15, isoform CRA_a
mmu -miR -98- 5p	Fam 126b	Miran da_R NAhy brid	-20. 99	151	3947	3969	-25.6	0.953 668	6215	6241	NM_ 1725 13.3	Fam 126b	m RN A	chr1:585 22806-5 8586154	-	mmu :213 056	Protein FAM126B
mmu -miR -98- 5p	Ccdc 93	Miran da_R NAhy brid	-22. 26	160	3028	3049	-25.2	0.941 303	3028	3049	NM_ 0299 55.3	Ccdc 93	m RN A	chr1:121 431067- 1215064 60	+	mmu :708 29	Coiled-coil domain-con taining protein 93
mmu -miR -98- 5p	LOC 1081 6772 5	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.129 609	99	122							
mmu -miR -98- 5p	Fasl	Miran da_R NAhy brid	-22. 97	167	350	371	-26.6	0.178 048	350	372	NM_ 0101 77.4	Fasl	m RN A	chr1:161 780691- 1617884 95	-	mmu :141 03	Fas ligand
mmu -miR -98- 5p	LOC 1052 4403 4	Miran da_R NAhy brid	-22. 73	165	157	179	-28.4	0.134 649	156	179							

mmu -miR -98- 5p	Gm3 9743	Miran da_R NAhy brid	-22. 73	165	289	311	-28.4	0.118 531	288	311							
mmu -miR -98- 5p	Gm2 1759	Miran da_R NAhy brid	-26. 29	172	77	96	-27.8	0.071 636	77	97							
mmu -miR -98- 5p	Gm4 2102	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.119 27	99	122							
mmu -miR -98- 5p	Fras 1	Miran da_R NAhy brid	-22. 7	165	145	169	-26.3	0.626 215	147	170	NM_ 1754 73.3	Fras 1	m RN A	chr5:963 73819-9 6784733	+	mmu :231 470	Extracellular matrix protein FRAS1
mmu -miR -98- 5p	LOC 1081 6800 3	Miran da_R NAhy brid	-22. 73	165	100	122	-28.4	0.124 318	99	122							
mmu -miR -98- 5p	Grin 2a	Miran da_R NAhy brid	-21. 08	155	2938	2963	-25.1	0.928 136	2938	2963	NM_ 0081 70.2	Grin 2a	m RN A	chr16:96 21275-9 995132	-	mmu :148 11	Glutamate receptor ionotropic, NMDA 2A
mmu -miR	Rabl 3	Miran da_R	-21. 34	156	95	116	-25	0.507 652	94	117	NM_ 0262	Rabl 3	m RN	chr16:37 539894-	+	mmu :676	Rab-like protein 3

-98-5p		NAhybrid									97.1		A	37572385		57	
mmu-miR-98-5p	Gm41476	Miranda_RNAhybrid	-22.73	165	100	122	-28.4	0.066718	99	122							
mmu-miR-98-5p	4930488N24Rik	Miranda_RNAhybrid	-23.17	158	328	352	-25.1	0.301515	330	353	XR_397312.1	4930488N24Rik	mRNA	chr17:14101817-14107866	-	mmu:75011	RIKEN cDNA4930488N24 gene
mmu-miR-98-5p	Wdr27	Miranda_RNAhybrid	-23.42	156	88	107	-26.9	0.28074	87	107	NM_175173.3	Wdr27	mRNA	chr17:14784829-14943151	-	mmu:71682	WD repeat-containing protein 27
mmu-miR-98-5p	Crb3	Miranda_RNAhybrid	-23.95	171	152	174	-29.4	0.203187	151	174	NM_177638.4	Crb3	mRNA	chr17:57061627-57065920	+	mmu:224912	Protein crumbs homolog 3
mmu-miR-98-5p	Gm37416	Miranda_RNAhybrid	-22.73	165	363	385	-28.4	0.161786	362	385							
mmu-miR-98-5p	Tbc1d13	Miranda_RNAhybrid	-21.83	155	1186	1208	-25	0.735875	1186	1208	NM_146252.2	Tbc1d13	mRNA	chr2:30142536-30152012	+	mmu:70296	TBC1 domain family member 13

mmu -miR -98- 5p	Pbx3	Miran da_R NAhy brid	-22. 34	165	858	879	-25	0.549 198	860	879	NM_ 0167 68.2	Pbx3	m RN A	chr2:341 71457-3 4371692	-	mmu :185 16	Pre-B-cell leukemia transcription factor 3
mmu -miR -98- 5p	Katn bl1	Miran da_R NAhy brid	-21. 23	161	1053	1072	-25.4	0.582 799	1053	1072	NM_ 0242 54.3	Katn bl1	m RN A	chr2:112 379211- 1124142 37	+	mmu :724 25	Putative uncharacteri zed protein
mmu -miR -98- 5p	Trp5 3bp 1	Miran da_R NAhy brid	-20. 34	168	3080	3101	-25.6	0.807 987	3074	3101	NM_ 0137 35.4	Trp5 3bp 1	m RN A	chr2:121 194835- 1212520 27	-	mmu :272 23	Tumor suppressor p53-binding protein 1
mmu -miR -98- 5p	Grpe l2	Miran da_R NAhy brid	-22. 35	172	2436	2457	-27	0.558 59	2436	2457	NM_ 0212 96.2	Grpe l2	mi sc RN A	chr18:61 712424- 6172636 0	-	mmu :177 14	GrpE protein homolog 2, mitochondri al
mmu -miR -98- 5p	Ptpn 2	Miran da_R NAhy brid	-23. 97	165	3401	3422	-25.3	0.972 319	3405	3423	NM_ 0089 77.3	Ptpn 2	m RN A	chr18:67 665501- 6772475 8	-	mmu :192 55	Tyrosine-pr otein phosphatas e non-recept or type 2
mmu -miR -98-	LOC 1081 6837	Miran da_R NAhy	-22. 73	165	100	122	-28.4	0.148 258	99	122							

5p	6	brid															
mmu -miR -10a -5p	Ankr d6	Miran da_R NAhy brid	-22. 41	153	1029	1055	-25.2	0.825 686	1031	1056	NM_ 0804 71.3	Ankr d6	m RN A	chr4:328 04027-3 2864810	-	mmu :140 577	Ankyrin repeat domain-con taining protein 6
mmu -miR -10a -5p	Tmo d1	Miran da_R NAhy brid	-23. 72	154	1455	1478	-25.3	0.729 402	1456	1479	NM_ 0218 83.2	Tmo d1	m RN A	chr4:460 38940-4 6104015	+	mmu :219 16	Tropomodul in-1
mmu -miR -10a -5p	Nr4a 3	Miran da_R NAhy brid	-25. 38	161	1046	1068	-28.7	0.441 534	1036	1069	NM_ 0157 43.2	Nr4a 3	m RN A	chr4:480 44889-4 8086447	+	mmu :181 24	Nr4a3 protein
mmu -miR -10a -5p	Cer1	Miran da_R NAhy brid	-20. 21	160	208	232	-25.1	0.489 133	207	232	NM_ 0098 87.2	Cer1	m RN A	chr4:828 81751-8 2885151	-	mmu :126 22	Cerberus 1 homolog (Xenopus laevis)
mmu -miR -10a -5p	Faf1	Miran da_R NAhy brid	-23. 84	167	1962	1987	-27.1	0.528 391	1964	1987	NM_ 0079 83.2	Faf1	m RN A	chr4:109 676627- 1099639 60	+	mmu :140 84	FAS-associa ted factor 1
mmu -miR -10a	Slc5 a9	Miran da_R NAhy	-22. 91	163	1690	1714	-26.2	0.688 54	1690	1715	NM_ 1455 51.4	Slc5 a9	mi sc RN	chr4:111 885528- 1119027	-	mmu :230 612	Sodium/glu cose cotransport

-5p		brid										A	83			er 4	
mmu -miR -10a -5p	D83 0031 N03 Rik	Miran da_R NAhy brid	-23. 06	164	2357	2383	-28	0.618 101	2357	2383	NM_ 0011 6791 8.1	D83 0031 N03 Rik	m RN A	chr4:123 403601- 1234119 11	-	mmu :442 834	Uncharacteri zed protein KIAA0754
mmu -miR -10a -5p	Gm1 3083	Miran da_R NAhy brid	-26. 26	165	656	678	-28.5	0.141 652	659	679	NM_ 0011 2632 4.1	Gm1 3083	m RN A	chr4:143 615060- 1436187 38	+	mmu :279 185	Protein Gm13083
mmu -miR -10a -5p	Agtr ap	Miran da_R NAhy brid	-22. 61	152	2808	2831	-26.5	0.805 866	2800	2832	NM_ 0096 42.4	Agtr ap	m RN A	chr4:148 077061- 1480880 64	-	mmu :116 10	Type-1 angiotensin II receptor-as sociated protein
mmu -miR -10a -5p	Vwa 1	Miran da_R NAhy brid	-21. 77	168	1062	1084	-26.2	0.623 187	1059	1084	NM_ 1477 76.4	Vwa 1	m RN A	chr4:155 769300- 1557727 98	-	mmu :246 228	von Willebrand factor A domain-con taining protein 1
mmu -miR -10a -5p	Nxp h1	Miran da_R NAhy brid	-24. 96	160	602	626	-26.2	0.996 515	603	627	NM_ 0087 51.5	Nxp h1	m RN A	chr6:894 7788-92 59863	+	mmu :182 31	Neurexophil in

mmu -miR -10a -5p	Irf5	Miran da_R NAhy brid	-25. 03	156	75	99	-26.3	0.181 801	75	99	NM_ 0120 57.4	Irf5	m RN A	chr6:295 29243-2 9537320	+	mmu :270 56	Interferon regulatory factor 5 bone marrow variant
mmu -miR -10a -5p	Svop l	Miran da_R NAhy brid	-20. 92	163	201	222	-29.5	0.169 62	196	222	NM_ 1772 00.4	Svop l	m RN A	chr6:379 84752-3 8047012	-	mmu :320 590	Putative transporter SVOPL
mmu -miR -10a -5p	Adck 2	Miran da_R NAhy brid	-20. 73	159	824	845	-28.7	0.184 261	805	846	NM_ 1788 73.3	Adck 2	m RN A	chr6:395 73876-3 9588769	+	mmu :578 69	Uncharacteri zed aarF domain-con taining protein kinase 2
mmu -miR -10a -5p	Arhg ap25	Miran da_R NAhy brid	-21. 74	156	75	97	-25.8	0.565 15	67	98	NM_ 1754 76.4	Arhg ap25	mi sc RN A	chr6:874 58545-8 7496327	-	mmu :232 201	Rho GTPase activating protein 25
mmu -miR -10a -5p	Prtr3	Miran da_R NAhy brid	-24. 33	154	209	233	-25.2	0.367 342	199	234	NM_ 1724 87.4	Prtr3	m RN A	chr6:113 493638- 1135018 43	-	mmu :210 673	Proline-rich transmembr ane protein 3, isoform CRA_b

mmu -miR -10a -5p	Vgll 4	Miran da_R NAhy brid	-22. 94	153	1407	1429	-26.7	0.473 74	1405	1430	NM_ 1776 83.2	Vgll 4	m RN A	chr6:114 860621- 1149010 36	-	mmu :232 334	Transcriptio n cofactor vestigial-like protein 4
mmu -miR -10a -5p	Syn2	Miran da_R NAhy brid	-21. 74	160	1888	1913	-27.1	0.557 856	1885	1914	NM_ 0136 81.3	Syn2	m RN A	chr6:115 134902- 1152765 63	+	mmu :209 65	Synapsin-2
mmu -miR -10a -5p	Tmc c1	Miran da_R NAhy brid	-25. 05	162	1079	1101	-28.4	0.527 493	1087	1102	NM_ 1774 12.1	Tmc c1	m RN A	chr6:116 018611- 1161933 73	-	mmu :330 401	Transmemb rane and coiled-coil domains protein 1
mmu -miR -10a -5p	Crac r2a	Miran da_R NAhy brid	-22. 59	153	893	917	-26.6	0.878 015	894	918	NM_ 0010 3346 4.3	Crac r2a	mi sc RN A	chr6:127 594740- 1276676 64	+	mmu :381 812	EF-hand calcium-bin ding domain-con taining protein 4B
mmu -miR -10a -5p	Ascc 2	Miran da_R NAhy brid	-22. 73	155	1133	1158	-25.4	0.867 102	1138	1159	NM_ 0292 91.1	Ascc 2	m RN A	chr11:46 37698-4 685699	+	mmu :754 52	Putative uncharacteri zed protein
mmu -miR -10a	Lcp2	Miran da_R NAhy	-26. 23	174	467	489	-27.5	0.370 749	468	490	NM_ 0106 96.3	Lcp2	m RN A	chr11:34 047201- 3409228	+	mmu :168 22	Lymphocyte cytosolic protein 2

-5p		brid												0			
mmu -miR -10a -5p	Cyfi p2	Miran da_R NAhy brid	-21. 08	150	992	1011	-25	0.894 121	997	1012	NM_ 1337 69.3	Cyfi p2	m RN A	chr11:46 193855- 4631236 4	-	mmu :768 84	Cytoplasmic FMR1-intera cting protein 2
mmu -miR -10a -5p	Shro om1	Miran da_R NAhy brid	-22. 27	163	359	380	-29.8	0.047 559	351	380	NM_ 0279 17.3	Shro om1	m RN A	chr11:53 457205- 5346776 6	+	mmu :717 74	Shroom family member 1, isoform CRA_a
mmu -miR -10a -5p	Slc2 a4	Miran da_R NAhy brid	-21. 9	150	958	978	-25.1	0.589 607	952	978	NM_ 0092 04.2	Slc2 a4	m RN A	chr11:69 942286- 6994819 0	-	mmu :205 28	Solute carrier family 2, facilitated glucose transporter member 4
mmu -miR -10a -5p	Ccdc 92b	Miran da_R NAhy brid	-21. 93	157	1723	1745	-27.3	0.633 664	1721	1746							
mmu -miR -10a -5p	Mett l16	Miran da_R NAhy brid	-21. 22	153	3532	3558	-25.5	0.997 327	3530	3558	NM_ 0261 97.3	Mett l16	m RN A	chr11:74 770837- 7482582 3	+	mmu :674 93	Methyltransf erase-like protein 16

mmu -miR -10a -5p	Mmd	Miranda_RNAhybrid	-22.03	152	1196	1220	-29.2	0.225849	1193	1220	NM_026178.2	Mmd	mRNA	chr11:90249297-90251618	+	mmu:67468	Putative uncharacterized protein
mmu -miR -10a -5p	Smarca1	Miranda_RNAhybrid	-21.88	151	439	459	-25.5	0.497762	438	460	NM_020618.4	Smarca1	mRNA	chr11:99209047-99231339	-	mmu:57376	Smarca1 variant 3
mmu -miR -10a -5p	Zfp385c	Miranda_RNAhybrid	-25.55	156	526	545	-27.9	0.494522	525	546	NM_177790.4	Zfp385c	mRNA	chr11:100627543-100692450	-	mmu:278304	Zinc finger protein 385C
mmu -miR -10a -5p	Mapt	Miranda_RNAhybrid	-21.53	153	631	653	-25.2	0.95993	628	654	NM_010838.4	Mapt	mRNA	chr11:104231327-104332090	+	mmu:17762	Microtubule-associated protein tau
mmu -miR -10a -5p	Limd2	Miranda_RNAhybrid	-25.07	151	843	873	-28.9	0.333068	842	873	NM_172397.3	Limd2	mRNA	chr11:106158035-106159965	-	mmu:67803	LIM domain-containing protein 2
mmu -miR -10a -5p	Prkca	Miranda_RNAhybrid	-24.17	155	2587	2608	-26.9	0.911773	2586	2608	NM_011101.3	Prkca	mRNA	chr11:107933387-108343888	-	mmu:18750	Protein kinase C alpha type

mmu -miR -10a -5p	Map 2k6	Miran da_R NAhy brid	-28. 04	168	31	55	-29.7	0.338 874	33	56	NM_ 0119 43.2	Map 2k6	m RN A	chr11:11 0399103 -110516 201	+	mmu :263 99	Dual-specifi city mitogen-act ivated protein kinase kinase 6
mmu -miR -10a -5p	Nplo c4	Miran da_R NAhy brid	-20. 07	162	1268	1291	-25.2	0.893 754	1267	1291	NM_ 1994 69.2	Nplo c4	m RN A	chr11:12 0379798 -120437 700	-	mmu :217 365	Nuclear protein localization protein 4 homolog
mmu -miR -10a -5p	Slc2 a12	Miran da_R NAhy brid	-23. 29	158	25	47	-27	0.466 585	23	47	NM_ 1789 34.4	Slc2 a12	m RN A	chr10:22 612730- 2270318 3	+	mmu :353 169	Solute carrier family 2 (Facilitated glucose transporter), member 12
mmu -miR -10a -5p	C2c d4c	Miran da_R NAhy brid	-24. 47	157	3971	3993	-26.7	0.895 855	3970	3994	NM_ 1986 14.3	C2c d4c	m RN A	chr10:79 606854- 7961401 8	-	mmu :237 397	C2 calcium-dep endent domain-con taining protein 4C

mmu -miR -10a -5p	Gna 11	Miran da_R NAhy brid	-20. 28	150	544	566	-25.2	0.822 181	1315	1341	NM_ 0103 01.3	Gna 11	m RN A	chr10:81 528732- 8154504 6	-	mmu :146 72	Guanine nucleotide- binding protein subunit alpha-11
mmu -miR -10a -5p	Zfp4 33	Miran da_R NAhy brid	-22. 15	165	1306	1325	-25.2	0.860 484	1305	1325	NM_ 0012 4306 7.1	Zfp4 33	m RN A	chr10:81 704192- 8172197 6	+	mmu :736 10	Protein Zfp433
mmu -miR -10a -5p	Gm3 2687	Miran da_R NAhy brid	-22. 15	165	1306	1325	-25.2	0.858 336	1305	1325							
mmu -miR -10a -5p	Gm3 3378	Miran da_R NAhy brid	-22. 15	165	1304	1323	-25.2	0.904 552	1303	1323							
mmu -miR -10a -5p	Vezt	Miran da_R NAhy brid	-24. 21	159	3428	3450	-25.8	0.998 613	3420	3451	NM_ 1725 38.4	Vezt	m RN A	chr10:93 961522- 9403579 9	-	mmu :215 008	Vezatin
mmu -miR -10a -5p	Ankr d33 b	Miran da_R NAhy brid	-24. 97	153	995	1019	-26.2	0.950 2	996	1020	NM_ 0274 96.3	Ankr d33 b	m RN A	chr15:31 291479- 3136775 9	-	mmu :674 34	Ankyrin repeat domain-con taining

																	protein 33B
mmu -miR -10a -5p	Kcnv 1	Miran da_R NAhy brid	-23. 85	164	12575	12597	-28.2	0.939 758	12571	12598	NM_ 0262 00.3	Kcnv 1	m RN A	chr15:45 096086- 4511649 0	-	mmu :674 98	Potassium voltage-gat ed channel subfamily V member 1
mmu -miR -10a -5p	Trap pc9	Miran da_R NAhy brid	-22. 89	154	1083	1105	-25.1	0.751 305	1066	1106	NM_ 1806 62.2	Trap pc9	m RN A	chr15:72 589620- 7305581 2	-	mmu :765 10	Trafficking protein particle complex subunit 9
mmu -miR -10a -5p	1810 041L 15Ri k	Miran da_R NAhy brid	-26. 22	155	173	200	-29.2	0.557 78	173	201	NM_ 0011 6314 5.1	1810 041L 15Ri k	m RN A	chr15:84 379203- 8444666 6	-	mmu :723 01	Protein 1810041L15 Rik
mmu -miR -10a -5p	Ttll8	Miran da_R NAhy brid	-24. 22	161	276	297	-27.1	0.421 372	276	298	NM_ 1728 18.3	Ttll8	m RN A	chr15:88 917458- 8895564 2	-	mmu :239 591	Protein monoglycyl ase TTLL8
mmu -miR -10a -5p	Slc3 8a2	Miran da_R NAhy brid	-22. 09	155	903	925	-26.7	0.699 58	904	925	NM_ 1751 21.3	Slc3 8a2	m RN A	chr15:96 687392- 9669972 4	-	mmu :677 60	Putative uncharacteri zed protein
mmu -miR	Insr	Miran da_R	-24. 4	166	772	794	-26	0.937 264	773	795	NM_ 0105	Insr	m RN	chr8:315 0922-32	-	mmu :163	Insulin receptor

-10a -5p		NAhy brid									68.2		A	79649		37	isoform B
mmu -miR -10a -5p	Ppp 1r3b	Miran da_R NAhy brid	-23. 47	155	674	695	-26.4	0.804 762	666	696	NM_ 1777 41.3	Ppp 1r3b	m RN A	chr8:353 75667-3 5388139	+	mmu :244 416	Protein phosphatas e 1 regulatory subunit 3B
mmu -miR -10a -5p	Nfix	Miran da_R NAhy brid	-22. 22	157	1803	1829	-25.9	0.912 115	1793	1829	NM_ 0109 06.3	Nfix	m RN A	chr8:847 04717-8 4780806	-	mmu :180 32	Nuclear factor 1 X-type
mmu -miR -10a -5p	Nfat 5	Miran da_R NAhy brid	-22. 45	161	1178	1200	-26.7	0.968 588	1176	1200	NM_ 1339 57.3	Nfat 5	m RN A	chr8:107 331084- 1073744 74	+	mmu :544 46	Nuclear factor of-activated T-cells 5
mmu -miR -10a -5p	Disc 1	Miran da_R NAhy brid	-22. 66	156	156	178	-27	0.748 996	152	179	NM_ 1748 54.2	Disc 1	m RN A	chr8:125 054195- 1252611 51	+	mmu :244 667	Disrupted in schizophreni a 1 homolog
mmu -miR -10a -5p	Myc s	Miran da_R NAhy brid	-24. 43	162	243	268	-28.3	0.127 982	244	269	NM_ 0108 50.2	Myc s	m RN A	chrX:546 6904-54 69265	-	mmu :178 70	Protein S-Myc
mmu -miR -10a	Atp7 a	Miran da_R NAhy	-24	165	755	777	-26.5	0.817 899	759	777	NM_ 0097 26.5	Atp7 a	m RN A	chrX:106 027224- 1061281	+	mmu :119 77	Copper-tran sporting ATPase 1

-5p		brid												60			
mmu -miR -10a -5p	Ndub5	Miranda_RNAhybrid	-29.19	174	149	171	-32.8	0.004626	148	172	NM_025316.2	Ndub5	mirNA	chr3:32737107-32751236	+	mmu:66046	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 5, mitochondrial
mmu -miR -10a -5p	E130311K13Rik	Miranda_RNAhybrid	-26.14	163	210	232	-30.7	0.029636	202	233	NM_177856.4	E130311K13Rik	mirNA	chr3:63914696-63929385	-	mmu:329659	Protein C3orf33 homolog
mmu -miR -10a -5p	Tmigd3	Miranda_RNAhybrid	-21.57	151	696	716	-25	0.586638	700	716							
mmu -miR -10a -5p	Adora3	Miranda_RNAhybrid	-21.57	151	696	716	-25	0.586638	700	716	NM_027025.4	Adora3	mirNA	chr3:105904421-105908928	+	mmu:11542	Adenosine receptor A3
mmu -miR -10a	Arsj	Miranda_RNAhy	-22.23	155	325	350	-26.2	0.371378	327	351	NM_173451.3	Arsj	mirNA	chr3:126363852-1264403	+	mmu:271970	Arylsulfatase J

-5p		brid												74			
mmu -miR -10a -5p	Tnni 3k	Miran da_R NAhy brid	-25. 47	171	135	157	-29.7	0.025 451	133	158	NM_ 1770 66.5	Tnni 3k	m RN A	chr3:154 792779- 1550554 02	-	mmu :435 766	Serine/threo nine-protei n kinase TNNI3K
mmu -miR -10a -5p	Neg r1	Miran da_R NAhy brid	-23. 49	161	5674	5696	-27	0.893 983	5674	5697	NM_ 1772 74.4	Neg r1	m RN A	chr3:156 561799- 1572284 95	+	mmu :320 840	Neuronal growth regulator 1
mmu -miR -10a -5p	E2f3	Miran da_R NAhy brid	-23. 45	157	3212	3231	-25.8	0.883 688	3004	3037	NM_ 0100 93.3	E2f3	m RN A	chr13:29 906575- 2998439 1	-	mmu :135 57	E2F transcription factor 3
mmu -miR -10a -5p	Ssr1	Miran da_R NAhy brid	-26. 36	150	5481	5503	-26.5	0.976 044	5481	5504	NM_ 0259 65.3	Ssr1	m RN A	chr13:37 971401- 3799419 0	-	mmu :107 513	Putative uncharacteri zed protein
mmu -miR -10a -5p	Jarid 2	Miran da_R NAhy brid	-21. 78	162	1163	1186	-25.5	0.704 618	1163	1186	NM_ 0218 78.3	Jarid 2	m RN A	chr13:44 729535- 4492163 8	+	mmu :164 68	Protein Jumonji
mmu -miR -10a -5p	Id4	Miran da_R NAhy brid	-21. 57	151	989	1010	-26	0.449 168	989	1010	NM_ 0311 66.2	Id4	m RN A	chr13:48 261427- 4826403 6	+	mmu :159 04	DNA-bindin g protein inhibitor ID-4

mmu -miR -10a -5p	2010 111l 01Ri k	Miran da_R NAhy brid	-21. 42	151	1375	1395	-26.4	0.865 974	1376	1396	NM_ 0280 79.2	2010 111l 01Ri k	m RN A	chr13:62 964893- 6330287 7	+	mmu :720 61	2010111l01 Rik protein
mmu -miR -10a -5p	Zfp3 67	Miran da_R NAhy brid	-24. 77	160	209	236	-27.1	0.561 023	210	237	NM_ 1754 94.4	Zfp3 67	m RN A	chr13:64 133025- 6415238 2	-	mmu :238 673	Zinc finger protein 367
mmu -miR -10a -5p	Zfp6 5	Miran da_R NAhy brid	-23. 4	157	1559	1580	-26.1	0.782 461	1561	1580	NM_ 1456 22.2	Zfp6 5	m RN A	chr13:67 705306- 6772917 3	-	mmu :235 907	Protein Zfp65
mmu -miR -10a -5p	Slc6 a19	Miran da_R NAhy brid	-21. 56	158	1117	1138	-26.6	0.568 953	1114	1139	NM_ 0288 78.3	Slc6 a19	m RN A	chr13:73 679745- 7369290 5	-	mmu :743 38	Sodium-de pendent neutral amino acid transporter B(0)AT1
mmu -miR -10a -5p	Cdk 7	Miran da_R NAhy brid	-23. 98	176	1901	1923	-26.9	0.921 474	1901	1923	NM_ 0098 74.3	Cdk 7	m RN A	chr13:10 0697024 -100730 942	-	mmu :125 72	Cyclin-depe ndent kinase 7 (Homolog of Xenopus MO15 cdk-activati ng kinase),

																	isoform CRA_a
mmu -miR -10a -5p	Zfp2 6	Miran da_R NAhy brid	-23. 92	164	5000	5022	-28.4	0.821 215	4999	5023	NM_ 0117 53.3	Zfp2 6	m RN A	chr9:204 33181-2 0460169	-	mmu :226 88	Zinc finger protein 26
mmu -miR -10a -5p	Eep d1	Miran da_R NAhy brid	-23. 35	157	41	63	-26	0.192 268	34	64	NM_ 0261 89.3	Eep d1	m RN A	chr9:254 81524-2 5489939	+	mmu :674 84	Endonucleas e/exonuclea se/phosphat ase family domain-con taining protein 1
mmu -miR -10a -5p	Kcnj 5	Miran da_R NAhy brid	-22. 38	153	539	560	-27.9	0.530 774	1889	1913	NM_ 0106 05.4	Kcnj 5	m RN A	chr9:323 14706-3 2344380	-	mmu :165 21	Potassium inwardly-rec tifying channel subfamily J member 5
mmu -miR -10a -5p	Tmp rss5	Miran da_R NAhy brid	-27. 34	161	478	500	-30	0.036 427	482	501	NM_ 0307 09.2	Tmp rss5	m RN A	chr9:490 80719-4 9117591	+	mmu :808 93	Transmemb rane protease, serine 5 (Spinesin)

mmu -miR -10a -5p	Prtg	Miran da_R NAhy brid	-21. 67	151	1785	1807	-26.3	0.923 548	1781	1808	NM_ 1754 85.4	Prtg	m RN A	chr9:728 07274-7 2917307	+	mmu :235 472	Protogenin
mmu -miR -10a -5p	Tfdp 2	Miran da_R NAhy brid	-22. 26	155	4878	4900	-25.2	0.988 859	4877	4901	NM_ 1786 67.4	Tfdp 2	m RN A	chr9:961 96246-9 6323646	+	mmu :211 586	Transcriptio n factor Dp-2
mmu -miR -10a -5p	Twf2	Miran da_R NAhy brid	-27. 24	157	23	44	-27.2	0.076 524	25	44	NM_ 0118 76.3	Twf2	m RN A	chr9:106 203108- 1062153 87	+	mmu :239 99	Twinfilin-2
mmu -miR -10a -5p	Tmp pe	Miran da_R NAhy brid	-20. 79	151	3579	3599	-28.4	0.679 376	243	271	NM_ 0012 0000 2.1	Tmp pe	m RN A	chr9:114 401095- 1144112 01	+	mmu :100 5047 15	Protein Tmpe
mmu -miR -10a -5p	Rbm s3	Miran da_R NAhy brid	-21. 86	163	3789	3812	-26.5	0.937 595	3791	3812	NM_ 1786 60.4	Rbm s3	m RN A	chr9:116 572750- 1180403 55	-	mmu :207 181	Rbms3 protein
mmu -miR -10a -5p	Ctds pl	Miran da_R NAhy brid	-21. 91	153	94	116	-27.2	0.710 993	2657	2689	NM_ 1337 10.3	Ctds pl	m RN A	chr9:118 929872- 1190441 19	+	mmu :692 74	CTD small phosphatas e-like protein
mmu -miR	Atl3	Miran da_R	-23. 35	154	1794	1816	-25.3	0.971 8	1795	1816	NM_ 1460	Atl3	m RN	chr19:74 94040-7	+	mmu :109	Atlantin-3

-10a -5p		NAhy brid									91.4		A	538609		168	
mmu -miR -10a -5p	Syt7	Miran da_R NAhy brid	-25. 78	158	2246	2269	-27.5	0.775 259	2246	2270	NM_ 1730 68.2	Syt7	m RN A	chr19:10 389090- 1045318 1	+	mmu :545 25	Synaptotag min-7
mmu -miR -10a -5p	Prpf 19	Miran da_R NAhy brid	-21. 65	150	2073	2093	-26.8	0.845 199	2070	2094	NM_ 1341 29.4	Prpf 19	m RN A	chr19:10 898645- 1090955 9	+	mmu :280 00	Pre-mRNA- processing factor 19
mmu -miR -10a -5p	Abli m1	Miran da_R NAhy brid	-32. 3	179	3682	3707	-34	0.079 7	3682	3707	NM_ 1786 88.3	Abli m1	m RN A	chr19:57 033264- 5721603 2	-	mmu :226 251	Ablim1 protein
mmu -miR -10a -5p	Mya dm	Miran da_R NAhy brid	-23. 77	158	1365	1386	-27.9	0.334 279	1361	1387	NM_ 0169 69.2	Mya dm	m RN A	chr7:329 2953-32 99355	+	mmu :509 18	Myeloid-ass ociated differentiati on marker
mmu -miR -10a -5p	Arhg ap35	Miran da_R NAhy brid	-26. 33	164	2238	2261	-26.7	0.754 374	2239	2262	NM_ 1727 39.4	Arhg ap35	m RN A	chr7:164 94473-1 6614993	-	mmu :232 906	Rho GTPase-acti vating protein 35
mmu -miR -10a -5p	Smg 9	Miran da_R NAhy brid	-24. 67	156	166	192	-26	0.141 912	167	193	NM_ 0280 47.2	Smg 9	m RN A	chr7:243 99926-2 4422777	+	mmu :719 97	Protein SMG9

mmu -miR -10a -5p	Zfp2 7	Miran da_R NAhy brid	-22. 09	166	564	586	-26.4	0.260 467	553	587	NM_ 0117 54.2	Zfp2 7	m RN A	chr7:298 93337-2 9906532	-	mmu :226 89	Mszf76
mmu -miR -10a -5p	Tyro bp	Miran da_R NAhy brid	-20. 2	172	91	113	-27.1	0.020 515	90	114	NM_ 0116 62.2	Tyro bp	m RN A	chr7:304 13788-3 0417582	+	mmu :221 77	TYRO protein tyrosine kinase-bindi ng protein
mmu -miR -10a -5p	Rhp n2	Miran da_R NAhy brid	-21. 61	166	844	865	-28.9	0.167 764	835	866	NM_ 0278 97.4	Rhp n2	m RN A	chr7:353 34237-3 5392287	+	mmu :524 28	Rhpn2 protein
mmu -miR -10a -5p	Chrn a7	Miran da_R NAhy brid	-25. 07	156	234	260	-26.8	0.143 23	236	261	NM_ 0073 90.3	Chrn a7	m RN A	chr7:630 98692-6 3212526	-	mmu :114 41	Neuronal acetylcholin e receptor subunit alpha-7
mmu -miR -10a -5p	Chd 2	Miran da_R NAhy brid	-20. 12	154	418	439	-29.8	0.298 041	1472	1495	NM_ 0010 8134 5.2	Chd 2	m RN A	chr7:734 26652-7 3541746	-	mmu :244 059	Chromodo main-helica se-DNA-bin ding protein 2
mmu -miR -10a	Crtc 3	Miran da_R NAhy	-20. 99	153	2251	2273	-25.2	0.926 077	1699	1721	NM_ 1738 63.2	Crtc 3	m RN A	chr7:805 86627-8 0688942	-	mmu :704 61	CREB-regul ated transcription

-5p		brid															coactivator 3
mmu -miR -10a -5p	Olfr6 58	Miran da_R NAhy brid	-21. 88	157	1135	1157	-25.3	0.696 116	1132	1158	NM_ 1470 49.4	Olfr6 58	m RN A	chr7:104 642880- 1046473 05	-	mmu :259 051	Olfactory receptor
mmu -miR -10a -5p	lqck	Miran da_R NAhy brid	-21. 23	153	454	474	-26.2	0.824 508	453	474	NM_ 0010 8144 6.1	lqck	m RN A	chr7:118 855753- 1189155 74	+	mmu :434 232	Protein lqck
mmu -miR -10a -5p	Ano 1	Miran da_R NAhy brid	-20. 54	159	240	262	-27.2	0.377 973	237	263	NM_ 1786 42.5	Ano 1	m RN A	chr7:144 588549- 1447520 45	-	mmu :101 772	Anoctamin- 1
mmu -miR -10a -5p	Rpl3 1	Miran da_R NAhy brid	-30. 23	177	75	97	-33.2	0.007 008	80	98	NM_ 0532 57.3	Rpl3 1	m RN A	chr1:393 67851-3 9371911	+	mmu :114 641	MCG126194 , isoform CRA_b
mmu -miR -10a -5p	Mars 2	Miran da_R NAhy brid	-27. 93	168	980	1003	-27.2	0.275 374	981	1004	NM_ 1754 39.3	Mars 2	m RN A	chr1:552 37177-5 5240058	+	mmu :212 679	Methionine- tRNA synthetase 2 (Mitochondr ial)
mmu -miR -10a	Aox 2	Miran da_R NAhy	-21. 37	153	299	321	-26.9	0.190 926	291	322	NM_ 0010 0841	Aox 2	m RN A	chr1:582 78326-5 8379264	+	mmu :213 043	Aldehyde oxidase 2

-5p		brid									9.2						
mmu -miR -10a -5p	Tns1	Miran da_R NAhy brid	-21. 47	153	669	689	-25.3	0.965 733	664	690	NM_ 1771 69.2	Tns1	m RN A	chr1:739 10232-7 4098332	-	mmu :219 61	Protein Tns1
mmu -miR -10a -5p	Cnot 9	Miran da_R NAhy brid	-21. 73	156	1111	1133	-25.1	0.823 993	1099	1133							
mmu -miR -10a -5p	Hda c4	Miran da_R NAhy brid	-25. 32	168	2303	2329	-29.1	0.525 638	2305	2330	NM_ 2072 25.1	Hda c4	m RN A	chr1:919 28779-9 2180231	-	mmu :208 727	Histone deacetylase 4
mmu -miR -10a -5p	Tnfrs f11a	Miran da_R NAhy brid	-22. 07	168	1560	1583	-26	0.843 111	1557	1583	NM_ 0093 99.3	Tnfrs f11a	m RN A	chr1:105 780747- 1058457 98	+	mmu :219 34	Tumor necrosis factor receptor superfamily member 11A
mmu -miR -10a -5p	Ptpn 4	Miran da_R NAhy brid	-21. 08	158	6627	6649	-25.4	0.994 37	6624	6650	NM_ 0199 33.2	Ptpn 4	m RN A	chr1:119 652467- 1198374 57	-	mmu :192 58	Tyrosine-pr otein phosphatas e non-recept

																	or type 4
mmu -miR -10a -5p	Pou 2f1	Miran da_R NAhy brid	-21. 11	153	25	47	-26.4	0.991 216	22	48	NM_ 1989 34.3	Pou 2f1	m RN A	chr1:165 865150- 1659530 71	-	mmu :189 86	POU domain, class 2, transcription factor 1
mmu -miR -10a -5p	Hnrn pu	Miran da_R NAhy brid	-20. 6	161	2916	2937	-26.7	0.961 819	7717	7741	NM_ 0168 05.2	Hnrn pu	m RN A	chr1:178 321108- 1783378 10	-	mmu :518 10	Protein Gm28062
mmu -miR -10a -5p	Grm 3	Miran da_R NAhy brid	-22. 2	157	262	285	-27.3	0.113 12	258	285	NM_ 1818 50.2	Grm 3	m RN A	chr5:948 5236-97 25352	-	mmu :108 069	Grm3 protein
mmu -miR -10a -5p	Htr5 a	Miran da_R NAhy brid	-22. 92	166	1447	1469	-26.9	0.802 53	1443	1469	NM_ 0083 14.2	Htr5 a	m RN A	chr5:278 41702-2 7853143	+	mmu :155 63	5-hydroxytr yptamine receptor 5A
mmu -miR -10a -5p	Nat8 l	Miran da_R NAhy brid	-20. 78	160	143	166	-25.6	0.962 235	143	166	NM_ 0010 0198 5.3	Nat8 l	m RN A	chr5:339 95984-3 4005916	+	mmu :269 642	N-acetylasp artate synthetase
mmu -miR	Golg a3	Miran da_R	-21. 56	155	1187	1214	-27	0.732 723	1187	1214	NM_ 0081	Golg a3	m RN	chr5:110 176658-	+	mmu :269	Golgin subfamily A

-10a -5p		NAhy brid									46.3		A	1102264 70		682	member 3
mmu -miR -10a -5p	Ddx 51	Miran da_R NAhy brid	-21. 63	168	1988	2013	-25.7	0.858 299	1989	2014	NM_ 0271 56.3	Ddx 51	m RN A	chr5:110 653451- 1106604 96	+	mmu :696 63	ATP-depen dent RNA helicase DDX51
mmu -miR -10a -5p	Slc8 b1	Miran da_R NAhy brid	-20. 86	161	336	358	-25.7	0.443 352	324	359	NM_ 1332 21.2	Slc8 b1	m RN A	chr5:120 511168- 1205278 14	+	mmu :170 756	Sodium/pot assium/calci um exchanger 6, mitochondri al
mmu -miR -10a -5p	Pvrig	Miran da_R NAhy brid	-22. 8	163	1457	1482	-27.2	0.815 313	1462	1483	Pvrig -ps	Pvrig -ps	m RN A	chr5:138 341770- 1383598 00	+		poliovirus receptor related immunoglo bulin domain containing, pseudogene
mmu -miR -10a -5p	Katn al1	Miran da_R NAhy brid	-25. 36	168	863	886	-26.9	0.841 1	852	887	NM_ 1535 72.2	Katn al1	m RN A	chr5:148 871584- 1489287 37	-	mmu :231 912	Katanin p60 ATPase-con taining subunit A-like 1

mmu -miR -10a -5p	Myt 1l	Miran da_R NAhy brid	-23. 34	165	1617	1639	-27.3	0.604 913	1617	1639	NM_ 0086 66.3	Myt 1l	m RN A	chr12:29 533358- 2992321 6	+	mmu :179 33	Myelin transcription factor 1-like protein
mmu -miR -10a -5p	lft43	Miran da_R NAhy brid	-23. 28	151	1000	1022	-26.9	0.792 936	1001	1023	NM_ 0296 01.3	lft43	m RN A	chr12:86 082561- 8616245 9	+	mmu :764 11	Intraflagellar transport protein 43 homolog
mmu -miR -10a -5p	Gpat ch2l	Miran da_R NAhy brid	-22. 07	154	2079	2103	-25.9	0.966 385	2078	2103	NM_ 0274 05.2	Gpat ch2l	m RN A	chr12:86 241838- 8629179 3	+	mmu :703 73	Putative uncharacteri zed protein
mmu -miR -10a -5p	Bdkr b1	Miran da_R NAhy brid	-24. 13	152	177	198	-30.8	0.005 117	174	199	NM_ 0075 39.2	Bdkr b1	m RN A	chr12:10 5604091 -105605 428	+	mmu :120 61	MCG1159
mmu -miR -10a -5p	Rcor 1	Miran da_R NAhy brid	-21. 66	151	2002	2024	-27.4	0.730 884	1998	2025	NM_ 1980 23.2	Rcor 1	m RN A	chr12:11 1039798 -111113 389	+	mmu :217 864	REST corepressor 1
mmu -miR -10a -5p	Zfp3 86	Miran da_R NAhy brid	-23. 99	155	2330	2352	-26.2	0.768 888	2329	2353	NM_ 0195 65.4	Zfp3 86	m RN A	chr12:11 6047724 -116063 209	+	mmu :562 20	Zinc finger protein 386 (Kruppel-lik e) isoform a
mmu -miR	Hic2	Miran da_R	-22. 44	156	322	347	-25.6	0.948 006	322	347	NM_ 1789	Hic2	m RN	chr16:17 233587-	+	mmu :581	Hypermethy lated in

-10a -5p		NAhy brid									22.3		A	1726343 0		80	cancer 2 protein
mmu -miR -10a -5p	Crkl	Miran da_R NAhy brid	-22. 69	160	2841	2864	-26.6	0.813 342	2839	2865	NM_ 0077 64.5	Crkl	m RN A	chr16:17 451985- 1748744 0	+	mmu :129 29	V-crk sarcoma virus CT10 oncogene homolog (Avian)-like
mmu -miR -10a -5p	Senp 5	Miran da_R NAhy brid	-22. 45	150	2005	2026	-25.3	0.949 225	2005	2026	NM_ 1771 03.4	Senp 5	m RN A	chr16:31 961906- 3201074 4	-	mmu :320 213	Sentrin-spe cific protease 5
mmu -miR -10a -5p	Hsp bap 1	Miran da_R NAhy brid	-21. 53	168	881	903	-25.8	0.862 532	883	903	NM_ 1751 11.3	Hsp bap 1	mi sc RN A	chr16:35 769655- 3582650 4	+	mmu :666 67	HSPB1-asso ciated protein 1
mmu -miR -10a -5p	Gtf2 e1	Miran da_R NAhy brid	-23. 09	155	1200	1224	-25.8	0.632 564	1202	1225	NM_ 0288 12.3	Gtf2 e1	m RN A	chr16:37 509796- 3753976 9	-	mmu :741 97	Putative uncharacteri zed protein
mmu -miR -10a -5p	Itsn1	Miran da_R NAhy brid	-25. 79	155	607	630	-28.7	0.802 109	605	631	NM_ 0105 87.2	Itsn1	m RN A	chr16:91 803274- 9192059 1	+	mmu :164 43	MAA-13 protein
mmu -miR	Atp8 a2	Miran da_R	-21. 28	168	1486	1510	-25.4	0.736 295	1487	1511	NM_ 0158	Atp8 a2	m RN	chr14:59 647741-	-	mmu :507	Phospholipi d-transporti

-10a -5p		NAhy brid									03.2		A	6008683 4		69	ng ATPase IB
mmu -miR -10a -5p	Jmjd 8	Miran da_R NAhy brid	-23. 42	159	384	405	-26.4	0.438 114	381	405	NM_ 0281 01.4	Jmjd 8	m RN A	chr17:25 829043- 2583184 3	+	mmu :721 06	JmjC domain-con taining protein 8
mmu -miR -10a -5p	D17 Wsu 92e	Miran da_R NAhy brid	-23. 87	159	1234	1259	-26.1	0.788 438	1236	1259	NM_ 0012 7151 1.1	D17 Wsu 92e	m RN A	chr17:27 751232- 2782054 2	-	mmu :224 647	Uncharacteri zed protein C6orf106 homolog
mmu -miR -10a -5p	Zfp8 71	Miran da_R NAhy brid	-23. 21	154	8698	8720	-25.9	0.992 993	8702	8720	NM_ 1724 58.3	Zfp8 71	m RN A	chr17:32 765496- 3278828 7	-	mmu :208 292	Protein Zfp871
mmu -miR -10a -5p	Zfp7 99	Miran da_R NAhy brid	-23. 43	155	2478	2506	-26.7	0.820 563	2478	2507	NM_ 1773 59.5	Zfp7 99	m RN A	chr17:32 815449- 3283026 1	-	mmu :240 064	Protein Zfp799
mmu -miR -10a -5p	Zfp8 70	Miran da_R NAhy brid	-24. 45	150	2085	2105	-27.5	0.662 876	2085	2105	NM_ 2072 45.2	Zfp8 70	m RN A	chr17:32 879221- 3289143 3	-	mmu :240 066	Protein Zfp870
mmu -miR -10a -5p	C4b	Miran da_R NAhy brid	-23. 72	168	55	77	-27	0.008 255	46	78	NM_ 0097 80.2	C4b	m RN A	chr17:34 728380- 3474389 7	-	mmu :122 68	Complemen t component 4B (Childo

																	blood group)
mmu-miR-10a-5p	C4a	Miranda_RNAhybrid	-22.5	164	55	77	-26.5	0.010902	48	78	NM_011413.2	C4a	mRNA	chr17:34809092-34823454	-	mmu:625018	C4a protein
mmu-miR-10a-5p	Nfya	Miranda_RNAhybrid	-20.23	152	2215	2237	-25.8	0.788622	1247	1275	NM_010913.2	Nfya	mRNA	chr17:48386885-48409901	-	mmu:18044	Nuclear transcription factor Y subunit alpha
mmu-miR-10a-5p	Lbh	Miranda_RNAhybrid	-30.14	156	1249	1274	-32.5	0.084434	1248	1275	NM_029999.4	Lbh	mRNA	chr17:72918305-72941946	+	mmu:77889	Protein LBH
mmu-miR-10a-5p	Kcng3	Miranda_RNAhybrid	-22.51	167	3790	3812	-26	0.986205	3791	3812	NM_153512.1	Kcng3	mRNA	chr17:83579949-83631993	-	mmu:225030	Potassium voltage-gated channel subfamily G member 3
mmu-miR-10a-5p	Msr b2	Miranda_RNAhybrid	-24.74	155	191	219	-25.9	0.260059	192	220	NM_029619.2	Msr b2	mRNA	chr2:19371411-19380814	+	mmu:76467	Methionine-R-sulfoxide reductase B2, mitochondrial

mmu -miR -10a -5p	Gad 2	Miran da_R NAhy brid	-23. 92	168	3150	3173	-27.1	0.732 273	3150	3173	NM_ 0080 78.2	Gad 2	m RN A	chr2:226 21422-2 2656274	+	mmu :144 17	Glutamate decarboxyla se 2
mmu -miR -10a -5p	Zer1	Miran da_R NAhy brid	-25. 18	151	58	84	-30.2	0.118 5	52	85	NM_ 1786 94.4	Zer1	m RN A	chr2:301 06732-3 0125258	-	mmu :227 693	Zyg-11 homolog B (C. elegans)-lik e
mmu -miR -10a -5p	Smt nl1	Miran da_R NAhy brid	-21. 92	156	792	817	-26.1	0.377 746	790	818	NM_ 0242 30.2	Smt nl1	m RN A	chr2:848 11176-8 4822652	-	mmu :686 78	Smoothelin- like protein 1
mmu -miR -10a -5p	Map kbp1	Miran da_R NAhy brid	-21. 64	154	364	386	-25.2	0.823 562	362	387	NM_ 0119 41.3	Map kbp1	m RN A	chr2:119 972390- 1200274 03	+	mmu :263 90	Mitogen-act ivated protein kinase-bindi ng protein 1
mmu -miR -10a -5p	LOC 1081 6873 4	Miran da_R NAhy brid	-24. 9	163	371	393	-26.9	0.103 756	373	394							
mmu -miR -10a -5p	Dbn dd2	Miran da_R NAhy brid	-28. 63	151	1734	1762	-30	0.274 627	1733	1762	NM_ 0267 97.2	Dbn dd2	m RN A	chr2:164 467153- 1644933 19	+	mmu :528 40	Dysbindin domain-con taining protein 2

mmu -miR -10a -5p	Zma t2	Miran da_R NAhy brid	-20. 71	155	1134	1161	-27.5	0.380 433	1133	1161	NM_ 0255 94.3	Zma t2	m RN A	chr18:36 793923- 3679966 0	+	mmu :664 92	Zinc finger matrin-type protein 2
mmu -miR -10a -5p	Slc2 5a2	Miran da_R NAhy brid	-27. 92	172	210	232	-32.3	0.003 294	209	233	NM_ 0011 5927 5.1	Slc2 5a2	m RN A	chr18:37 637378- 3763872 3	-	mmu :838 85	Mutant ornithine transporter 2
mmu -miR -10a -5p	Spry 4	Miran da_R NAhy brid	-25. 29	165	247	267	-27.6	0.657 235	247	267	NM_ 0118 98.2	Spry 4	m RN A	chr18:38 586265- 3860126 8	-	mmu :240 66	Protein sprouty homolog 4
mmu -miR -10a -5p	Tica m2	Miran da_R NAhy brid	-20. 92	160	1388	1412	-25.2	0.826 137	1389	1412	NM_ 1733 94.3	Tica m2	m RN A	chr18:46 558231- 4657453 3	-	mmu :225 471	TIR domain-con taining adapter molecule 2
mmu -miR -10a -5p	Ppar gc1b	Miran da_R NAhy brid	-23. 75	154	4066	4088	-26.9	0.942 964	4041	4089	NM_ 1332 49.2	Ppar gc1b	m RN A	chr18:61 291445- 6140146 2	-	mmu :170 826	Peroxisome proliferative activated receptor, gamma, coactivator 1 beta
mmu -miR	Rnf1 65	Miran da_R	-22. 57	160	3689	3712	-25	0.994 871	2893	2916	NM_ 0011	Rnf1 65	m RN	chr18:77 456110-	-	mmu :225	RING finger protein 165

-10a		NAhy									6450		A	7756513		743	
-5p		brid									4.1			6			