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Differentially deregulated microRNAs contribute to ultraviolet radiation-induced photocarcinogenesis through immunomodulation: An-analysis of microRNAs expression profiling

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Running title: miRNAs expression profiling in UVB induced skin tumors

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Abstract

MicroRNAs (miRNAs) are short non-coding RNA molecules (18-25 nucleotides) that regulate several fundamental biological processes. Emerging evidence has shown more than 1500 miRNAs functions in the cell cycle, proliferation, apoptosis, oxidative stress, immune response, DNA damage, and epigenetics alterations. miRNAs are bidirectionally in nature and act as a tumor suppressor and as an oncogene through crosstalk between tumor cells and immune cells. Although the roles of miRNAs in several cancers are well studied, little is known about ultraviolet B (UVB) radiation-induced skin cancer. Here, we performed a comprehensive screening of 1281 miRNAs in tumor tissues and compared their expression with normal skin. Our results demonstrate that the expression levels of 587 miRNAs were altered in tumor tissues compared to their expression in normal skin. The expression of 337 miRNAs was upregulated from 1.5-12 folds, while the expression of 250 miRNAs was downregulated up to 1.5-10 folds in tumors. Further, intraperitoneal injection of a mimic of down-regulated miR-15b (30nM) and an inhibitor of upregulated miR-133a (20nM) protect UVB-induced suppression of contact hypersensitivity (CHS) response. In conclusion, we identified a network of altered miRNAs in tumors that can serve as prognostic biomarkers and therapeutic targets to manage photocarcinogenesis effectively.

Keywords: Meta-analysis, microRNAs, skin tumor, photocarcinogenesis

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1. Introduction

Skin, an important protective shield of the entire body, acts as a barrier to block the penetration of ultraviolet radiation (UV) and contact with foreign particles. Solar UV radiation is one of the critical risk factors that initiate carcinogenic events and promote skin cancer by inducing inflammatory responses, oxidative stress, immunosuppression, DNA damage, and gene mutations, all of which have been implicated in a variety of skin diseases, including the development of skin cancers [1-4]. UV radiation-induced inflammation plays a crucial role in all three stages of tumor development (initiation, promotion, and progression). Chronic exposure to UV radiation is a well-recognized etiological factor for all types of skin cancers, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma, and which accounts for the approximately 1.3 million new cases of skin cancer each year in the USA [5]. The incidence of skin cancer is nearly equal to other malignancies in all other organs [6], thus representing a significant public health problem. Skin cancer development and progression is a complex process accompanied by multiple molecular changes at cellular levels. Despite intensive investigations, the precise mechanisms by which UVB radiation causes skin cancer remains unclear. Therefore, to uncover the molecular mechanisms involved in photocarcinogenesis, more novel makers must be discovered in this area.

MicroRNAs (miRNAs) are small non-coding RNA molecules (18-25 nucleotides) that play an essential role in various physiological functions in mammals and other multicellular organisms. A single miRNA targets up to hundreds of mRNAs. Approximately 30-60% of all human genes are affected by miRNA regulation. It has been reported that miRNAs affect several diseases and cancer-related processes such as proliferation, cell cycle control, apoptosis, differentiation, migration, and metabolism [7-10] and function as oncogenes or tumor-suppressor genes. This dual role of miRNAs has been reported in various studies. As tumor suppressors, they repress oncogenic targets but are usually downregulated in cancer tissues [11]. Others are upregulated and have a stimulating role in cancer progression [12,13]. The biogenesis of miRNA is a three-step process; (i) transcription of primary miRNA (pri-miRNA) from the miRNA genes, (ii) partially processed precursor miRNA (pre-miRNA) in nuclei, and (iii) the generation of mature miRNAs into the cytoplasm **(Fig. 1).** Pri-miRNA is typically large transcripts and forms stem-loop structures.

Further, the stem-loop is cleaved off by the microprocessor machinery. Drosha (ribonuclease enzyme III) and its cofactor Pasha (DiGeorge syndrome critical region gene 8) form pre-miRNA (~60-100 nucleotide). After successful cleavage, the pre-miRNA is bound by

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exportin-5 and exported from the nucleus to the cytoplasm [14,15]. In the cytoplasm, pre-miRNA undergoes the next step of processing mediated by Dicer to produce the mature miRNA. The Dicer (ribonuclease enzyme III) cleaves RNAs into ~22 nucleotide products [16,17]. After cleavage, one strand of the miRNA duplex is preferentially incorporated into the RISC complex and binds to Argonaute (AGO) protein. The other strand, shown in **Fig. 1**, referred to as miRNA* (a complementary strand labeled by a star in the figure), normally degraded.

In some cases, miRNAs* can also be functional [18]. Although miRNAs are tiny in size but heavily involved in mammalian development through the regulation of various genes and represent a novel class of potential biomarkers or therapeutic targets. As a new layer of gene regulation mechanism, miRNAs have diverse functions, and deregulation alters normal cell growth and development, leading to various disorders, including human cancers. MiRNAs play a central role in immune regulation by modulating immune cells [19]. The expression of miRNAs has been demonstrated to be highly specific for tissues and developmental stages. Here to determine the effect of UVB radiation on miRNAs expression and their role in photocarcinogenesis, we performed a miRNAs expression profiling for more than 1000 miRNAs and provided a wide range of altered miRNAs expression in tumors.

2. Results

2.1. UVB radiation-induced alterations in miRNAs expression

First, to determine the effect of UVB radiation on miRNA expression in skin tumors, we performed miRNA array profiling using 7th-generation sequencing, which contains 3100 capture probes targeting human, mouse, and rat miRNAs registered in the miRBASE 18.0. These 3100 capture probes target 1281 mouse miRNAs **(Fig. 2A)**. Our miRNAs profiling revealed that the expression levels of 587 miRNAs were changed in UVB-induced tumors, while the levels of 694 miRNAs remained unchanged **(Fig. 2B)**. Out of 587 altered miRNAs, the expression levels of 250 miRNAs were downregulated, while the expression levels of 337 miRNAs were upregulated **(Fig. 2C)** in tumors.

2.2. Down-regulation of miRNAs in UVB tumors

The loss of miRNA expression is closely related to tumor cell growth and has been implicated in tumorigenesis [20]. Therefore, we next identified the total number of down-regulated miRNAs in the tumor tissue. As shown in **Fig. 3A**, Out of 250 down-regulated miRNAs (**Table-1**), the expression of 165 miRNAs was reduced between 1.01-2.0 fold, while about 55

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miRNAs' expression was reduced between 2.01-4.0 fold in the tumors. The expression of 17 miRNAs was decreased within the range of 4.01-6.0 fold, and 13 miRNAs were downregulated more than 6 folds in the tumors compared to the normal skin. These down-regulated miRNAs may act as tumor suppressors.

2.3. Upregulation of miRNAs in UVB tumors

UV radiation causes several mutations in gene status to induce tumors, such as the p53 mutation regulated by miRNAs. In our miRNAs profiling results, we observed that the levels of 3377 miRNAs were upregulated in tumors **(Fig. 3B, Table 2).** In the tumor tissue, out of 337 upregulated miRNAs, the expression of 285 miRNAs was increased up to 2.0 fold, while about 45 miRNAs' expression was increased between 2.01-4.0 fold. The expression of 7 miRNAs was highly upregulated more than 6 folds in the UVB-induced tumors compared with their expression in the normal skin. These upregulated miRNAs may act as an oncogene to promote photocarcinogenesis.

2.4. Effect of mimic of miR-15b and an inhibitor of miR-133a on UVB-induced immune suppression of the CHS response

UVB-induced immunosuppression has been considered a key mechanism in photocarcinogenesis [21,22]. Therefore, to identify the role of miRNAs altered in UVB-induced tumors, the two miRNAs (miR-15b and miR-133a) were randomly selected for their role in immunosuppression in the CHS study. As shown in **Fig. 4A and 4B**, UVB exposure suppresses the CHS response of DNFB upto 86.45% ($p<0.0018$; bar 3) compared with the non-UVB exposed group (bar 2). Intraperitoneal injections of mimic of downregulated miR-15b (30nM) block UVB-induced immunosuppression upto 42.05% ($p<0.0218$; bar 4, **Fig. 4A**), while treatment with an inhibitor of upregulated miR-133a (20 nM) blocks UVB mediated immune suppression upto 69.89% ($p<0.0041$; bar 4, **Fig. 4B**). These observations revealed that maintenance of UVB mediated miRNAs protect mice from UVB induced immune suppression.

Discussion

Exposure to UV radiation is the principal cause of non-melanoma skin cancer, the most prevalent human cancer, and is also associated with the induction of malignant melanoma. The global incidence of both types of skin cancer (non-melanoma and melanoma) has been increasing over the past few years. Approximately 2-3 million non-melanoma and 132,000

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melanoma skin cancers occur worldwide yearly. According to the skin care foundation, one in every three cancers is skin cancer diagnosed globally [23]. UV radiation is a complete carcinogen, which can initiate skin cancer followed by promotion and progression. Exposure to UV radiation of the skin causes inflammation, apoptosis, DNA damage, oxidative stress, immunosuppression, and premature aging of the skin [24,25].

Cancer formation is the combined interaction of tumor suppressors and oncogenes. Although several genes have been identified in human and animal models, the mechanism of cancer formation is yet to be determined. A recent study demonstrated that more than 50% of miRNA genes are located in cancer-associated genomic regions or fragile sites [26], suggesting that miRNAs may play a more critical role in the pathogenesis of a limited range of human cancers. Various studies have shown that miRNAs play essential roles in DNA methylation, cell proliferation, differentiation, angiogenesis, cell survival, and activation of several molecular pathways in cancers, such as miRNA-106b regulating cell survival pathways and enhancing cell proliferation and tumor of melanoma cells by targeting p21 expression [27]. Several other miRNAs, such as miRNA-17, miRNA-18, miRNA-19, miRNA-21, miRNA-29c, etc., have been reported for their roles in non-melanoma skin cancer [28,29].

In the miRNA profiling of UVB tumor tissues, we observed that the expression levels of several miRNAs were altered either upregulated or downregulated, and they may have an important role in photocarcinogenesis. When cells exhibit abnormal growth and loss of apoptosis function, it usually results in cancer formation. Recent studies indicate that miRNA regulates cell growth and apoptosis [30,31]. For example, *miR-15* and *miR-16* induce apoptosis by targeting anti-apoptotic gene B cell lymphoma 2 (*BCl2*) mRNA [32], which is a key player in many types of human cancers, including skin cancer. Our profiling demonstrated that expression levels of *miR-15* and *miR*-16 were upregulated, suggesting that these miRNAs may have been involved in UVB-induced tumor formation through the regulation of cell growth and apoptosis. The expression of miRNA cluster miRNA-17-92 was also observed to be upregulated in UVB tumors. Recent studies reported that the expression of miRNA cluster miR-17–92 is remarkably increased in several other cancers, including lung cancer [33], by targeting two tumor suppressor genes, *PTEN* and *RB1* [33]. *PTEN* promotes apoptosis through the P13K-Akt-PKB pathway [34]. In our results, we also observed that these miRNAs were upregulated in UVB-induced tumors and provided evidence for their role in photocarcinogenesis. Cancer is the manifestation of genetic and epigenetic events. Exposure to UVB radiation causes DNA hypermethylation and silenced tumor suppressor genes to promote tumor growth. Recent

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studies indicate that loss of miRNA-29s expression has a role in DNA methylation by targeting DNA methyltransferases and TET enzymes [35,36]. Our profiling results demonstrated that the levels of miRNA-29s were down regulated in UVB tumors.

Briefly, miRNAs expression profiling helps to identify a new range of miRNAs that regulate several biological processes and may involve in various diseases, including carcinogenesis and provides a better platform for distinguishing cancer tissues from normal tissues. Our observations suggest that miRNAs can be used as biomarkers and a powerful diagnostic tool for detecting cancers.

In conclusion, for the first time, we have shown that such an expression profiling approach is a suitable and effective solution for identifying aberrant miRNAs involved in cancer progression caused by UV radiation. The results of this miRNAs expression profiling in UVB-induced tumors will provide new insights into discovering potential biomarkers in photocarcinogenesis. Further mechanistic and external validation studies are needed for their clinical significance and role in the development of skin cancer.

4. Material and methods

4.1. Animals

SKH-1 hairless mice (6-7 weeks old) were purchased from Charles River Laboratory (Wilmington, MA). The mice were kept for at least one week in our animal resource facility before use in experiments. Mice were maintained under standard conditions of a 12-h dark/12-h light cycle, a temperature of 24 ± 2°C, and relative humidity of 50 ± 10%. The animal study was approved by the Institutional Animal Care and Use Committee (IACUC) of the University of Alabama at Birmingham.

4.2. UVB irradiation and photocarcinogenesis protocol

The mice were exposed to UVB radiation, as described previously [37]. Briefly, the dorsal skin of SKH-1 hairless mice was exposed to UVB radiation from a band of four FS24T1 UVB lamps (Daavlin, UVA/UVB Research Irradiation Unit, Bryan, OH) equipped with a regulator for UVB dosa. Under the standard photocarcinogenesis protocol, mice were UVB irradiated (180 mJ/cm^2; 3X/week) for upto 24 weeks. At the end of the study, mice from both cohorts were humanly euthanized, and samples were collected and stored at -80^0C.

4.3. Tissue collection and RNA isolation

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At the end of the photocarcinogenesis experiment, tumor and skin tissues were harvested after the euthanization of experimental mice. Total RNAs, including small ones, were extracted from the skin/tumor tissues using the Qiagen miRNeasy® mini kit. Briefly, a small portion of tissue (10mg) was lysed in 700µL Qiazol lysis reagent using a tissue lyzer with one 5mm stainless steel bead. The tissue lysate was transferred to a new tube with 140 µL chloroform, mixed, incubated for 2 min at room temperature, and centrifuged at 12,000 x g for 15 min at 4^0C. The upper aqueous phase was separated, and 525µL of 100% ethanol was added. The contents were mixed gently, transferred into RNeasy mini spin column in a collection tube, and centrifuged at 8,000 x g for 15 sec at room temperature. The RNeasy mini spin column was rinsed with 700 µL RWT buffer and centrifuged at 8,000 x g for 15 sec at room temperature, followed by another rinse with 500 µL RPE buffer and centrifuged at 8,000 x g for 15 sec at room temperature. The rinse step with RPE buffer was repeated two times. After centrifugation, the flow-through was discarded, RNeasy mini spin column was transferred to a new collection tube, and the lid was left uncapped for 1 min to allow the column to dry. Total RNA was eluted by adding 50 µL of RNase-free water to the membrane of the RNeasy mini spin column and incubating for 1 min before centrifugation at room temperature. The RNAs, including small RNAs, were stored at -80^0C until used.

4.4. miRNAs array profiling

All microRNAs array was conducted at Exiqon Services, Denmark. An Agilent 2100 Bioanalyzer profile verified the quality of the total RNA. 750 ng total RNA from both sample and reference was labeled with Hy3™ and Hy5™ fluorescent labels, respectively, using the miRCURY LNA™ microRNA Hi-Power labeling kit, Hy3™/Hy5™ (Exiqon, Denmark) following the procedure described by the manufacturer. The Hy3™ labeled samples and a Hy5™ labeled reference RNA sample was mixed pairwise and hybridized to the miRCURY LNA™ microRNA array 7th Gen (Exiqon, Denmark), which contains capture probes targeting all microRNAs for human, mouse, and rat registered in the miRBASE 18.0. The hybridization was performed according to the miRCURY LNA™ microRNA array instruction manual using a Tecan HS4800™ hybridization station (Tecan, Austria). After hybridization, the microarray slides were scanned and stored in an ozone-free environment (ozone level below 2.0 ppb) to prevent potential bleaching of the fluorescent dyes. The miRCURY LNA™ microRNA array slides were scanned using the Agilent G2565BA Microarray Scanner System (Agilent Technologies, Inc., USA), and the image analysis was carried out using the ImaGene® 9 (miRCURY LNA™ microRNA Array

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Analysis Software, Exiqon, Denmark). The quantified signals were normalized using the global LOWESS (Locally Weighted Scatterplot Smoothing) regression algorithm and background corrected [38]. As per the recommendations provided by Exiqon, smaller fold changes (≤1.0 fold) may tend to be relatively more affected by technical variance, and such changes could be associated with the increased risk of false-positive signals. Therefore the cut-off value was ≤1.0 fold change in our study. The data for miRNAs expression showing ≤1.0 fold change were eliminated during comparison within the groups.

4.5. Contact hypersensitivity (CHS) assay

The effect of miRNA-15b and miRNA-133a mimic/inhibitor on UVB-induced immune suppression in mice was assessed using the contact hypersensitivity model described previously [21,22]. Briefly, dorsal skin-shaved mice were exposed to UVB radiation (150 mJ/cm^2) on four consecutive days. During the UVB exposure, ears were protected from UV irradiation by covering. After 24 hours of last UVB exposure, mice were sensitized with skin contact sensitizer 2, 4-dinitrofluorobenzene (DNFB) by topical application [(0.5% in 25 µl of acetone: olive oil mixture (4:1, v/v)]. After five days, CHS response was elicited by treating with 20 µl of 0.2% DNFB (ears). The thickness of ear skin was measured 24 h after the challenge using an engineer's micrometer (Mitutoyo, Tokyo, Japan). The CHS response was calculated by comparing the ear thickness before the challenge. To determine the effect of miRNAs on UVB-induced immune suppression, mice were administered with the mimic of miRNA-15b (30nM; i.p) and an inhibitor of miRNA-133a (20nM; i.p.). The experimental mice were treated with miRNAs mimic/inhibitor daily, 30 mins before UVB exposure.

4.6. Statistical Analysis

Data were evaluated for outliers and adherence to a normal distribution using GraphPad Prism software (San Diego, CA, USA), version 8.1. Statistical significance of normally and non-normally distributed data were assessed via one-way ANOVA and Tukey's multiple comparison test, respectively, with $\alpha = 0.05$.

Author Contributions: A.A., V.K., H.F., V.K.S, and R.P. conceived the study and participated in the design. R.P. participated in sample collection and CHS study. All authors wrote, edited, and consented to the published version of the manuscript.

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Figure legends

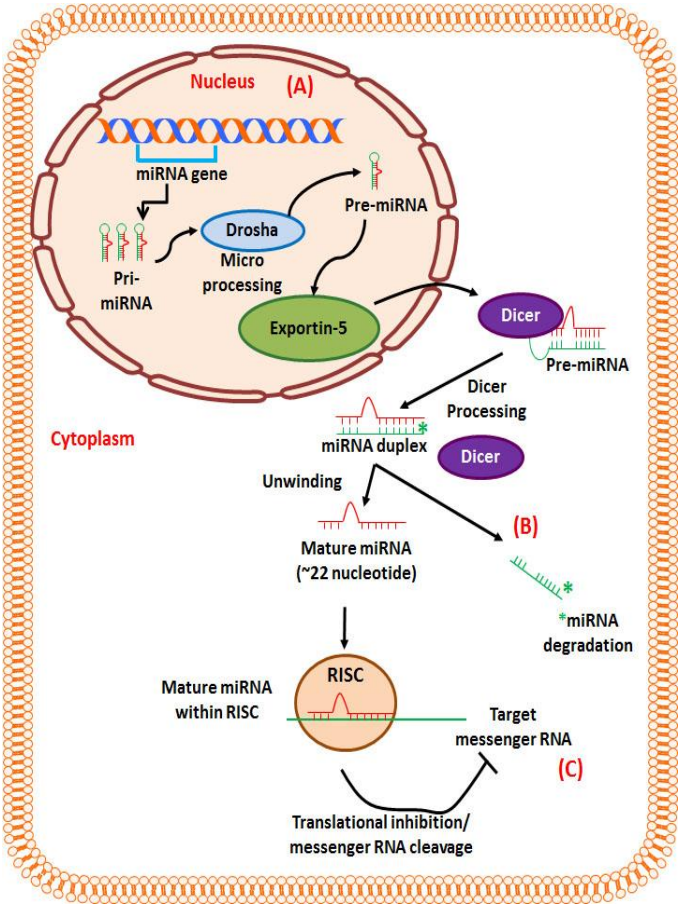

Figure 1: Biogenesis of miRNAs. **(A)** In the nucleus, ribonuclease enzyme II transcribes the pri-miRNA transcript. Drosha and its co factor Pasha form the microprocessor complex that cleaves pri-miRNA transcript into pre-miRNA which share a stem loop structure. These pre-miRNAs are transported by exportin-5 into cytoplasm from nucleus. **(B)** In the cytoplasm, Dicer unwind the miRNA duplex into mature miRNA and complementary strand (miRNA*, which rapidly degraded), and loaded mature miRNA into RNA-induced silencing complex (RISC). **(C)** Depending on the degree of complementarity between the target mRNA and the miRNA, the binding ether stops the translation by cleaving the target mRNA or suppress translation by binding to impeding ribosomal reading of the mRNA (incomplete complementarity). miRNA, microRNA; pri-miRNA, primary microRNA; pre-miRNA, precursor -microRNA; RISC, RNA-induced silencing complex.

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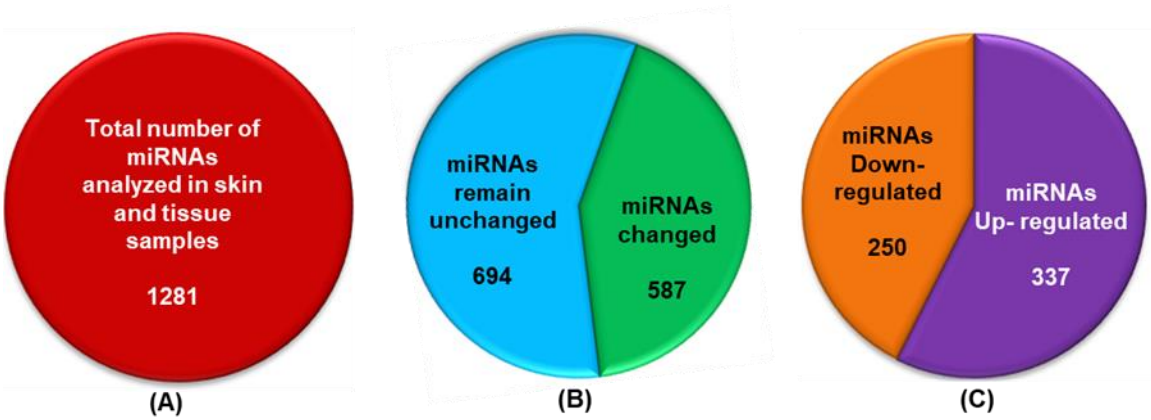

Figure 2: Total number of miRNAs profiled in tumors and normal skin of SKH-1 hairless mice. SKH-1 hairless mice were exposed to UVB radiation (180mJ/cm^2) for up to 24 weeks, and tumor and skin tissue were harvested for miRNAs isolation using Trizol-chloroform extraction method. **(A)** Total number of miRNAs measured in tumors and skin tissues, **(B)** The number of altered miRNAs expression in tumors, **(C)**The number of downregulated, upregulated and aberrantly expressed miRNAs.

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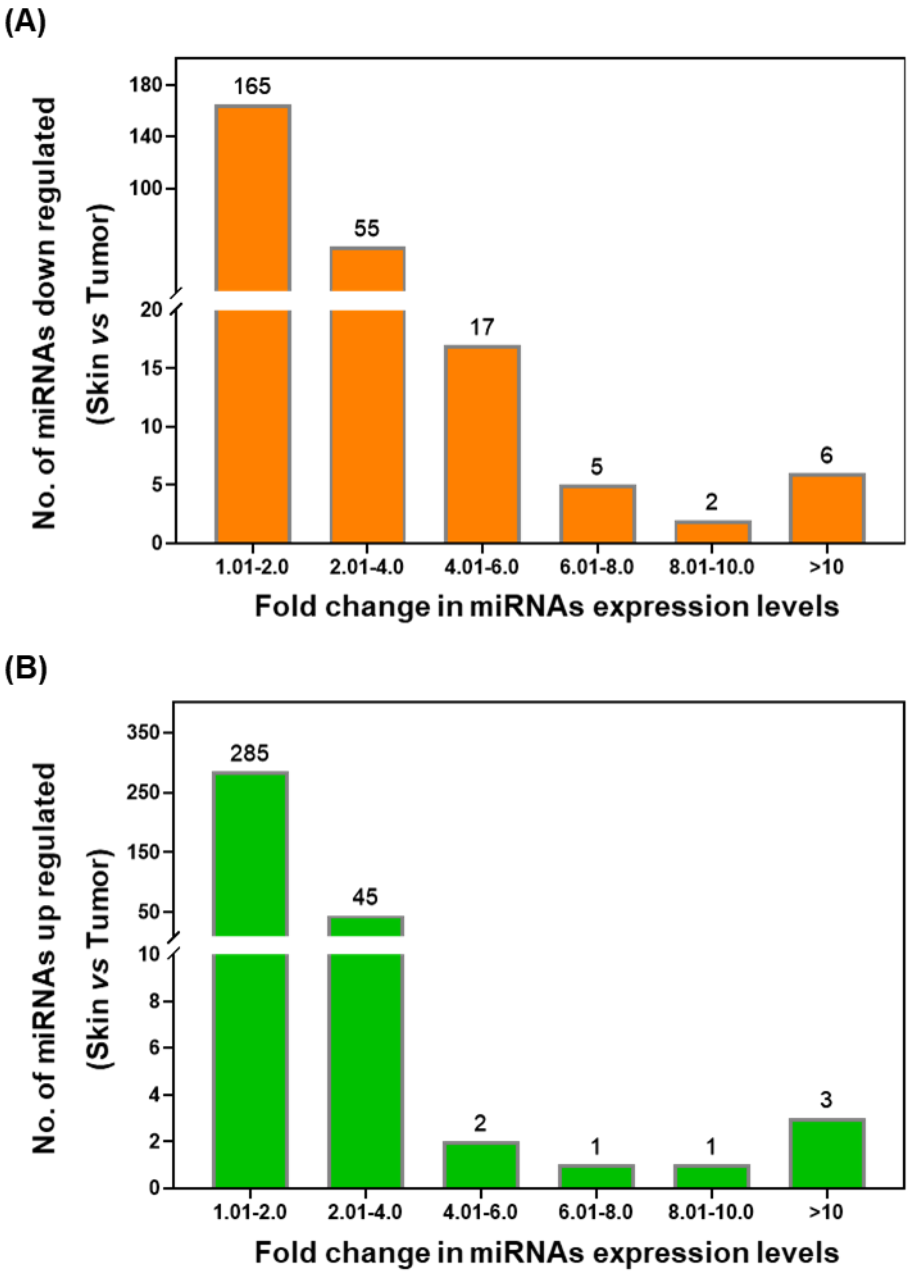

Figure 3: Graphical representation of fold change in the expression of miRNAs in UVB induced tumors. Graph showing difference in down regulated miRNAs **(A)** and upregulated miRNAs **(B).**

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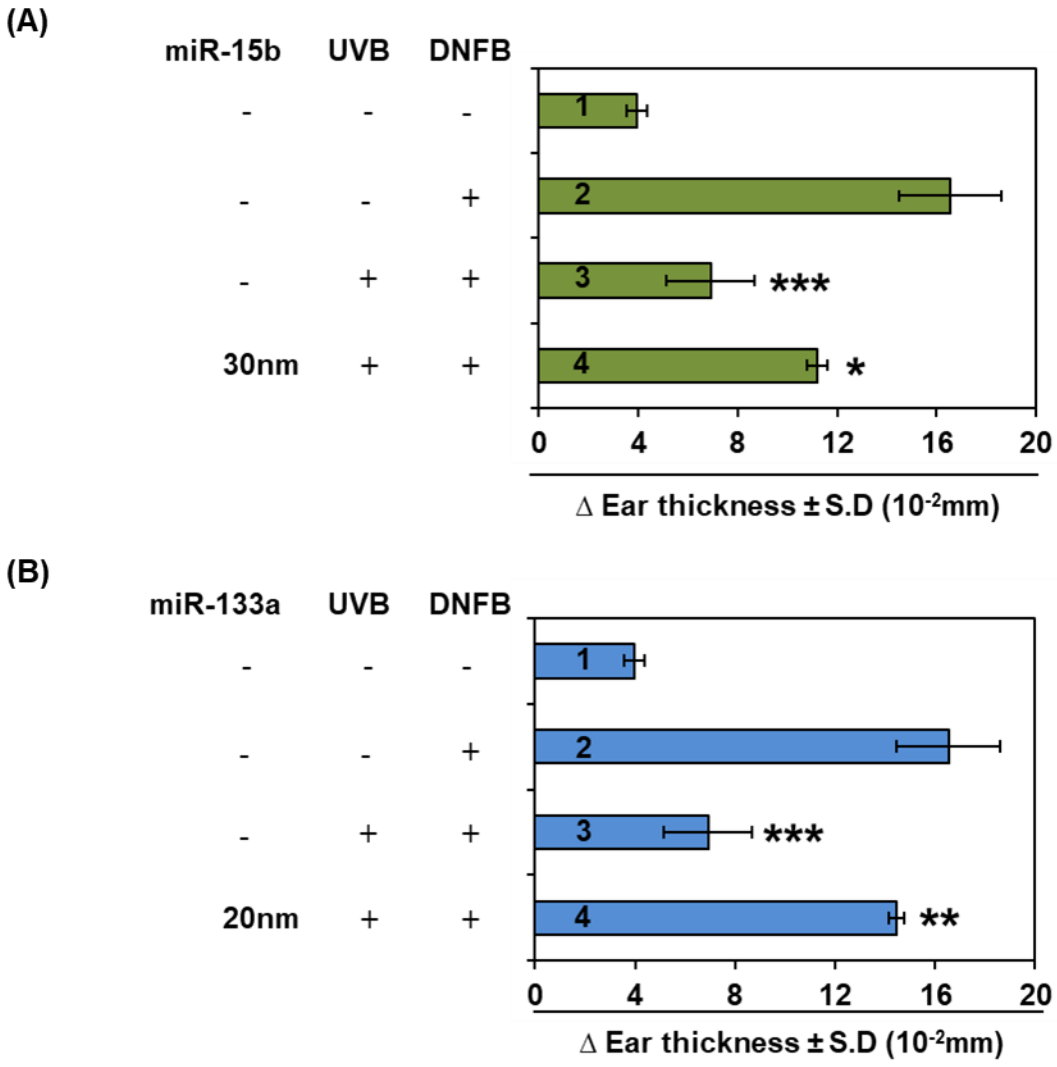

Figure 4. The effect of intraperitoneal injections of mimic of miR-15b **(A)** and inhibitor of miR-133a **(B)** on UVB induced immunosuppression. The mice were treated with mimic/inhibitor 30 mins prior to UVB exposure. The data is presented as change in mean ear thickness ± S.E. n = 4, Statistical differences; *p<0.05, **p<0.01, ***p<0.001.

Table 1: Fold change expression of down-regulated miRNAs in UVB-induced tumors (UT). Data were compared with non-UVB exposed normal skin (CS).

Probe ID	Annotation	AvgHy3	UT	CS	logFC	Fold Change (CS vs. UT)
42866	mmu-miR-451a	14.22	3.31	-3.46	-6.77	-109.45
29802	mmu-miR-144-3p	11.65	3.57	-2.79	-6.36	-82.18
32946	mmu-miR-3107-5p/mmu-miR-486-5p	9.44	3.02	-1.21	-4.23	-18.75
169104	mmu-miR-5099	12.49	2.80	-1.12	-3.91	-15.05
169268	mmu-miR-5112	8.49	2.45	-1.07	-3.52	-11.48
17280	mmu-miR-15b-5p	11.39	2.70	-0.71	-3.41	-10.66
148472	mmu-miR-201-5p	8.55	2.36	-1.05	-3.41	-10.62
42682	mmu-miR-25-3p	9.25	2.64	-0.66	-3.30	-9.84
46320	mmu-miR-31-3p	9.29	2.46	-0.62	-3.08	-8.46
30687	mmu-miR-93-5p	10.13	2.50	-0.47	-2.97	-7.85
10967	mmu-miR-16-5p	13.27	2.54	-0.41	-2.95	-7.72
19599	mmu-miR-106a-5p	10.38	2.37	-0.49	-2.86	-7.25
148578	mmu-miR-541-3p	10.32	2.38	-0.44	-2.82	-7.07
169075	mmu-miR-92a-3p	9.63	2.18	-0.50	-2.68	-6.40
11052	mmu-miR-31-5p	10.26	2.23	-0.31	-2.54	-5.81

145845	mmu-miR-20a-5p	10.97	2.06	-0.47	-2.54	-5.80
148344	mmu-miR-669l-3p	12.23	2.10	-0.39	-2.49	-5.61
42640	mmu-miR-20b-5p	9.30	1.96	-0.49	-2.45	-5.45
169336	mmu-miR-17-5p	10.42	2.04	-0.40	-2.44	-5.43
10947	mmu-miR-142-3p	12.53	1.96	-0.39	-2.36	-5.12
10997	mmu-miR-19a-3p	9.96	1.88	-0.46	-2.34	-5.06
42630	mmu-miR-140-3p	9.88	2.09	-0.24	-2.32	-5.01
148101	mmu-miR-669d-2-3p/mmu-miR-669d-3p	12.42	1.98	-0.33	-2.31	-4.96
19603	SNORD13	9.85	2.00	-0.31	-2.31	-4.96
27720	mmu-miR-15a-5p	12.24	2.15	-0.14	-2.29	-4.91
19582	mmu-miR-106b-5p	11.34	1.99	-0.26	-2.25	-4.75
146164	mmu-miR-1958	11.82	1.95	-0.16	-2.12	-4.34
146155	mmu-miR-2137	12.40	1.96	-0.15	-2.12	-4.33
14302	mmu-miR-374b-5p/mmu-miR-374c-5p	7.96	1.83	-0.28	-2.11	-4.32
147506	mmu-miR-21a-5p	13.80	1.25	-0.80	-2.04	-4.12
46204	SNORD38B	9.68	1.88	-0.12	-2.01	-4.01
145852	mmu-miR-210-3p	9.08	1.89	-0.07	-1.96	-3.89
18739	mmu-miR-186-5p	7.64	1.92	-0.03	-1.95	-3.87
13143	mmu-miR-301a-3p	8.53	1.87	-0.04	-1.91	-3.76

14290	mmu-miR-541-5p	8.20	1.53	-0.37	-1.90	-3.72
13147	mmu-miR-96-5p	8.59	1.80	-0.09	-1.89	-3.70
168556	mmu-miR-3096b-5p	9.50	1.50	-0.35	-1.86	-3.62
11024	mmu-miR-223-3p	11.55	1.80	-0.04	-1.85	-3.59
168706	mmu-miR-5129-5p	8.60	1.33	-0.50	-1.84	-3.57
148233	mmu-miR-3096a-3p	10.79	1.38	-0.44	-1.82	-3.53
11245	mmu-miR-433-5p	10.60	1.48	-0.33	-1.81	-3.51
168880	mmu-miR-489-5p	7.39	1.16	-0.65	-1.81	-3.51
14289	mmu-miR-540-3p	9.68	1.43	-0.38	-1.81	-3.50
148098	mmu-miR-374b-5p	8.54	1.70	-0.09	-1.79	-3.46
148238	mmu-miR-3096a-5p	9.47	1.59	-0.18	-1.78	-3.43
148528	mmu-miR-196a-1-3p	8.40	1.15	-0.63	-1.78	-3.43
145798	mmu-miR-142-5p	10.46	1.55	-0.22	-1.78	-3.43
148087	mmu-miR-669d-2-3p	9.70	1.63	-0.03	-1.66	-3.16
146192	mmu-miR-669m-3p	11.14	1.75	0.10	-1.65	-3.14
10998	mmu-miR-19b-3p	10.88	1.55	-0.10	-1.65	-3.13
42811	mmu-miR-542-5p	8.23	1.68	0.07	-1.61	-3.04
148035	mmu-miR-3084-5p	9.95	1.55	-0.04	-1.59	-3.00
169340	mmu-miR-3096a-3p/mmu-miR-3096b-3p	9.99	1.00	-0.53	-1.53	-2.88

146012	mmu-miR-1949	9.75	0.93	-0.52	-1.44	-2.72
145633	mmu-let-7d-3p	8.99	1.36	-0.07	-1.43	-2.69
46917	mmu-miR-205-5p	13.85	1.41	0.01	-1.40	-2.64
4700	mmu-miR-140-5p	8.84	1.41	0.02	-1.40	-2.64
17608	mmu-miR-425-5p	7.84	1.30	-0.10	-1.40	-2.63
17427	mmu-miR-200c-3p	10.57	1.42	0.02	-1.40	-2.63
19585	mmu-miR-148b-3p	8.26	1.43	0.06	-1.37	-2.59
27558	mmu-miR-155-5p	7.66	1.31	-0.02	-1.33	-2.52
169347	mmu-miR-5622-5p	9.16	1.22	-0.05	-1.26	-2.40
42702	mmu-miR-30c-1-3p	7.63	1.24	-0.02	-1.26	-2.40
17610	mmu-miR-677-5p	8.36	1.27	0.02	-1.25	-2.38
10975	mmu-miR-182-5p	8.49	1.17	-0.07	-1.24	-2.36
42919	mmu-miR-203-5p	8.96	1.40	0.16	-1.23	-2.35
148484	mmu-miR-3084-3p	11.53	1.02	-0.20	-1.22	-2.33
9938	mmu-let-7i-5p	11.74	1.21	-0.01	-1.21	-2.32
10946	mmu-miR-141-3p	10.95	1.17	-0.03	-1.20	-2.30
19007	SNORD3@	12.94	0.93	-0.26	-1.20	-2.30
148676	mmu-miR-1186b	10.48	0.92	-0.28	-1.20	-2.29
169277	mmu-miR-3970	9.60	1.06	-0.12	-1.17	-2.26

145661	SNORD65	8.08	1.06	-0.09	-1.15	-2.22
27533	mmu-miR-320-3p	8.77	1.31	0.16	-1.15	-2.22
46438	mmu-let-7g-5p	11.41	1.35	0.21	-1.14	-2.20
42730	mmu-miR-423-3p	8.51	0.94	-0.18	-1.12	-2.17
29490	mmu-miR-7a-5p	10.34	1.00	-0.10	-1.09	-2.13
42571	mmu-miR-129-1-3p	7.53	0.91	-0.17	-1.08	-2.11
168966	mmu-miR-28a-5p/mmu-miR-28c	8.67	1.01	-0.06	-1.07	-2.10
168872	mmu-miR-24-1-5p	9.44	1.14	0.07	-1.06	-2.09
11022	mmu-miR-221-3p	9.36	1.08	0.03	-1.06	-2.08
31388	mmu-miR-291a-5p	10.55	0.73	-0.31	-1.05	-2.07
17854	mmu-miR-106b-3p	8.53	1.18	0.14	-1.04	-2.06
168859	mmu-miR-3962	10.72	1.20	0.17	-1.03	-2.04
10985	mmu-miR-191-5p	9.98	1.25	0.22	-1.03	-2.04
29190	mmu-miR-708-5p	8.99	1.28	0.27	-1.00	-2.01
42707	mmu-miR-294-5p	12.23	0.57	-0.43	-1.00	-2.00
146004	mmu-miR-2136	7.47	1.12	0.13	-0.99	-1.99
148051	mmu-miR-770-3p	7.89	0.97	-0.01	-0.97	-1.96
146111	mmu-miR-767	8.42	0.85	-0.12	-0.97	-1.96
147199	mmu-miR-27b-3p	11.90	0.91	-0.05	-0.96	-1.94

28547	mmu-miR-675-5p	9.89	0.94	0.00	-0.95	-1.93
11184	mmu-miR-99b-5p	9.63	0.95	0.00	-0.94	-1.92
11023	mmu-miR-222-3p	9.70	0.92	-0.02	-0.94	-1.92
148416	mmu-miR-3102-5p	7.87	0.68	-0.26	-0.93	-1.91
169330	mmu-miR-23b-3p	13.09	1.01	0.12	-0.89	-1.86
28450	mmu-miR-291b-5p	9.91	0.72	-0.17	-0.89	-1.85
145663	SNORD68	11.57	0.92	0.03	-0.89	-1.85
11260	mmu-miR-151-5p	8.24	1.04	0.16	-0.88	-1.84
168630	mmu-miR-5121	9.19	0.57	-0.30	-0.87	-1.83
17752	mmu-let-7f-5p	9.95	1.18	0.31	-0.87	-1.83
10990	mmu-miR-196a-5p	7.51	0.40	-0.45	-0.86	-1.81
145666	SNORD110	8.73	0.83	-0.02	-0.85	-1.81
19008	SNORD2	12.27	0.61	-0.24	-0.84	-1.79
146199	mmu-miR-1961	8.41	1.05	0.21	-0.84	-1.79
146112	mmu-miR-30b-5p	11.23	1.15	0.31	-0.83	-1.78
11256	mmu-miR-470-5p	9.04	0.79	-0.04	-0.83	-1.78
145968	mmu-let-7d-5p	11.44	1.02	0.19	-0.83	-1.77
27575	mmu-miR-711	9.56	1.17	0.35	-0.82	-1.77
148523	mghv-miR-M1-8-3p	11.82	0.50	-0.31	-0.81	-1.75

10988	mmu-miR-194-5p	7.42	0.72	-0.08	-0.80	-1.74
10936	mmu-miR-130b-3p	7.66	0.69	-0.11	-0.80	-1.74
146087	mmu-miR-1894-3p	8.36	0.88	0.08	-0.80	-1.74
30831	mmu-miR-804	7.40	1.21	0.42	-0.79	-1.73
17506	mmu-miR-24-3p	13.49	1.04	0.25	-0.78	-1.72
147162	mmu-let-7a-5p	11.08	0.98	0.20	-0.78	-1.72
17478	mmu-miR-429-3p	8.89	1.14	0.37	-0.78	-1.71
146172	mmu-miR-1892	8.93	0.65	-0.12	-0.77	-1.70
42953	mmu-miR-101b-3p	9.31	0.99	0.23	-0.76	-1.69
17597	mmu-miR-467b-3p	9.91	1.00	0.25	-0.74	-1.67
148100	mmu-miR-1947-3p	12.96	0.37	-0.36	-0.73	-1.66
145859	mmu-miR-33-5p	9.39	0.79	0.06	-0.73	-1.65
11020	mmu-miR-22-3p	12.57	0.93	0.21	-0.72	-1.65
28966	mmu-miR-574-3p	8.91	0.73	0.02	-0.71	-1.64
42923	mmu-miR-30c-5p	11.58	0.95	0.26	-0.69	-1.61
148107	mmu-miR-3104-3p	7.93	0.92	0.23	-0.69	-1.61
168824	mmu-miR-5100	15.78	0.89	0.20	-0.68	-1.61
168842	mmu-miR-5105	7.38	0.68	0.01	-0.67	-1.59
28191	mmu-miR-30e-5p	10.73	0.95	0.28	-0.67	-1.59

145838	mmu-miR-125b-1-3p	8.42	0.74	0.07	-0.67	-1.59
148362	mmu-miR-592-3p	9.08	1.06	0.40	-0.66	-1.58
42605	mmu-miR-503-3p	11.29	0.54	-0.12	-0.66	-1.58
168819	mmu-miR-200a-3p	10.35	0.87	0.22	-0.65	-1.57
145753	mmu-miR-484	7.61	0.82	0.18	-0.64	-1.56
42827	mmu-miR-652-3p	8.04	0.75	0.13	-0.62	-1.54
145897	mmu-miR-92b-3p	8.50	0.23	-0.39	-0.62	-1.53
169190	mmu-miR-5117-3p	11.20	0.73	0.11	-0.61	-1.53
169105	mmu-miR-3963	15.95	1.14	0.53	-0.61	-1.53
11053	mmu-miR-32-5p	8.82	0.78	0.18	-0.60	-1.52
145993	mmu-miR-1899	8.41	0.60	0.00	-0.59	-1.51
19600	mmu-miR-17-3p	9.34	0.41	-0.17	-0.59	-1.50
11215	mmu-miR-292-3p	7.57	1.95	1.37	-0.59	-1.50
145701	mmu-miR-668-3p	7.90	0.81	0.23	-0.58	-1.49
14301	mmu-miR-361-5p	9.27	0.80	0.22	-0.58	-1.49
14285	mmu-miR-487b-3p	8.04	0.56	-0.01	-0.58	-1.49
148059	mmu-miR-493-5p	8.92	0.24	-0.33	-0.57	-1.48
169248	mmu-miR-5108	7.39	0.40	-0.16	-0.57	-1.48
169250	mmu-miR-5109	13.60	0.69	0.13	-0.56	-1.48

148197	mmu-miR-3081-5p	8.34	0.46	-0.10	-0.56	-1.47
42888	mmu-miR-875-3p	12.08	0.47	-0.09	-0.56	-1.47
168708	mmu-miR-296-5p	7.47	0.78	0.22	-0.56	-1.47
11227	mmu-miR-329-3p	9.38	0.98	0.43	-0.54	-1.46
46210	mmu-miR-1249-3p	7.70	1.14	0.61	-0.53	-1.44
169246	mmu-miR-5618-5p	7.82	0.47	-0.05	-0.52	-1.44
17489	mmu-miR-710	10.34	0.54	0.03	-0.51	-1.43
30768	mmu-miR-674-5p	9.18	0.57	0.07	-0.50	-1.42
10138	mmu-miR-130a-3p	10.45	0.80	0.31	-0.49	-1.40
19606	SNORD12	8.89	0.30	-0.18	-0.48	-1.39
168807	mmu-miR-3473c	7.55	0.59	0.12	-0.47	-1.39
10955	mmu-miR-148a-3p	8.03	0.50	0.04	-0.46	-1.38
169374	mmu-miR-184-5p	11.08	0.34	-0.12	-0.46	-1.38
148261	mmu-miR-208a-5p	7.23	0.46	0.00	-0.46	-1.38
168762	mmu-miR-3964	7.99	0.18	-0.27	-0.45	-1.37
11182	mmu-miR-98-5p	10.38	0.77	0.34	-0.44	-1.35
11234	mmu-miR-350-3p	7.72	0.57	0.14	-0.44	-1.35
168586	mmu-miR-34a-5p	9.78	0.11	-0.32	-0.43	-1.35
46483	mmu-miR-27a-3p	11.82	0.44	0.01	-0.43	-1.34

147186	mmu-miR-200b-3p	10.53	0.67	0.27	-0.41	-1.33
46636	mcmv-miR-M23-1-5p	8.00	-0.09	-0.49	-0.39	-1.31
13140	mmu-miR-138-5p	8.44	0.41	0.04	-0.37	-1.29
148654	mmu-miR-184-3p	7.29	0.47	0.10	-0.37	-1.29
10986	mmu-miR-193a-3p	9.90	0.60	0.23	-0.37	-1.29
21498	mmu-miR-654-3p	7.21	0.63	0.26	-0.36	-1.29
19605	SNORD6	7.44	0.69	0.34	-0.34	-1.27
148046	mmu-miR-344-5p	7.42	-0.03	-0.37	-0.34	-1.27
42744	mmu-miR-23a-3p	13.14	0.65	0.32	-0.33	-1.26
42636	mmu-miR-28a-3p	7.39	0.48	0.16	-0.32	-1.25
148391	mmu-miR-3068-5p	8.04	0.07	-0.25	-0.31	-1.24
148424	mmu-miR-201-3p	8.42	0.14	-0.17	-0.31	-1.24
46251	mmu-miR-1193-3p	7.35	0.03	-0.28	-0.31	-1.24
42724	mmu-miR-34b-3p	9.92	0.23	-0.08	-0.30	-1.24
145643	mmu-miR-382-5p	7.96	0.47	0.16	-0.30	-1.24
17810	mmu-miR-29b-1-5p	9.05	0.38	0.07	-0.30	-1.23
146065	mmu-miR-1927	7.27	0.35	0.05	-0.30	-1.23
148218	mghv-miR-M1-11-3p	7.84	0.42	0.13	-0.29	-1.22
148485	mghv-miR-M1-12-3p	8.22	0.40	0.11	-0.29	-1.22

146106	mmu-miR-1931	8.20	0.19	-0.10	-0.29	-1.22
42494	mmu-miR-712-3p	7.58	0.27	-0.02	-0.29	-1.22
42452	mmu-miR-141-5p	7.69	0.33	0.05	-0.28	-1.22
148166	mmu-miR-3069-3p	8.84	0.28	0.00	-0.28	-1.21
42879	mmu-miR-92a-2-5p	8.29	0.65	0.38	-0.27	-1.21
42488	mmu-miR-466h-5p	7.32	0.92	0.66	-0.26	-1.20
14328	mmu-miR-124-3p	7.45	0.50	0.24	-0.25	-1.19
148470	mmu-miR-1264-3p	10.00	0.12	-0.13	-0.25	-1.19
148370	mmu-miR-466n-3p	9.63	0.22	-0.02	-0.24	-1.18
10919	mmu-miR-103-3p	10.69	0.57	0.32	-0.24	-1.18
148172	mmu-miR-216a-3p	8.11	-0.10	-0.32	-0.23	-1.17
42570	mmu-miR-194-2-3p	7.35	0.33	0.11	-0.22	-1.16
42769	mmu-let-7b-3p	7.38	0.21	0.01	-0.20	-1.15
29852	mmu-miR-9-3p	7.32	0.08	-0.12	-0.19	-1.14
145676	mmu-miR-30e-3p	8.54	0.50	0.31	-0.19	-1.14
13150	mmu-miR-322-5p	8.43	0.36	0.17	-0.19	-1.14
146133	mmu-miR-1936	8.27	0.10	-0.09	-0.18	-1.14
19013	SNORD14B	7.68	0.42	0.24	-0.18	-1.13
168566	mmu-miR-5625-3p	8.24	-0.29	-0.46	-0.17	-1.13

145638	mmu-miR-29a-5p	8.21	0.47	0.30	-0.17	-1.12
148179	mmu-miR-3095-3p	10.46	0.04	-0.12	-0.16	-1.12
168687	mmu-miR-29a-3p	12.14	0.29	0.12	-0.16	-1.12
168662	mmu-miR-5132-5p	8.87	-0.01	-0.17	-0.16	-1.12
146086	mmu-miR-30a-5p	10.06	0.62	0.47	-0.15	-1.11
27536	mmu-miR-190a-5p	7.52	0.87	0.73	-0.15	-1.11
17953	mmu-miR-183-3p	10.40	0.07	-0.08	-0.15	-1.11
145640	mmu-miR-328-3p	8.53	0.02	-0.13	-0.14	-1.10
33114	mmu-miR-455-3p	7.46	0.05	-0.09	-0.14	-1.10
17273	mghv-miR-M1-6-3p	8.28	0.67	0.53	-0.14	-1.10
28019	mmu-miR-10a-3p	7.92	0.14	0.01	-0.13	-1.09
148242	mmu-miR-205-3p	8.63	-0.14	-0.27	-0.13	-1.09
148121	mmu-miR-155-3p	9.32	0.18	0.05	-0.13	-1.09
11251	mmu-miR-465a-5p	7.75	0.68	0.56	-0.13	-1.09
168968	mmu-miR-147-3p	8.94	0.27	0.15	-0.12	-1.09
147283	mmu-miR-137-5p	8.05	0.50	0.39	-0.12	-1.08
19596	mmu-miR-30d-5p	9.79	0.59	0.47	-0.12	-1.08
17818	mmu-miR-27a-5p	7.25	0.30	0.18	-0.11	-1.08
148546	mmu-miR-500-5p	7.30	0.33	0.21	-0.11	-1.08

146008	mmu-miR-26b-5p	11.47	0.55	0.43	-0.11	-1.08
148646	mmu-miR-467a-3p	11.52	0.27	0.16	-0.11	-1.08
168797	mmu-miR-3968	11.65	-0.28	-0.38	-0.10	-1.07
42808	mmu-miR-874-3p	7.44	-0.12	-0.22	-0.10	-1.07
42738	mmu-miR-340-3p	7.65	0.19	0.10	-0.09	-1.07
10923	mmu-miR-107-3p	10.15	0.39	0.30	-0.09	-1.06
42950	mmu-miR-24-2-5p	9.57	0.38	0.30	-0.09	-1.06
11040	mmu-miR-29b-3p	11.90	0.32	0.24	-0.08	-1.06
17825	mmu-miR-338-5p	7.72	0.13	0.05	-0.08	-1.06
42532	mmu-miR-22-5p	9.41	0.45	0.38	-0.08	-1.05
148225	mmu-miR-3102-5p.2-5p	7.38	-0.03	-0.09	-0.07	-1.05
10977	mmu-miR-183-5p	9.22	-0.11	-0.17	-0.06	-1.04
14272	mmu-miR-542-3p	7.86	0.34	0.28	-0.06	-1.04
42464	mghv-miR-M1-2-3p	9.14	0.67	0.62	-0.05	-1.04
148128	mmu-miR-3090-5p	9.16	-0.10	-0.15	-0.05	-1.03
11078	mmu-miR-365-3p	9.43	0.42	0.37	-0.04	-1.03
16681	mmu-miR-721	9.22	-0.05	-0.09	-0.04	-1.02
30787	mmu-miR-125b-5p	12.75	0.37	0.34	-0.03	-1.02
148689	mmu-miR-3099-5p	9.18	0.18	0.15	-0.03	-1.02

42929	mmu-miR-25-5p	10.96	0.71	0.69	-0.03	-1.02
17942	mmu-miR-125a-3p	7.67	0.02	-0.01	-0.03	-1.02
42804	mmu-miR-712-5p	8.16	0.00	-0.02	-0.02	-1.02
46292	mmu-miR-5097	11.74	-0.68	-0.69	-0.02	-1.01
148303	mmu-miR-3106-5p	7.42	-0.26	-0.27	-0.02	-1.01
169060	mmu-miR-3961	12.40	-0.25	-0.27	-0.01	-1.01
148270	mmu-miR-669b-3p	11.78	0.28	0.27	-0.01	-1.01
145678	mmu-miR-150-5p	9.57	0.11	0.10	-0.01	-1.01

Table 2: Fold change expression of up-regulated miRNAs in UVB-induced tumors (UT). Data were compared with non-UVB exposed normal skin (CS).

Probe ID	Annotation	AvgHy3	UT	CS	logFC	Fold Change (CS vs UT)
42927	mmu-miR-673-3p	9.40	0.19	0.19	0.01	1.01
14288	mmu-miR-503-5p	10.65	0.07	0.08	0.01	1.01
148076	mmu-miR-3103-5p	7.90	-0.14	-0.12	0.02	1.01
146029	mmu-miR-365-2-5p	7.37	0.01	0.03	0.02	1.01
42609	mmu-miR-135a-1-3p	7.89	-0.18	-0.16	0.02	1.01
148286	mmu-miR-3066-3p	7.32	-0.07	-0.05	0.03	1.02
148656	mmu-miR-3099-3p	8.54	0.18	0.20	0.03	1.02
13148	mmu-miR-195a-5p	11.20	0.40	0.43	0.03	1.02
42475	mmu-miR-221-5p	8.07	-0.14	-0.10	0.04	1.02
168596	mmu-miR-5620-3p	8.23	-0.22	-0.18	0.04	1.03
148200	mmu-miR-3100-3p	12.41	-0.15	-0.12	0.04	1.03
148468	mmu-miR-677-3p	11.21	0.12	0.16	0.04	1.03
148114	mmu-miR-26a-2-3p	7.39	0.04	0.08	0.04	1.03
146082	mmu-miR-1956	8.11	0.14	0.18	0.04	1.03
145846	mmu-let-7e-5p	12.12	0.13	0.18	0.05	1.03

146099	mmu-miR-1950	7.59	0.02	0.06	0.05	1.03
145820	mmu-let-7c-5p	12.26	0.39	0.44	0.05	1.04
11074	mmu-miR-34c-5p	8.99	0.13	0.19	0.05	1.04
42474	mmu-miR-362-3p	7.88	0.11	0.16	0.06	1.04
148146	mmu-miR-3076-3p	8.31	0.03	0.09	0.06	1.04
28979	mmu-miR-670-5p	7.28	0.31	0.37	0.06	1.04
148450	mmu-miR-210-5p	7.80	-0.27	-0.21	0.06	1.04
169394	mmu-miR-1843a-5p	7.63	0.03	0.09	0.06	1.04
11231	mmu-miR-345-5p	8.78	-0.37	-0.30	0.07	1.05
148614	mmu-miR-7a-2-3p	8.45	-0.19	-0.11	0.07	1.05
148052	mmu-miR-374c-3p	7.94	0.28	0.37	0.08	1.06
146088	mmu-miR-1983	12.82	-0.25	-0.16	0.09	1.06
146143	mmu-miR-1904	7.64	-0.18	-0.08	0.10	1.07
169408	mmu-miR-181d-5p	8.36	-0.02	0.08	0.10	1.07
27565	mmu-miR-423-5p	10.75	-0.06	0.05	0.11	1.08
42902	mmu-miR-185-5p	9.72	-0.07	0.04	0.11	1.08
147165	mmu-let-7b-5p	12.16	0.46	0.58	0.12	1.09
42519	mmu-miR-465c-5p	9.06	-0.24	-0.12	0.12	1.09
42528	mmu-miR-296-3p	8.60	-0.15	-0.03	0.12	1.09

148278	mmu-miR-138-2-3p	9.39	-0.27	-0.14	0.13	1.09
148651	mmu-miR-3072-3p	8.66	0.49	0.62	0.13	1.09
148440	mmu-miR-452-3p	7.41	-0.58	-0.45	0.13	1.09
168876	mmu-miR-1843b-5p	8.00	-0.04	0.10	0.13	1.10
148191	mmu-miR-3081-3p	8.45	-0.40	-0.26	0.14	1.10
148230	mmu-miR-450a-1-3p	9.48	-0.13	0.01	0.14	1.10
17676	mmu-miR-152-3p	8.39	0.07	0.21	0.14	1.10
46774	mcmv-miR-m01-2-5p	8.08	-0.22	-0.07	0.14	1.11
146156	mmu-miR-1960	8.64	-0.07	0.07	0.15	1.11
148097	mmu-miR-329-5p	7.97	-0.17	-0.03	0.15	1.11
148560	mmu-miR-3066-5p	7.88	0.02	0.17	0.15	1.11
17431	mghv-miR-M1-8-5p	11.01	-0.18	-0.02	0.16	1.12
10943	mmu-miR-136-5p	8.34	0.18	0.34	0.16	1.12
148309	mmu-miR-3068-3p	11.98	-0.12	0.05	0.17	1.12
11208	mmu-miR-207	10.85	-0.53	-0.37	0.17	1.12
27572	mmu-miR-298-5p	8.34	-0.32	-0.15	0.17	1.13
17352	mghv-miR-M1-5-5p	9.76	-0.28	-0.10	0.17	1.13
42619	mmu-miR-709	13.63	-0.23	-0.06	0.18	1.13
148630	mmu-miR-3472	7.53	-0.41	-0.23	0.18	1.13

148103	mghv-miR-M1-4-3p	8.40	-0.35	-0.18	0.18	1.13
42790	mmu-miR-337-3p	8.47	-0.48	-0.29	0.19	1.14
11108	mmu-miR-425-3p	7.59	-0.30	-0.11	0.19	1.14
11226	mmu-miR-325-5p	7.92	-0.22	-0.03	0.19	1.14
147701	mmu-miR-491-3p	15.22	-0.11	0.08	0.19	1.14
11235	mmu-miR-351-5p	11.61	-0.41	-0.21	0.19	1.14
148480	mmu-miR-494-5p	7.59	-0.11	0.09	0.19	1.14
42887	mmu-miR-331-3p	8.28	-0.43	-0.23	0.20	1.15
42585	mmu-miR-297a/miR-297b/miR-297c-3p	11.24	0.00	0.20	0.20	1.15
148192	mmu-miR-421-3p	7.94	0.01	0.21	0.20	1.15
168977	mmu-miR-5128	10.04	-0.45	-0.25	0.20	1.15
27574	mmu-miR-705	10.68	-0.29	-0.09	0.20	1.15
11229	mmu-miR-341-3p	9.68	-0.68	-0.47	0.20	1.15
168752	mmu-miR-5627-3p	7.36	-0.20	0.01	0.20	1.15
42670	mmu-miR-500-3p	7.98	-0.02	0.20	0.22	1.16
168828	mmu-miR-5125	10.65	-0.30	-0.08	0.22	1.17
148252	mmu-miR-496a-5p	7.20	-0.12	0.11	0.22	1.17
11065	mmu-miR-335-5p	7.58	0.35	0.58	0.23	1.17
148099	mmu-miR-344h-3p	10.60	-0.28	-0.05	0.23	1.17

42878	mmu-miR-882	12.20	-0.19	0.04	0.23	1.17
168592	mmu-miR-5622-3p	7.35	-0.11	0.12	0.23	1.17
46385	mmu-miR-1186a	8.65	-0.20	0.04	0.24	1.18
145745	mmu-miR-335-3p	12.80	-0.37	-0.13	0.24	1.18
42471	mmu-miR-290-5p	11.89	-0.26	-0.01	0.24	1.18
33596	mmu-miR-126-5p	9.30	0.09	0.33	0.25	1.19
169111	mmu-miR-5616-3p	9.65	-0.29	-0.04	0.25	1.19
148558	mmu-miR-3064-5p	8.42	-0.08	0.16	0.25	1.19
169373	mmu-miR-5626-5p	9.14	0.40	0.65	0.25	1.19
148281	mmu-miR-467e-3p	12.79	-0.19	0.06	0.25	1.19
17632	mmu-miR-691	12.33	-0.19	0.06	0.25	1.19
148226	mmu-miR-467c-3p	10.54	-0.07	0.18	0.25	1.19
28944	mmu-miR-667-3p	11.64	-0.65	-0.39	0.26	1.20
42835	mmu-miR-16-1-3p	8.71	-0.27	-0.01	0.26	1.20
169420	mmu-miR-193b-5p	7.81	-0.47	-0.20	0.26	1.20
17540	mmu-miR-669b-5p	7.90	-0.05	0.22	0.27	1.20
148198	mmu-miR-653-3p	8.88	-0.14	0.13	0.27	1.21
168890	mmu-miR-1306-5p	7.62	-0.34	-0.06	0.27	1.21
148657	mmu-miR-381-5p	7.52	-0.02	0.27	0.28	1.22

17313	mmu-miR-297b-5p	7.58	0.04	0.33	0.28	1.22
42767	mmu-miR-34c-3p	8.97	-0.41	-0.13	0.29	1.22
145692	mmu-miR-499-3p	7.11	-0.25	0.04	0.29	1.22
14316	mmu-miR-664-3p	9.26	-0.40	-0.09	0.30	1.23
148155	mghv-miR-M1-1-5p	7.87	-0.36	-0.05	0.30	1.23
148427	mmu-miR-3101-3p	8.14	-0.15	0.15	0.30	1.24
11202	mmu-miR-151-3p	7.51	-0.38	-0.07	0.31	1.24
11210	mmu-miR-215-5p	7.26	-0.09	0.22	0.31	1.24
146171	mmu-miR-1907	8.02	-0.15	0.16	0.31	1.24
168689	mmu-miR-361-3p	8.92	0.41	0.74	0.33	1.26
148609	mmu-miR-487b-5p	8.40	-0.52	-0.19	0.33	1.26
11044	mmu-miR-302c-3p	7.59	-0.16	0.17	0.34	1.26
42709	mmu-miR-743b-5p	7.87	-0.47	-0.13	0.34	1.27
42445	mmu-miR-693-5p	9.98	-0.43	-0.09	0.34	1.27
17291	mghv-miR-M1-4-5p	11.55	-0.35	-0.01	0.35	1.27
11004	mmu-miR-203-3p	12.94	0.33	0.68	0.35	1.27
28309	mmu-miR-741-3p	8.33	-0.46	-0.11	0.35	1.27
148336	mmu-miR-3071-5p	7.32	-0.44	-0.09	0.35	1.28
11018	mmu-miR-218-5p	7.67	-0.32	0.03	0.35	1.28

17511	mmu-miR-713	9.11	-0.47	-0.12	0.35	1.28
145637	mmu-miR-187-3p	8.06	-0.13	0.22	0.36	1.28
42627	mmu-miR-212-3p	7.80	-0.65	-0.29	0.36	1.28
148473	mmu-miR-3473a	12.66	-0.54	-0.18	0.36	1.28
148575	mmu-miR-700-5p	8.09	-0.36	0.01	0.36	1.29
42739	mmu-miR-339-5p	8.19	-0.31	0.06	0.36	1.29
17433	mmu-miR-679-5p	8.28	-0.36	0.01	0.37	1.29
10306	mmu-miR-146b-5p	10.26	-0.11	0.26	0.37	1.29
148415	mmu-miR-668-5p	7.89	-0.40	-0.03	0.37	1.30
169344	mmu-miR-3473b	15.31	-0.33	0.05	0.38	1.30
148632	mmu-miR-2861	8.98	-0.48	-0.10	0.39	1.31
148548	mmu-miR-3090-3p	7.21	-0.84	-0.45	0.39	1.31
148199	mmu-miR-3102-3p	7.47	0.02	0.42	0.39	1.31
148355	mmu-miR-3077-3p	8.99	-0.46	-0.07	0.40	1.32
169051	mmu-miR-5120	9.84	-0.54	-0.14	0.40	1.32
42502	mmu-miR-204-3p	10.70	-0.37	0.03	0.40	1.32
11093	mmu-miR-379-5p	7.19	-0.21	0.19	0.41	1.33
11105	mmu-miR-378a/miR-378b/miR-378c	10.30	0.34	0.75	0.41	1.33
11014	mmu-miR-214-3p	10.82	-0.55	-0.14	0.41	1.33

146145	mmu-miR-1895	9.98	-0.47	-0.05	0.41	1.33
148531	mmu-miR-544-5p	10.07	-0.45	-0.03	0.42	1.34
148446	mmu-miR-346-3p	11.31	-0.22	0.20	0.42	1.34
42626	mmu-miR-30b-3p	10.70	-0.31	0.11	0.42	1.34
46639	mmu-miR-467f	11.87	-0.33	0.09	0.42	1.34
4610	mmu-miR-126-3p	11.41	-0.17	0.26	0.42	1.34
17422	mmu-miR-695	9.46	0.15	0.58	0.43	1.35
168580	mmu-miR-5626-3p	7.89	-0.41	0.02	0.43	1.35
148036	mghv-miR-M1-3-5p	8.28	-0.56	-0.12	0.44	1.36
17495	mmu-miR-697	10.23	-0.68	-0.23	0.44	1.36
148109	mmu-miR-669a/miR-669o-3p	11.46	-0.20	0.24	0.44	1.36
13485	mmu-miR-10a-5p	9.59	-0.31	0.13	0.44	1.36
42708	mmu-miR-99a-5p	9.62	-0.16	0.30	0.45	1.37
42868	mmu-miR-762	10.25	-0.19	0.26	0.45	1.37
42692	mmu-miR-127-5p	7.33	-0.72	-0.27	0.46	1.37
168713	mmu-miR-5135	7.30	-0.16	0.30	0.46	1.37
10928	mmu-miR-125a-5p	11.22	-0.28	0.17	0.46	1.37
17669	mmu-miR-690	15.12	-0.67	-0.21	0.46	1.37
42687	mmu-miR-883b-5p	10.25	-0.26	0.20	0.46	1.38

147203	mmu-miR-302a-3p	11.41	-0.28	0.18	0.46	1.38
42638	mmu-miR-23a-5p	8.43	-0.47	-0.01	0.47	1.38
169329	mmu-miR-370-3p	7.94	-0.70	-0.23	0.47	1.39
148423	mmu-miR-652-5p	7.29	-0.48	-0.01	0.47	1.39
17898	mmu-miR-99b-3p	9.28	-0.57	-0.09	0.47	1.39
148649	mmu-miR-3470a	9.37	-0.48	0.00	0.48	1.40
46288	mmu-miR-1196-5p	13.09	-0.70	-0.22	0.48	1.40
148094	mmu-miR-669c-3p	12.22	-0.26	0.23	0.49	1.40
148175	mmu-miR-1843a-3p	10.42	-0.65	-0.15	0.49	1.41
168787	mmu-miR-5114	9.60	-0.52	-0.02	0.50	1.41
146176	mmu-miR-1971	12.83	-0.28	0.22	0.50	1.41
148171	mmu-miR-7b-3p	8.62	-0.69	-0.20	0.50	1.41
30033	mmu-miR-877-5p	9.98	-0.38	0.12	0.50	1.41
42658	mmu-miR-681	8.26	-0.40	0.10	0.50	1.42
148210	mmu-miR-3060-3p	9.32	-0.91	-0.40	0.51	1.42
148508	mmu-miR-3062-3p	7.84	-0.66	-0.15	0.51	1.43
148448	mmu-miR-3112-3p	8.04	-0.49	0.03	0.51	1.43
42865	mmu-miR-181a-5p	8.90	-0.07	0.45	0.52	1.43
29650	mmu-miR-714	11.24	-1.02	-0.50	0.52	1.43

27672	mmu-miR-615-3p	9.14	-0.75	-0.23	0.52	1.43
148579	mmu-miR-3544-3p	7.32	-0.35	0.17	0.52	1.44
46205	SNORD48	9.35	-0.48	0.05	0.52	1.44
147198	mmu-miR-26a-5p	9.78	0.03	0.56	0.53	1.44
168738	mmu-miR-5127	8.29	-0.94	-0.42	0.53	1.44
145840	mmu-let-7f-1-3p	8.65	-0.57	-0.04	0.53	1.44
145943	mmu-miR-100-5p	8.06	-0.26	0.27	0.54	1.45
28624	mmu-miR-666-5p	9.25	-1.06	-0.52	0.54	1.45
168794	mmu-miR-5107-5p	9.64	-0.54	0.00	0.54	1.45
17465	mmu-miR-678	9.53	-0.50	0.04	0.54	1.45
42592	mmu-miR-338-3p	8.49	0.07	0.61	0.54	1.46
168688	mmu-miR-1843b-3p	14.11	-1.04	-0.50	0.55	1.46
17918	mmu-miR-222-5p	7.36	-0.82	-0.27	0.55	1.46
30681	mmu-miR-376c-3p	8.09	-0.49	0.07	0.56	1.47
11253	mmu-miR-467d-3p	9.11	-0.23	0.33	0.56	1.47
169053	mmu-miR-130b-5p	7.90	-0.52	0.05	0.56	1.48
148045	mmu-miR-3094-3p	7.19	-0.83	-0.26	0.57	1.48
146195	mmu-miR-2139	8.52	-0.56	0.01	0.57	1.48
42826	mmu-miR-300-5p	13.43	-0.40	0.18	0.58	1.50

168817	mmu-miR-5621-3p	8.37	-0.97	-0.39	0.58	1.50
168740	mmu-miR-5113	13.87	-0.50	0.09	0.59	1.50
42490	mmu-miR-505-5p	9.96	-0.46	0.13	0.59	1.50
146023	mmu-miR-1946b	9.68	-0.28	0.31	0.59	1.51
146130	mmu-miR-1946a	7.64	-0.55	0.07	0.61	1.53
169148	mmu-miR-5130	8.24	-0.71	-0.10	0.61	1.53
42574	mmu-miR-467e-5p	10.21	-0.49	0.13	0.62	1.54
42462	mmu-miR-883a-5p	13.01	-0.50	0.12	0.63	1.54
148022	mmu-miR-664-5p	8.47	-0.58	0.05	0.63	1.55
146147	mmu-miR-1897-5p	14.16	-0.66	-0.03	0.63	1.55
42770	mmu-miR-665-3p	12.72	-0.54	0.12	0.65	1.57
32608	mmu-miR-761	8.58	-0.45	0.20	0.66	1.58
168617	mmu-miR-5131	7.17	-0.59	0.07	0.66	1.58
31026	mmu-miR-101a-3p	10.81	-0.14	0.53	0.67	1.59
168777	mmu-miR-5615-5p	9.09	-0.52	0.15	0.67	1.59
27855	mmu-miR-763	10.93	-1.09	-0.42	0.67	1.59
148122	mmu-miR-669p-3p	12.47	-0.45	0.22	0.67	1.60
146187	mmu-miR-1941-3p	9.28	-0.73	-0.06	0.67	1.60
17527	mmu-miR-717	8.33	-0.62	0.06	0.68	1.60

168913	mmu-miR-5115	10.51	-0.26	0.42	0.68	1.60
42916	mmu-miR-471-5p	8.73	-0.92	-0.24	0.68	1.61
148668	mmu-miR-378a-3p	11.24	0.01	0.69	0.68	1.61
148655	mmu-miR-3471	7.19	-0.66	0.03	0.69	1.61
148553	mmu-miR-1948-5p	7.73	-0.77	-0.08	0.69	1.62
148158	mghv-miR-M1-5-3p	8.84	-1.14	-0.45	0.69	1.62
42723	mmu-miR-195a-3p	9.08	-0.80	-0.10	0.70	1.63
146193	mmu-miR-1957a	10.63	-0.89	-0.18	0.71	1.63
17904	mmu-miR-185-3p	13.39	-0.42	0.30	0.72	1.65
148426	mmu-miR-466a/miR-466b/miR-466c-3p	9.88	-0.38	0.35	0.72	1.65
46206	SNORD44	8.83	-0.69	0.03	0.72	1.65
145994	mmu-miR-1900	11.60	-0.64	0.08	0.73	1.66
148020	mmu-miR-3078-3p	9.31	-0.72	0.01	0.73	1.66
148527	mmu-miR-669a-3-3p	11.99	-0.45	0.28	0.73	1.66
148212	mmu-miR-3103-3p	11.39	-0.79	-0.06	0.73	1.66
27568	mmu-miR-744-5p	11.33	-0.17	0.56	0.73	1.66
148259	mmu-miR-3070a/miR-3070b-5p	8.45	-1.05	-0.31	0.75	1.68
10952	mmu-miR-146a-5p	9.53	-0.33	0.42	0.75	1.68
42587	mmu-miR-881-5p	10.63	-0.59	0.16	0.75	1.68

148090	mmu-miR-495-5p	9.72	-0.73	0.02	0.75	1.68
148180	mmu-miR-669e-3p	9.66	-0.41	0.35	0.76	1.69
148244	mmu-miR-3098-3p	11.19	-0.91	-0.15	0.76	1.69
146021	mmu-miR-1935	11.52	-0.57	0.19	0.76	1.70
42694	mmu-miR-485-3p	9.82	-1.02	-0.25	0.77	1.70
6880	mmu-miR-297a-5p	9.37	-0.50	0.27	0.77	1.71
46979	mmu-miR-669h-3p	7.91	-0.53	0.24	0.77	1.71
11221	mmu-miR-300-3p	8.63	-0.65	0.13	0.77	1.71
29872	mmu-miR-340-5p	10.63	-1.06	-0.28	0.77	1.71
147366	mmu-miR-320-5p	9.36	-0.89	-0.11	0.77	1.71
146125	mmu-miR-1903	9.84	-0.83	-0.05	0.78	1.72
169127	mmu-miR-101a/miR-101c	9.94	-0.39	0.40	0.79	1.73
17537	mghv-miR-M1-3-3p	10.44	-0.71	0.08	0.79	1.73
168694	mmu-miR-5616-5p	9.74	-0.76	0.03	0.79	1.73
146163	mmu-miR-224-3p	9.99	-1.16	-0.37	0.80	1.74
42576	mmu-miR-342-5p	7.38	-0.83	-0.03	0.80	1.74
42861	mmu-miR-466d-3p	9.66	-0.42	0.38	0.81	1.75
42518	mmu-miR-465b-5p	11.44	-1.09	-0.28	0.81	1.75
46807	mmu-miR-466f-3p	12.19	-0.54	0.28	0.81	1.76

148533	mmu-miR-1943-3p	9.65	-0.88	-0.06	0.81	1.76
148535	mmu-miR-3097-5p	9.64	-0.75	0.07	0.82	1.76
46485	mmu-miR-669f-3p	11.96	-0.59	0.23	0.82	1.76
146055	mmu-miR-1954	10.72	-0.93	-0.11	0.82	1.76
148567	mmu-miR-1249-5p	7.87	-1.12	-0.30	0.82	1.76
146050	mmu-miR-669n	13.21	-0.67	0.15	0.82	1.76
42978	mmu-miR-466a/miR-466e-3p	8.12	-0.44	0.38	0.82	1.76
46976	mmu-miR-467g	11.59	-0.50	0.32	0.82	1.77
168651	mmu-miR-466q	11.49	-0.59	0.24	0.83	1.78
148184	mmu-miR-466m-3p	8.04	-0.58	0.26	0.84	1.79
46374	mmu-miR-466i-3p	10.39	-0.57	0.27	0.84	1.79
146097	mmu-miR-1934-5p	10.50	-1.31	-0.47	0.84	1.79
46978	mmu-miR-669i	8.29	-0.47	0.38	0.85	1.80
10925	mmu-miR-10b-5p	9.58	-0.62	0.23	0.85	1.80
146054	mmu-miR-1952	11.76	-1.19	-0.34	0.85	1.81
42703	mmu-miR-490-3p	10.59	-1.20	-0.35	0.86	1.81
17388	mmu-miR-669a-5p/mmu-miR-669p-5p	10.28	-0.66	0.20	0.86	1.82
168771	mmu-miR-5624-3p	10.06	-0.67	0.19	0.86	1.82
147953	mmu-miR-491-5p	7.66	-0.91	-0.05	0.86	1.82

146030	mmu-miR-2183	10.40	-1.09	-0.22	0.87	1.83
10995	mmu-miR-199a-3p/mmu-miR-199b-3p	10.66	-0.95	-0.08	0.87	1.83
148608	mmu-miR-551b-5p	10.23	-1.30	-0.42	0.88	1.85
168835	mmu-miR-5621-5p	7.98	-1.06	-0.17	0.89	1.85
148647	mmu-miR-3470b	10.85	-0.95	-0.05	0.90	1.86
42895	mmu-miR-881-3p	9.22	-0.84	0.06	0.90	1.87
146221	mmu-miR-669c-5p	13.66	-0.77	0.13	0.90	1.87
46453	mmu-miR-466f-5p	10.81	-0.73	0.19	0.92	1.89
42706	mmu-miR-325-3p	10.87	-1.30	-0.38	0.92	1.90
16528	mmu-miR-706	14.07	-1.02	-0.09	0.93	1.90
146081	mmu-miR-1929-5p	10.58	-0.74	0.20	0.94	1.91
148248	mmu-miR-344e-3p	8.33	-1.06	-0.12	0.94	1.92
42752	mmu-miR-872-3p	11.41	-1.50	-0.56	0.94	1.92
45985	mmu-miR-546	7.99	-1.00	-0.06	0.94	1.92
148631	mmu-miR-466j	10.56	-0.75	0.21	0.96	1.95
148378	mmu-miR-511-3p	8.17	-0.58	0.38	0.97	1.95
148068	mmu-miR-758-5p	10.64	-0.89	0.08	0.97	1.96
46734	mmu-miR-467h	10.43	-0.76	0.21	0.97	1.96
148636	mmu-miR-466f	13.10	-0.90	0.09	0.98	1.97

148325	mmu-miR-1981-3p	10.17	-1.25	-0.26	0.99	1.99
148490	mmu-miR-1224-3p	10.43	-1.25	-0.26	0.99	1.99
169364	mmu-miR-3572-3p	10.78	-1.13	-0.13	1.00	2.00
42945	mmu-miR-297c-5p	10.30	-0.79	0.22	1.00	2.00
168981	mmu-miR-378b	10.91	-0.37	0.63	1.00	2.01
148267	mmu-miR-3082-5p	13.72	-1.07	-0.04	1.02	2.03
11254	mmu-miR-468-3p	10.80	-0.95	0.08	1.03	2.04
11041	mmu-miR-29c-3p	10.29	-0.59	0.45	1.04	2.05
42606	mmu-miR-330-3p	9.34	-1.07	-0.02	1.04	2.06
169058	mmu-miR-1231-3p	9.02	-1.09	-0.04	1.06	2.08
148521	mmu-miR-466m-5p/mmu-miR-669m-5p	10.41	-0.91	0.16	1.07	2.10
27740	mmu-miR-574-5p	12.31	-0.91	0.17	1.08	2.12
145677	mmu-miR-139-5p	11.11	-2.01	-0.92	1.08	2.12
148444	mghv-miR-M1-2-5p	10.19	-0.89	0.20	1.08	2.12
168826	mmu-miR-5624-5p	11.38	-1.43	-0.34	1.08	2.12
146039	mmu-miR-669o-5p	12.20	-0.88	0.24	1.12	2.17
29575	mmu-miR-32-3p	13.38	-1.06	0.06	1.12	2.18
46346	mmu-miR-669e-5p	11.60	-0.99	0.14	1.13	2.18
148249	mghv-miR-M1-6-5p	12.12	-1.08	0.05	1.13	2.18

148403	mmu-miR-3065-3p	9.41	-0.49	0.64	1.13	2.19
148690	mmu-miR-466d-5p	12.57	-1.05	0.08	1.13	2.19
42894	mmu-miR-466e-5p	11.78	-0.99	0.15	1.13	2.19
169153	mmu-miR-5116	13.65	-1.25	-0.11	1.14	2.21
42530	mmu-let-7a-2-3p	10.14	-1.44	-0.30	1.14	2.21
148354	mmu-miR-466a-5p	11.40	-1.00	0.15	1.15	2.22
46310	mmu-miR-1187	11.55	-0.95	0.20	1.15	2.22
148433	mmu-miR-466i-5p	14.06	-1.22	-0.05	1.17	2.25
148570	mmu-miR-466n-5p	11.25	-1.01	0.17	1.19	2.28
146002	mmu-miR-669l-5p	12.05	-1.05	0.18	1.22	2.33
42803	mmu-miR-466c-5p	12.03	-1.10	0.13	1.23	2.35
147994	mmu-miR-669d-5p	12.46	-1.15	0.09	1.24	2.36
169024	mmu-miR-3960	10.80	-0.80	0.45	1.25	2.37
42847	mmu-miR-497-5p	7.82	-1.07	0.18	1.25	2.38
46381	mmu-miR-1298-5p	8.38	-0.77	0.48	1.25	2.38
148034	mmu-miR-669f-5p	12.47	-1.16	0.11	1.26	2.40
148339	mmu-miR-665-5p	11.48	-1.32	-0.06	1.27	2.41
46306	mmu-miR-466a-5p/mmu-miR-466p-5p	12.43	-1.12	0.15	1.27	2.41
29562	mmu-miR-199a-5p	10.89	-1.36	-0.07	1.29	2.44

148409	mmu-miR-669k-5p	12.59	-1.12	0.19	1.31	2.48
148143	mmu-miR-466b-5p/mmu-miR-466o-5p	11.83	-1.13	0.18	1.32	2.49
169291	mmu-miR-5126	9.84	-1.18	0.18	1.36	2.56
148653	mmu-miR-3474	13.12	-1.37	-0.01	1.36	2.57
42659	mmu-miR-290-3p	12.03	-1.29	0.08	1.36	2.57
42641	mmu-miR-145a-5p/mmu-miR-145b	9.12	-1.03	0.34	1.38	2.60
11205	mmu-miR-199b-5p	10.30	-1.29	0.16	1.46	2.74
148536	mmu-miR-1a-1-5p	7.62	-0.98	0.66	1.64	3.11
148279	mmu-miR-449a-3p	7.55	-1.42	0.25	1.67	3.19
42538	mmu-miR-196a-2-3p	9.41	-2.01	-0.15	1.86	3.62
11007	mmu-miR-206-3p	9.57	-1.03	0.86	1.88	3.69
13177	mmu-miR-143-3p	11.03	-1.51	0.54	2.05	4.14
42765	mmu-miR-339-3p	9.64	-1.90	0.29	2.19	4.56
17517	mmu-miR-688	11.16	-2.37	0.38	2.76	6.75
17653	mmu-miR-133a-5p	7.71	-2.06	1.03	3.09	8.50
146137	mmu-miR-133a-3p	10.30	-3.39	1.16	4.55	23.35
146160	mmu-miR-133b-3p	10.87	-3.50	1.15	4.65	25.09
10916	mmu-miR-1a-3p	11.21	-4.97	1.21	6.18	72.36