

Original Article

MicroRNA-130a expression is decreased in Xinjiang Uyghur patients with type 2 diabetes mellitus

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Abstract: Aims: MicroRNAs play important roles in energy metabolism, insulin synthesis, insulin transport and the development of diabetes. This study aims to investigate the expression and effect of microRNA-130a in Uyghur patients with type 2 diabetes mellitus (T2DM). Materials and methods: Peripheral blood and omental adipose tissues were collected from individuals with normal glucose tolerance and patients with T2DM. The microRNA expression profile of peripheral blood was established by microarray analysis. The differentially expressed microRNAs and possible target genes were identified by bioinformatics analysis. MicroRNA-130a mimics and inhibitors were transfected into 3T3-L1 preadipocytes. Results: Our results showed that microRNA-130a expression level was significantly decreased in peripheral blood and omental adipose tissues of T2DM patients ($P < 0.01$). Peroxisome proliferator-activated receptors γ (PPAR γ) were predicted as target genes of microRNA-130a. This prediction was verified by the results that PPAR γ mRNA expression in omental adipose tissues of T2DM patients were significantly increased ($P < 0.01$). The glucose consumption level after microRNA-130a transfection was significantly decreased ($P < 0.05$). And, microRNA-130a mimics inhibited PPAR γ expression at both mRNA and protein level, further suggesting that PPAR γ is a target gene of microRNA-130a. Additionally, adiponectin, lipoprotein lipase, CCAAT enhancer binding protein α , and the downstream genes of PPAR γ , were significantly decreased after microRNA-130a mimics transfection. Conclusions: In conclusion, microRNA-130a is decreased in Uyghur patients with T2DM and it may play a role in T2DM through targeting PPAR γ .

Keywords: microRNAs, Uyghur, type 2 diabetes, microarray, peroxisome proliferator-activated receptors γ , tumor necrosis factor α

Introduction

Diabetes mellitus (DM) is now an increasingly serious health problem faced by many countries and its prevalence rate is increasing [1, 2]. China has become one of the countries that have the fastest growing rate in DM prevalence. Ning et al [3] reported that the average prevalence rate of DM in Chinese adults was 11.6%. An epidemiological study has shown that the prevalence rate of type 2 DM (T2DM) was 8.42% in Uyghur, Xinjiang, China [4].

MicroRNAs (miRNAs) are a class of small non-coding RNA molecules, with the length of 21

to 25 nucleotides. They can bind with the 3'-untranslated region of the target genes, promote the degradation of mRNA, or inhibit the translation of mRNA, thus inhibiting the expression of the target proteins [5]. MiRNAs play important roles in many events, such as cell differentiation [6] and animal development [7]. Poy et al [8] reported that miR-375 overexpression in pancreatic β cells inhibited glucose-induced insulin secretion. miR-14 can regulate the size of lipid droplets and the levels of triglycerides [9]. miR-122 is involved in the regulation of lipid metabolism [10]. miR-133 and miRNA-1 are muscle specific miRNAs and play important

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Table 1. Biochemical index of 6 individuals with NGT and 6 patients with T2DM

Subjects	Age (years)	BMI (kg/m ²)	SBP (mmHg)	DBP (mmHg)	FPG (mmol/L)	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
NGT	53 ± 7	23.4 ± 5.5	138 ± 38	81 ± 14	4.85 ± 0.41	4.13 ± 0.71	1.58 ± 0.79	0.91 ± 0.16	2.29 ± 0.45
T2DM	54 ± 11	30.4 ± 2.5*	131 ± 14	85 ± 10	10.36 ± 4.49*	5.67 ± 1.76	3.63 ± 1.96*	0.92 ± 0.32	3.00 ± 0.81

Note: Body mass index (BMI), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Fasting blood glucose (FBG), Total cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), Normal glucose tolerance group (NGT), Type 2 diabetes mellitus (T2DM). *P < 0.05, T2DM vs NGT.

Table 2. Clinical data of 24 individuals with NGT and 12 patients with T2DM

Subjects	Age (years)	BMI (kg/m ²)	SBP (mmHg)	DBP (mmHg)	FPG (mmol/L)	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
NGT	49 ± 13	26.3 ± 3.6	124 ± 21	76 ± 10	4.99 ± 0.86	3.07 ± 1.08	1.82 ± 1.44	1.94 ± 0.89	2.96 ± 0.78
T2DM	56 ± 10	30.9 ± 5.8*	127 ± 19	78 ± 11	10.08 ± 4.35*	4.41 ± 0.89*	2.80 ± 2.33	0.96 ± 0.21*	2.67 ± 0.70

Note: Body mass index (BMI), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Fasting blood glucose (FBG), Total cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), Normal glucose tolerance group (NGT), Type 2 diabetes mellitus (T2DM). *P < 0.05, T2DM vs NGT.

roles in the regulation of muscle cell differentiation [11].

It is reported that miRNAs may also be involved in the pathogenesis of T2DM. Short non-coding miRNAs can control exocytosis, the final event in insulin secretion, and are the “ribo-regulators” of glucose homeostasis [12]. He et al [13] found that overexpression of miRNA-29 significantly inhibited insulin-stimulated glucose uptake, and promoted insulin resistance, resulting in the development of T2DM. Therefore, in this study, the miRNAs associated with the pathogenesis of T2DM were screened with micro-array in Uyghur patients with T2DM. The mechanisms underlying the role of the differentially expressed miRNAs in T2DM were also investigated.

Materials and methods

Clinical data

A total of 72 individuals from Xinjiang Uyghur, including 42 individuals with normal glucose tolerance (NGT) and 30 patients with T2DM, were enrolled in this study. Inclusion criteria: Their age was between 30 to 80 years old. They were Uyghur males and females for three generations of linear relatives and they were unrelated. They lived in Xinjiang Uyghur Autonomous Region for more than 20 years. Exclusion criteria: Pregnant or lactating women; Patients with a history of mental illness or drug abuse; Patients who underwent surgery or with other emergency situations; Patients who recently

took antibiotics, steroids or probiotics; Patients with obvious liver and kidney dysfunction, gastrointestinal diseases (such as chronic gastrointestinal disorders, diarrhea, biliary tract infection and enteritis), or serious diseases of the blood or the endocrine systems; Patients with severe heart diseases and with systolic blood pressure > 160 mmHg and diastolic blood pressure > 95 mmHg; Patients who required insulin treatment or had a history of ketoacidosis; Patients with type I DM, gestational DM or other particular types of DM. T2DM was diagnosed according to the 2011 American Diabetes Association Guidelines for Diagnosis. Patients with fasting blood glucose level ≥ 7.0 mmol/L (126 mg/dL) or blood glucose level ≥ 11.1 mmol/L (200 mg/dL) after 2 h of oral glucose tolerance test were diagnosed as T2DM. Patients with fasting blood glucose level < 6.1 mmol/L (110 mg/dL) and 2 h post-meal blood glucose level < 7.8 mmol/L (140 mg/dL) were determined as NGT.

Among the 72 individuals, peripheral blood was collected from 48 individuals. Peripheral blood of 6 individuals with NGT and 6 patients with T2DM were used for microarray assay. Their clinical data was shown in **Table 1**. Peripheral blood of 24 individuals with NGT and 12 patients with T2DM were used for detecting expression of miRNAs. Their clinical data was shown in **Table 2**. Among the 72 individuals, omental adipose tissue was collected from 24 individuals, including 12 NGT and 12 T2DM. Their clinical data was shown in **Table 3**.

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Table 3. Clinical data of 12 individuals with NGT and 12 patients with T2DM

Subjects	Age (years)	BMI (kg/m ²)	SBP (mmHg)	DBP (mmHg)	FPG (mmol/L)	TC (mmol/L)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)
NGT	53 ± 14	25.7 ± 4.2	116 ± 17	75 ± 17	4.88 ± 0.60	4.53 ± 0.88	1.04 ± 0.53	1.11 ± 0.40	2.79 ± 1.19
T2DM	57 ± 11	27.9 ± 4.2	120 ± 6	75 ± 7	10.20 ± 3.01*	4.68 ± 0.72	2.12 ± 1.59*	1.28 ± 0.38	2.53 ± 0.87

Note: Body mass index (BMI), Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Fasting blood glucose (FBG), Total cholesterol (TC), Triglyceride (TG), High-density lipoprotein cholesterol (HDL-C), Low-density lipoprotein cholesterol (LDL-C), Normal glucose tolerance group (NGT), Type 2 diabetes mellitus (T2DM). *P < 0.05, T2DM vs NGT.

Table 4. Primer sequences used in real-time PCR

Genes	Primer sequence
β-actin (human)	Forward: 5'-TGGCACCCAGCACAATGAA-3' Reverse: 5'-CTAAGTCATAGTCCGCCTAGAAGCA-3'
PPARγ (human)	Forward: 5'-CAC AGG CCG AGA AGGAGAA-3' Reverse: 5'-TTG GTC AGC GGG AAGGA-3'
β-actin (mouse)	Forward: 5'-GTGACGTTGACATCCGTAAGA-3' Reverse: 5'-GCCGGACTCATCGTACTCC-3'
PPARγ (mouse)	Forward: 5'-CTCCAAGAATACCAAGTGCGA-3' Reverse: 5'-GCCTGATGCTTTATCCCCACA-3'
LPL (mouse)	Forward: 5'-TGGCGTAGCAGGAAGTCTGA-3' Reverse: 5'-TGCTCCATTGGGATAAATGTC-3'
GLUT4 (mouse)	Forward: 5'-GTGACTGGAACACTGGTCCTA-3' Reverse: 5'-CCAGCCACGTTGCATTGTAG-3'
APM1 (mouse)	Forward: 5'-ACAAGGCCGTTCTCTCACC-3' Reverse: 5'-GTCCATTGTGGTCCCCATCC-3'
CEBPα (mouse)	Forward: 5'-CAAGAACAGCAACGAGTACCG-3' Reverse: 5'-GTCAGTGGTCAACTCCAGCAC-3'

Note: peroxisome proliferator-activated receptors γ (PPARγ), lipoprotein lipase (LPL), glucose transporter 4 (GLUT4), adiponectin (APM1), CCAAT enhancer binding protein α (CEBPα).

Prior written and informed consent were obtained from every patient and the study was approved by the ethics review board of Xinjiang Medical University.

3T3-L1 cell culture and treatment

The 3T3-L1 preadipocytes were obtained from Dr. Qiqun Tang from the Institute of Biological Science, Fudan University (Shanghai, China). They were cultured in DMEM high glucose medium (GIBCO, Carlsbad, CA, USA) supplemented with 10% fetal bovine serum (GIBCO, Carlsbad, CA, USA) and 1% penicillin-streptomycin (GIBCO, Carlsbad, CA, USA). And, they were kept in an incubator at 37 °C with 5% CO₂.

The 3T3-L1 preadipocytes at the exponential phase were seeded into 6 well plates at a concentration of 1 × 10⁶ cells/ml. After culturing for 5 days, 0.5 mM IBMX (Sigma-Aldrich, St. Louis, USA), 2.5 μM dexamethasone (Sigma-

Aldrich, St. Louis, USA), and 10 μg/ml insulin (ROCHE, Mannheim, Germany) were added to induce the differentiation of preadipocytes. The 3T3-L1 preadipocytes were transfected with miR-130a mimics and inhibitors (Qiagen, Valencia, CA, USA) using Hiperfect Transfection Reagent (Qiagen, Valencia, CA, USA). The constructs were custom synthesized from Qiagen. Cells were divided into the following groups: the control group, the mir-130a mimics group (75 nM) and the mir-130a inhibitor group (75 nM). After culturing for 72 h, cells were collected for further analysis.

Micro-array analysis

Total RNAs were extracted from peripheral blood using TRI REAGENT BD (ChinaGen, Inc, Shenzhen, China). For fluorescent probe labeling, miRNAs were labeled with Hy3TM or Hy5TM fluorophore using miRCURYTM Array Power labeling kit (Exiqon, Vedbaek, Denmark). Under standard conditions, fluorescence labeled probes were hybridized with miRCURYTM chip (Exiqon, Vedbaek, Denmark) in PhalanxTM hybridization bags (Exiqon, Vedbaek, Denmark). The fluorescence intensity was scanned on a GenePix 4000B scanner (Axon Instruments, Foster City, CA, USA) and the scanning results were converted into digital data. The results were analyzed by the softwares of targetscan, miRBase and miRanda.

Real-time PCR

Total RNAs were extracted from peripheral blood, omental adipose tissue and 3T3-L1 preadipocytes. Then, RNAs were reversely transcribed into cDNA. For amplification of miRNAs, the miRNA-specific forward primers and a reverse universal primer were designed and synthesized by Qiagen (Valencia, CA, USA). The real-time PCR for miRNA amplification was per-

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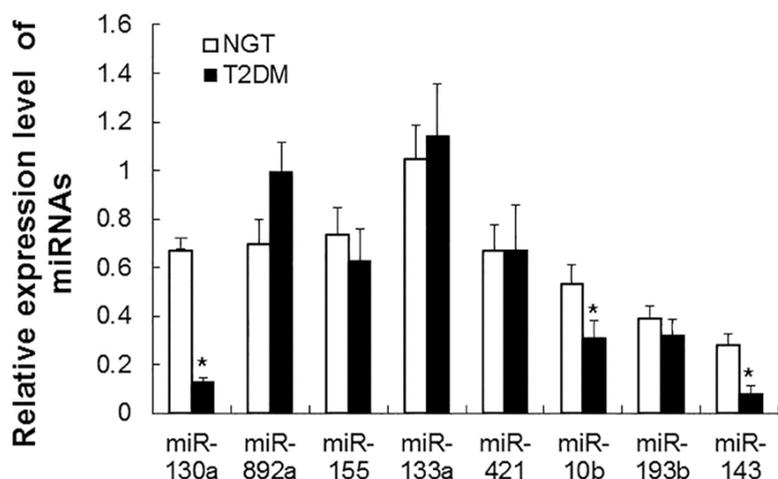


Figure 1. Analysis of miRNA expression in peripheral blood of NGT and T2DM patients. Real-time PCR was performed to analyze the expression levels of miR-130a, 892a, 155, 133a, 421, 10b, 193b, 29a, 143, and 107. β -actin was used as an internal control. Relative expression levels of miRNAs were calculated based on those of β -actin. Compared with NGT, * $P < 0.01$.

formed according to the instructions provided by the miScript SYBR® Green PCR kit (Qiagen). The following PCR procedures were used, initial activation at 95°C for 15 min, followed by 40 cycles of denaturation at 95°C for 15 seconds, annealing at 55°C for 30 seconds, and extension at 70°C for 30 seconds.

For mRNA quantification, RNA was extracted and reversely transcribed into cDNA. For amplification of peroxisome proliferator-activated receptors γ (PPAR γ), β -actin, lipoprotein lipase (LPL), adiponectin (APM1), CCAAT enhancer binding protein α (CEBP α) and their primers were designed by Primer 5.0 and synthesized by Sangon (Sangon Biotech Co., Ltd., Shanghai, China). The amplification was performed according to the instructions of miScript SYBR® Green PCR kit. The primer sequences were shown in **Table 4**. β -actin was used as an internal control. The $2^{-\Delta\Delta Ct}$ method was used to calculate the relative expression levels of genes.

Measurement of the content of glucose

At 72 h after transfection, cell culture supernatant was collected and the levels of glucose were detected by Glucose Assay Kit (BioVision, Mountain View, CA, USA) according to the manufacturers' instructions. Briefly, the standard curve was generated by measuring the glucose standard sample. The absorbance of cell culture supernatant was measured at 570 nm by

colorimetric assay. Finally, the levels of glucose consumption were calculated by $C = Sa/Sv$ (nmol/ μ l or μ μ mol/ml, or mM). Sa is the sample amount from standard curve. Sv is the sample volume added into the sample wells.

Western blot analysis

At 72 h after transfection, total proteins were extracted from 3T3-L1 preadipocytes. 3T3-L1 cells were immediately lysed in an ice-cold RIPA buffer. The protein was quantified by BCA assay (Pierce Endogen, IL, USA). Samples were then separated on 10-12% SDS

polyacrylamide gels and proteins were transferred to a PVDF membrane (BIO-RAD, CA, USA). The membrane was first incubated with primary antibodies against PPAR γ (Cell signaling, Boston, USA) and GAPDH (Santa Cruz Biotechnology Inc., CA, USA). Then, the membrane was incubated with secondary antibodies conjugated with horseradish peroxidase (HRP). The membrane was detected using the ECL Western blotting analysis system.

Statistical analysis

Data were analyzed with SPSS 17.0 software. All experimental data were presented as means \pm SD. Student's t-test was used to analyze comparison between groups). ANOVA followed by a Tukey analysis test was used for multiple comparisons. $P < 0.05$ was considered as statistically significant.

Results

Expression profile of miRNAs in NGT and T2DM patients

To identify the differentially expressed miRNAs between NGT and T2DM patients, microarray assay was performed. Total RNAs from peripheral blood of NGT and T2DM patients were used for analysis. The microarray assay results were analyzed by targetscan, miRBase and miRanda. A total of 59 kinds of differentially

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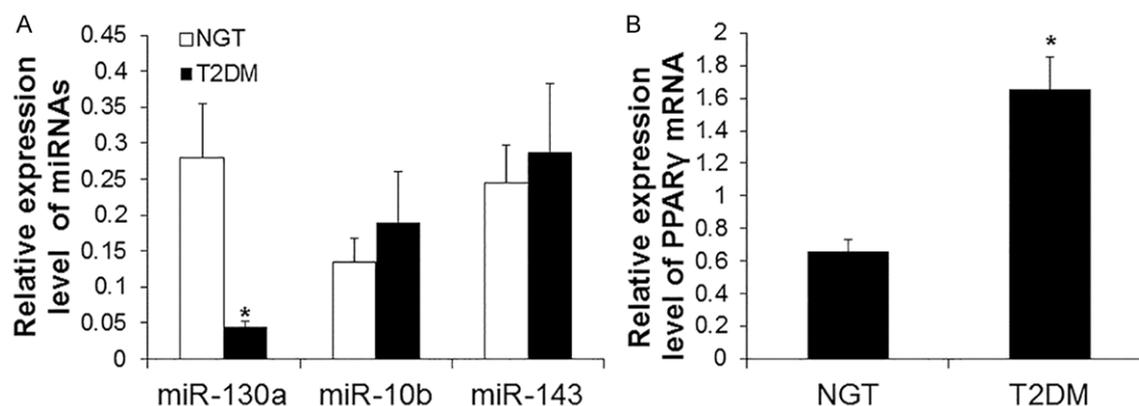


Figure 2. Analysis of miRNA and PPAR γ expression in omental adipose tissues of NGT and T2DM patients. Real-time PCR was performed to analyze the expression levels of miRNAs and PPAR γ . β -actin was used as an internal control. Relative expression levels were calculated based on those of β -actin. A. Expression levels of miR-130a, 107, 29a, and 143. Compared with NGT, * $P < 0.01$. B. Expression levels of PPAR γ mRNA. Compared with NGT, * $P < 0.05$.

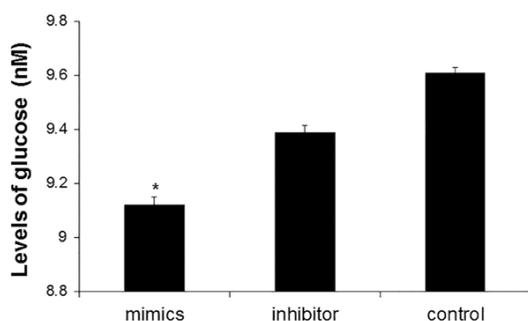


Figure 3. Analysis of glucose consumption level after miR-130a mimics transfection. At 72 h after transfection with miR-130a mimics, miR-130a inhibitors and control siRNA, cell culture supernatant of 3T3-L1 preadipocytes was collected and the levels of glucose were measured. Compared with control, * $P < 0.05$.

expressed miRNAs were identified. The fold change of miRNA expression in T2DM patients to that in NGT individuals was calculated. Among these 59 miRNAs, there were 8 miRNAs with fold change more than 2, including miR-130a, 892a, 155, 133a, 421, 10b, 193b, 143. Furthermore, the predicted target genes of these miRNAs were associated with glucose and lipid metabolism. For example, PPAR γ , which was the predicted target gene of miR-130a, is best known for its role in regulating adipogenic pathways. FGF1 (fibroblast growth factor 1), which was the predicted target gene of miR-133a, is a key regulator of human adipogenesis. These results indicate that these differentially expressed miRNAs in Xinjiang Uygur patients with T2DM might play an important role in glucose and lipid metabolism.

MicroRNAs of miR-130a, 10b and 143 are decreased in peripheral blood of T2DM patients

To further verify the microarray results, real-time PCR was conducted to detect the expression levels of miRNAs in peripheral blood of NGT and T2DM patients. Quantitative real-time PCR results were shown. As shown in **Figure 1**, the expression levels of miR-130a, 10b and 143 in T2DM patients were significantly lower than those in NGT individuals ($P < 0.01$). The expression levels of hsa-miR-155, 892a, 133a, 421 and 193b were not significantly different between NGT and T2DM patients. These results suggest that miR-130a, 10b and 143 are decreased in peripheral blood of Xinjiang Uygur patients with T2DM.

miR-130a levels are decreased while PPAR γ mRNA levels are elevated in omental adipose tissues of T2DM patients

The expression levels of miR-130a, 10b and 143 in omental adipose tissues of NGT and T2DM patients were further measured by real-time PCR. As shown in **Figure 2A**, the expression levels of miR-130a in T2DM patients were significantly lower than those in NGT individuals ($P < 0.01$). However, no significant difference was found in the expression levels of miR-10b and 143 between NGT and T2DM patients. These results suggest that miR-130a might play important role in adipocyte.

As predicted by targets can, miRBase and miRanda, PPAR γ were possible target genes of miR-130a. To determine the expression levels

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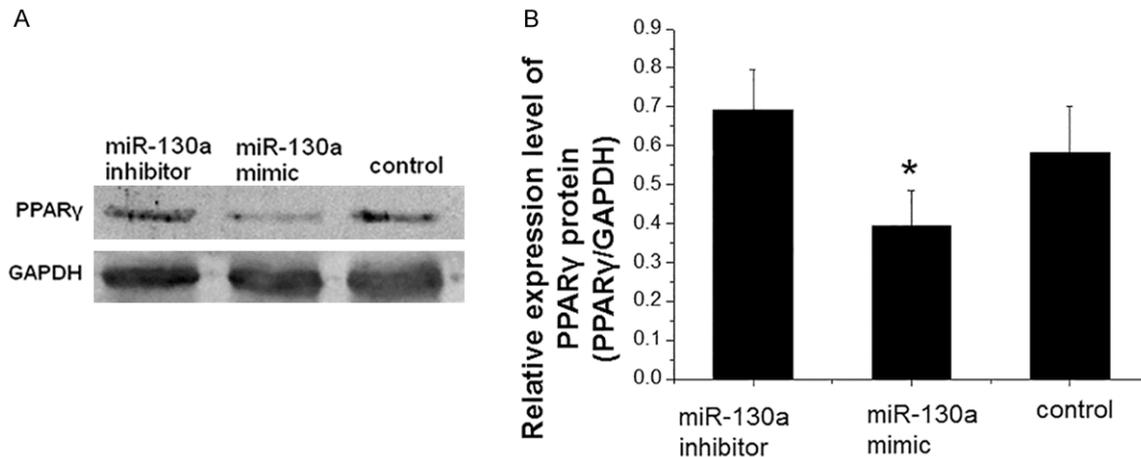


Figure 4. Analysis of PPAR γ protein level after miR-130a mimics transfection. At 72 h after transfection with miR-130a mimics, miR-130a inhibitors and control siRNA, preadipocytes were collected and total proteins were extracted. Western blotting was performed to detect the expression of PPAR γ protein. GAPDH was used as an internal control. A. Representative Western blotting results. B. Quantitative Western blotting results. Compared with control, * $P < 0.05$.

of PPAR γ mRNA in omental adipose tissues of NGT and T2DM patients, real-time PCR was performed. As shown in **Figure 2B**, T2DM patients had significantly higher levels of PPAR γ than NGT individuals ($P < 0.05$). These results indicate that PPAR γ is one of target genes of miR-130a.

The consumption of glucose is increased after transfection of miR-130a mimics

To determine the consumption of glucose, the levels of glucose in cell culture supernatant was measured at 72 h after transfection of miR-130a mimics and inhibitors in 3T3-L1 preadipocytes. The concentration of glucose transfected with miR-130a mimics, miR-130a inhibitors and control group were 9.12 ± 0.29 nM, 9.39 ± 0.23 nM, and 9.61 ± 0.02 nM (**Figure 3**). Compared with control cells, the consumption of glucose in cells transfected with miR-130a mimics was significantly increased ($P < 0.05$). These results suggest that miR-130 enhances the ability of glucose uptake.

PPAR γ protein level is decreased after transfection of miR-130a mimics

To measure determine the expression level of PPAR γ protein, Western blot analysis was performed at 72 h after transfection of miR130a mimics and inhibitors in 3T3-L1 preadipocytes. Representative and quantitative Western blotting results were shown in **Figure 4A** and **4B**,

respectively. The level of PPAR γ protein in cells transfected with miR130a mimics was lower than that in cells transfected with miR-130a inhibitors and control siRNA. Statistically, cells transfected with miR130a mimics had significantly lower level of PPAR γ protein than cells transfected with control siRNA ($P < 0.05$). These results showed that miR130a mimics inhibited the expression of PPAR γ protein, further suggesting that PPAR γ gene may be one of the target genes of miR-130a.

Expression levels of glucose and lipid metabolism related genes are decreased after transfection of miR-130a mimics

To detect the levels of APM1, LPL, CEBP α and PPAR γ after transfection of miR130a mimics (75 nM), real-time PCR was carried out at 72 h after transfection. As shown in **Figure 5**, the levels of APM1, LPL, CEBP α and PPAR γ were reduced after transfection of miR130a mimics. Statistically, the downstream genes of PPAR γ were significantly decreased after transfection with microRNA-130a mimics ($P < 0.05$), suggesting that miR-130a mimics inhibit the expression of APM1, LPL, CEBP α , and PPAR γ .

Discussion

It is reported that miR-130a is closely related with insulin secretion and adipogenesis. Hennessy et al [14] reported that miR-130a knock-down in MIN6 cells decreased the secretion of

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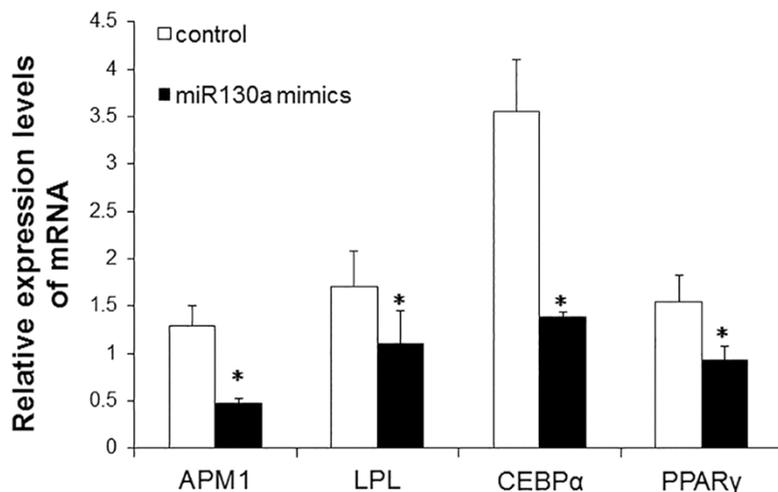


Figure 5. Analysis of APM1, LPL, CEBP α , PPAR γ , AP2 and GLUT4 expression at mRNA level after miR-130a mimics transfection. Real-time PCR was carried out at 72 h after miR130a mimics (75 nM) transfection. β -actin was used as an internal control. Relative expression levels were calculated based on those of β -actin. Compared with control, *P < 0.05.

insulin in response to glucose stimulation. Lee et al [15] found that in adipose tissues of obese women and in 3T3-L1 preadipocytes, miR-130 (including miR-130a and miR130b) inhibited adipogenesis through suppressing the expression of PPAR γ . In this study, many miRNAs were differentially expressed between NGT and T2DM patients of Xinjiang Uyghurs. Among them, the expression level of miR-130a was significantly decreased both in peripheral blood and omental adipose tissues of T2DM patients. This data suggests that miR-130a may be related with the development of T2DM.

Through analysis with targetscan, miRBase and miRanda, PPAR γ gene, which is involved in glucose and lipid metabolism, was predicted as possible target gene of miR-130a. PPAR γ is a kind of transcription factor, which belongs to the large family of nuclear hormone receptors. It is expressed mainly in adipose tissue. Furthermore, PPAR γ is an important factor in regulating the differentiation of preadipocytes into mature adipocytes process. It begins to express in the early stage of cell differentiation, and its expression level is gradually increased during cell differentiation [16-18]. Our results showed that the mRNA expression level of PPAR γ in omental adipose tissues of T2DM patients were higher than those of NGT individuals. As mentioned above, PPAR γ was a possible target gene of miR-130a. Thus, this increase

in mRNA expression levels of PPAR γ may be caused by the decreased levels of miRNA-130a.

Activated PPAR γ can regulate transcription of genes associated with the effects of insulin. The function of these genes includes transport and usage of glucose and regulation of lipid metabolism. In this study, after transfection of miR-130a mimics in 3T3-L1 preadipocytes, expression levels of PPAR γ protein and mRNA were reduced. These results further suggest that PPAR γ is one of the target genes of miR-130a. Further investigation showed that the expression levels of down-

stream target genes of PPAR γ , adipogenic gene products including APM1, LPL, and CEBP α , were also decreased after transfection of miR-130a mimics. This data indicates that miR-130a may indirectly affect generation and differentiation of adipocytes.

Furthermore, we previously reported that the level of miRNA130a expression in peripheral anticoagulant blood in Uyghur obesity population was significantly reduced, indicating that the level of miRNA130a expression may be related with Uyghur obesity [19]. And, the low expression of miR-130a in the obese persons may reflect a relative depletion of preadipocytes due to their recruitment into the adipocyte pool. Furthermore, the obesity is the basis of pathophysiology of insulin resistance. In this study, we found that miR-130 enhanced the ability of glucose uptake. These results suggest that the reduction of miR-130a might promote obesity, which may further lead to insulin resistance and T2DM.

In summary, the expression of miR-130a is decreased in Xinjiang Uyghur T2DM patients. Expression level of PPAR γ , target gene of miR-130a, is increased in omental tissues of T2DM patients. Consistently, expression levels of PPAR γ and its downstream genes are inhibited by miR130a mimics transfection. Our findings suggest that miR-130a may play an important

role in the development of insulin resistance and T2DM.

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Disclosure of conflict of interest

None.

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