Genetics and Molecular Research

Relationship between the polymorphisms in *KCNQ1* and type 2 diabetes in Chinese Kazakh population

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Genet. Mol. Res. 15 (2): gmr.15027503
Received August 24, 2015
Accepted December 21, 2015
Published May 13, 2016
DOI http://dx.doi.org/10.4238/gmr.15027503

ABSTRACT. Recently genome-wide association studies on East Asian populations reported an association between diabetes and several single nucleotide polymorphisms (SNPs) in a 40-kb linkage disequilibrium block in intron 15 of *KCNQ1*. However, the association between *KCNQ1* variants and type 2 diabetes mellitus (T2DM) in Chinese Kazakh populations is unknown. We investigated the relationship between rs2237892 and rs2237895 SNPs in *KCNQ1* and susceptibility to and clinical characteristics of T2DM in 100 Chinese Kazakh T2DM subjects and 100 healthy subjects. SNPs were genotyped by polymerase chain reaction-restriction fragment length polymorphism and the main anthropometric and biochemical parameters of individuals were assessed in the genotype groups (rs2237892: CC, CT, or TT, and rs2237895: AA, AC, or CC). Genotype distribution and allele frequencies of these

two SNPs were not significantly different between T2DM and control groups (P > 0.05). The frequencies of CT and TT genotypes and T allele for the rs2237892 SNP in females with T2DM were significantly higher than that in the control group (genotype: P = 0.016, allele: P = 0.004). However, there were no significant differences among individuals with different genotypes with respect to the rs2237895 SNP (P > 0.05). The main anthropometric and biochemical parameters did not correlate with the rs2237892 or rs2237895 SNPs in the T2DM group (P > 0.05). Thus, the T allele-containing genotypes of the rs2237892 SNP in *KCNQ1* may increase the susceptibility to T2DM in female Chinese Kazakh individuals, whereas the rs2237895 SNP may not be associated with T2DM in the Chinese Kazakh population.

Key words: Chinese Kazakh populations; Genetic susceptibility; *KCNQ1*; Population genetics; Single nucleotide polymorphism; Type 2 diabetes mellitus

INTRODUCTION

Diabetes is the most common metabolic disease that affects 246 million people (5.9% of adults) worldwide. Type 2 diabetes mellitus (T2DM) is characterized by the presence of insulin resistance and pancreatic β-cell dysfunction, and it is the result of both genetic and environmental factors. The International Diabetes Federation predicts that the total number of people living with diabetes will increase to 380 million within the next 20 years (International Diabetes Federation, 2006), with almost 80% of patients originating from developing countries (Sadikot, 2008). The total number of people with diabetes in China is estimated to increase from 20.8 million in 2000 to 42.3 million by 2030.

Genome-wide association studies (GWAS) have been carried out for complex diseases, including T2DM, and have identified a growing number of T2DM trait susceptibility loci (Prokopenko et al., 2008). Two independent GWAS studies identified a novel T2DM susceptibility gene, *KCNQ1*, in the East Asian subjects (Unoki et al., 2008; Yasuda et al., 2008). Very recently, two GWAS studies on Chinese Han and European populations confirmed *KCNQ1* as a T2DM susceptibility gene (Tsai et al., 2010; Voight et al., 2010). The association of T2DM with *KCNQ1* variants was replicated in studies on Chinese (Hu et al., 2009; Liu et al., 2009; Qi et al., 2009), Singaporean (Tan et al., 2009, 2010), Indian (Been et al., 2011), and some Euro-Caucasian subjects (Unoki et al., 2008; Holmkvist et al., 2009; Jonsson et al., 2009).

Different ethnic groups and geographic regions can show significant differences in the frequencies of some genetic variations. The rate of T2DM in the Kazakh population in China is much lower than in the Han population in this region, despite the significant incidence of obesity, insulin resistance, and other risk factors in the Kazakh population (Tao et al., 2008). Therefore, we investigated the contribution of *KCNQ1* to the etiology of T2DM in the Chinese Kazakh population to determine whether variants of *KCNQ1* were associated with susceptibility to T2DM and diabetes-related metabolic traits. The purpose of this study is to provide a scientific basis for the role of *KCNQ1* in the molecular genetics of diabetes in Chinese Kazakh subjects.

MATERIAL AND METHODS

Study subjects

This study was prospectively performed and approved by the Institutional Ethics Committees of the First Affiliated Hospital of Shihezi University School of Medicine in China. It was conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Written informed consent was obtained from all patients before they entered the study.

We recruited 100 Chinese Kazakh patients with T2DM (54 male and 46 female; mean age = 51.21 ± 11.60 years) who had been hospitalized for treatment of poor glucose control. Controls subjects (44 male and 56 female; mean age = 49.85 ± 12.41 years) were recruited from healthy individuals who completed health examinations in the same hospital. Diagnosis of T2DM was based on the criteria outlined by the World Health Organization: fasting glucose ≥7 mM (126 mg/dL), 2-h oral glucose tolerance test glucose level ≥11.1 mM (200 mg/dL), or clinical diagnosis of the disease. Any individuals suspected of having any infectious disease shortly before or during recruitment and patients with autoimmune diseases were excluded from study.

Data collection

All participants underwent physical examination and blood tests after overnight fasting. A standardized mercury sphygmomanometer was used to measure the systolic blood pressure (SBP) and diastolic blood pressure (DBP) according to the standard protocols. Body weight and height were measured with subjects wearing only light indoor clothing and without shoes. Body mass index (BMI) was calculated as weight (kg) divided by the square of the height (m^2). The waist circumference was measured midway between the caudal point of the costal arch, as palpated laterally, and the iliac crest. The hip circumference was measured at the symphysis-trochanter femoris level. The waist-to-hip ratio (WHR) was calculated as the waist circumference divided by the hip circumference. Blood specimens were drawn after overnight fasting, and detected within 2 h for levels of fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting insulin (FINS), and fasting C-peptide (FCP) using conventional methods with an Olympus Automatic Biochemical Analyzer (Japan). Homeostasis model assessment based on β-cell function (β) or insulin resistance (IR) (HOMA-β and HOMA-IR, respectively) were calculated from FINS and FPG using the homeostasis model assessment method (Matthews et al., 1985).

DNA extraction

Blood was treated with anticoagulant and preserved at -20°C for genomic DNA extraction. Genomic DNA was extracted from whole blood using a leukocyte genomic DNA isolation kit (Beijing Biotech Corporation, Beijing, China) according to the manufacturer instructions and stored at -20°C for further analysis.

Genotyping

We selected two single nucleotide polymorphisms (SNPs) to study in *KCNQ1*,

rs2237892 and rs2237895, both of which had previously been associated with T2DM (Hu et al., 2009). All control and patient samples were genotyped for these SNPs using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis.

Primers were designed using the Primer Premier 5.0 software (PREMIER Biosoft International, Vancouver, Canada) and synthesized by Shanghai Biological Engineering Co., Ltd. (Shanghai, China). The primer sequences for rs2237892 were: upstream primer, 5'-CTCAGAGGAAGAGCAAGGGTAG-3', and downstream primer, 5'-CCTGGGTCATCAGACTAGGG-3'. The primer sequences for rs2237895 were: upstream primer, 5'-GGAAAAGCCTTCCTCATGGAG-3', and downstream primer, 5'-CCATCTGCCTCTTGGTCTCATC-3'. PCR was performed with a 25-μL final reaction volume comprised of primers (1 μL each, 10 pM), 12.5 μL 2X Power TaqPCR Master Mix (Biotech Corporation, Beijing, China) and 3 μL DNA template. PCR cycling conditions were as follows: 94°C for 5 min; 35 cycles of 94°C for 30 s, 59°C for 30 s (rs2237892) or 58°C for 40 s (rs2237895), and 72°C for 30 s; and a final extension step at 72°C for 10 min. The PCR products of rs2237892 and rs2237895 were digested with the restriction enzymes *Ava*I and *Sma*I (Fermentas, Vilnius, Lithuania), respectively, at 37°C for 1 h. Following digestion, products were separated on a 2.5% agarose gel and visualized by staining with ethidium bromide. The desired genotypes of *KCNQ1* were confirmed by DNA sequencing of two randomly selected samples (Biomed Corporation, Beijing, China).

Statistical analysis

The SPSS17.0 software package (Chicago, IL, USA) was used for statistical analysis. All data are reported as means ± standard deviation. Quantitative traits with a skewed distribution were logarithmically transformed ($\log_e$) to approximate univariate normality. The genotype and allele frequencies were calculated manually and were found to meet Hardy-Weinberg equilibrium (HWE) in both control and T2DM groups. The differences in genotype and allele frequencies between the two groups were analyzed using the chi-squared test. For the measured data, the Student *t*-test for independent samples was used. A bilateral probability of $P < 0.05$ was considered statistically significant.

RESULTS

Clinical data and biochemical indicators in T2DM patients and healthy controls

Blood samples were collected from 100 T2DM and 100 healthy control Kazakh subjects. The demographic and biochemical parameters of the subjects are provided in Table 1. The T2DM subjects had a larger WHR; higher BMI, SBP, FPG, HOMA-IR, TG, TC, and LDL-C; and lower FINS, FCP, and HOMA-β than control subjects. However, no significant differences were found between control and T2DM subjects with respect to gender, age, HDL-C, or DBP.

Genotype frequencies and allele frequency distribution of *KCNQ1* rs2237892 and rs2237895 polymorphisms

The allele and genotype distributions are summarized in Table 2. The two SNPs included in this study did not deviate from HWE in either T2DM and normal Kazakh

individuals (P > 0.05). Three genotypes in both rs2237892 (CC, CT, and TT) and rs2237895 (AA, AC, and CC) were present in T2DM and healthy Kazakh subjects. Genotype and allele frequencies of the two sites did not show any significant differences between the Kazakh T2DM and healthy control groups.

Table 1. Demographic and biochemical parameters of the subjects.

Parameters	Type 2 diabetes (N = 100)	Control (N = 100)	P value
Gender (male/female)	55/45	46/54	0.294
Age (years)	51.21 ± 11.60	49.85 ± 12.41	0.116
WHR	0.93 ± 0.06	0.89 ± 0.04	0.027
BMI (kg/m^2)	25.59 ± 3.01	24.01 ± 2.86	0.000
SBP (mmHg)	137.48 ± 27.63	130.06 ± 17.76	0.022
DBP (mmHg)	85.51 ± 11.42	81.90 ± 8.44	0.059
FPG (mM)	7.54 ± 2.93	4.54 ± 0.38	0.000
TC (mM)	4.42 ± 1.64	3.99 ± 0.93	0.024
TG (mM)	2.25 ± 1.12	1.60 ± 0.45	0.017
LDL-C (mM)	2.85 ± 1.02	1.75 ± 0.60	0.008
HDL-C (mM)	1.21 ± 1.04	1.39 ± 0.45	0.132
FINS (pM)	37.24 ± 15.85	56.67 ± 12.36	0.002
FCP (nM)	1.17 ± 0.29	1.76 ± 0.48	0.001
HOMA-β	143.0 ± 124.9	182.3 ± 124.1	0.041
HOMA-IR	1.21 ± 0.19	1.05 ± 0.21	0.018

WHR = waist-to-hip ratio; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; FPG = fasting plasma glucose; TC = total cholesterol; TG = triglycerides; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; FINS = fasting insulin; FCP = fasting C-peptide; HOMA = homeostasis model assessment based on β-cell function (β) or insulin resistance (IR).

Table 2. Genotype and allele frequencies of *KCNQ1* SNPs at rs2237892 and rs2237895 in type 2 diabetes mellitus (T2DM) patients and healthy controls.

SNP	Group	Genotype frequency [N (%)]			P value	Allele frequency [N (%)]		P value
		CC	CT	TT		C	T	
rs2237892	T2DM	39 (39.0)	46 (46.0)	15 (15.0)	0.138	124 (62.0)	76 (38.0)	0.072
	Control	53 (53.0)	35 (35.0)	12 (12.0)		141 (70.5)	59 (29.5)	
		AA	AC	CC		A	C	
rs2237895	T2DM	40 (40.0)	49 (49.0)	11 (11.0)	0.330	129 (64.5)	71 (35.5)	0.151
	Control	32 (32.0)	51 (51.0)	17 (17.0)		115 (57.5)	85 (42.5)	

While the frequencies of the TT and CT genotypes and the T allele of the rs2237892 SNP in the T2DM group were higher than that in the control group (15.0 *vs* 12.0, 46.0 *vs* 35.0, and 38.0 *vs* 29.5%, respectively), these differences were not statistically significant (P > 0.05). There were also no significant differences in the frequencies of the AA genotype or A allele of the rs2237895 SNP between the T2DM and control groups (40.0 *vs* 32.0% and 64.5 *vs* 57.5%, respectively; P > 0.05).

Genotype and allele frequencies of rs2237892 and rs2237895 stratified by gender, age, and BMI

Epidemiological studies have shown that T2DM is associated with socioeconomic level, gender, age, and phenotype. Therefore, we stratified the *KCNQ1* rs2237892 and rs2237895 polymorphisms by gender, age, and BMI. The only significant difference found was for the rs2237892 SNP in terms of gender (Table 3). The frequency of the CT and TT genotypes and the T allele was significantly higher in females in the T2DM group compared to the control group [48.9 *vs* 31.5, 22.2 *vs* 11.1, and 46.7 *vs* 26.9%, respectively; genotype:

P = 0.016, allele: P = 0.004, odds ratio (OR) = 2.384, 95%CI = 1.316-4.316]. Furthermore, comparison of the frequency of T allele carriers (CT/TT genotypes) with the frequency of the CC genotype also showed a statistically significant difference (P = 0.004). However, no significant difference was found for the rs2237895 SNP genotype and allele frequencies, regardless of the stratification used (Table 4; all P > 0.05).

Table 3. Genotype and allele frequencies of rs2237892 stratified by sex, age, and BMI.

	Group	N	Genotype frequency [N (%)]			Allele frequency [N (%)]	
			CC	CT	TT	C	T
Gender							
Male	T2DM	55	26 (47.3)	24 (43.6)	5 (9.1)	76 (69.1)	34 (30.9)
	Control	46	22 (47.8)	18 (39.1)	6 (13.0)	62 (67.4)	30 (32.6)
P value			0.785			0.796	
Female	T2DM	45	13 (28.9)	22 (48.9)	10 (22.2)	48 (53.3)	42 (46.7)
	Control	54	31 (57.4)	17 (31.5)	6 (11.1)	79 (73.1)	29 (26.9)
P value			0.016			0.004	
Age							
<60 years	T2DM	53	18 (34.0)	26 (49.1)	9 (17.0)	62 (58.5)	44 (41.5)
	Control	51	25 (49.0)	19 (37.3)	7 (13.7)	69 (67.6)	33 (32.4)
P value			0.295			0.172	
≥60 years	T2DM	47	21 (44.7)	20 (42.6)	6 (12.8)	62 (66.0)	32 (34.0)
	Control	49	28 (57.1)	16 (32.7)	5 (10.2)	72 (73.5)	26 (26.5)
P value			0.474			0.252	
BMI							
<25 kg/m^2	T2DM	38	20 (52.6)	12 (31.6)	6 (15.8)	52 (66.0)	24 (34.0)
	Control	48	31 (64.6)	11 (22.9)	6 (12.5)	73 (73.5)	23 (26.5)
P value			0.295			0.172	
≥25 kg/m^2	T2DM	62	19(30.6)	34(54.8)	9 (14.5)	72 (58.1)	52 (41.9)
	Control	52	22 (42.3)	24 (46.2)	6 (11.5)	68 (65.4)	36 (34.6)
P value			0.432			0.258	

Table 4. Genotype and allele frequencies of rs2237895 stratified by gender, age, and body-mass index.

	Group	N	Genotype frequency [N (%)]			Allele frequency [N (%)]	
			AA	AC	CC	A	C
Gender							
Male	T2DM	55	23 (41.8)	24 (43.6)	8 (14.5)	70 (63.6)	40 (36.4)
	Control	46	12 (26.1)	25 (54.3)	9 (19.6)	49 (53.3)	43 (46.7)
P value			0.252			0.136	
Female	T2DM	45	17 (37.8)	25 (55.6)	3 (6.7)	59 (65.6)	31 (34.4)
	Control	54	20 (37.0)	26 (48.1)	8 (14.8)	66 (61.1)	42 (38.9)
P value			0.421			0.519	
Age							
<60 years	T2DM	53	22 (41.5)	26 (49.1)	5 (9.4)	70 (66.0)	36 (34.0)
	Control	51	16 (31.4)	27 (52.9)	8 (15.7)	59 (57.8)	43 (42.2)
P value			0.445			0.223	
≥60 years	T2DM	47	18 (38.3)	23 (48.9)	6 (12.8)	59 (62.8)	35 (37.2)
	Control	49	16 (32.7)	24 (49.0)	9 (18.4)	56 (57.1)	42 (42.9)
P value			0.706			0.427	
BMI							
<25 kg/m^2	T2DM	38	16 (42.1)	17 (44.7)	5 (13.2)	49 (64.5)	27 (35.5)
	Control	48	13 (27.1)	27 (56.3)	8 (16.7)	53 (55.2)	43 (44.8)
P value			0.343			0.219	
≥25 kg/m^2	T2DM	62	24 (38.7)	32 (51.6)	6 (9.7)	80 (64.5)	44 (35.5)
	Control	52	19 (36.5)	24 (46.2)	9 (17.3)	62 (59.6)	42 (40.4)
P value			0.482			0.447	

Levels of primary anthropometric biochemical parameters in T2DM patients with different *KCNQ1* genotypes

Since only 28 individuals with the TT genotype in the rs2237892 SNP and 27 individuals with the CC genotype in the rs2237892 SNP were included in the study, T2DM patients were divided into two groups for the rs2237892 (CC and CT/TT) and rs2237895 (AA and AC/CC) SNPs. Following this, the levels of anthropometric and biochemical parameters in these groups were analyzed (Tables 5 and 6). No statistically significant differences in any of the parameters were detected among T2DM subjects based on the genotypes of the rs2237892 or rs2237895 SNPs (all $P > 0.05$).

Table 5. Comparison of anthropometric and biochemical parameters among rs2237892 genotypes.

rs2237892	Genotype		P value
	CC	CT + TT	
WHR	0.93 ± 0.06	0.92 ± 0.08	0.69
BMI (kg/m^2)	25.21 ± 3.02	24.67 ± 2.87	0.68
SBP (mmHg)	137.03 ± 16.70	135.71 ± 14.54	0.62
DBP (mmHg)	82.54 ± 12.6	84.61 ± 10.52	0.43
FPG (mM)	7.23 ± 2.18	6.95 ± 2.86	0.47
TC (mM)	4.11 ± 1.45	4.29 ± 1.54	0.32
TG (mM)	1.89 ± 0.55	2.10 ± 1.12	0.27
LDL-C (mM)	2.81 ± 1.12	2.67 ± 0.68	0.49
HDL-C (mM)	1.20 ± 1.08	1.31 ± 0.67	0.58
FINS (pM)	46.98 ± 11.54	42.65 ± 6.87	0.28
FCP (nM)	1.56 ± 0.28	1.41 ± 0.29	0.34
HOMA-β	146.0 ± 124.9	150.0 ± 124.6	0.32
HOMA-IR	1.11 ± 0.51	1.25 ± 0.48	0.36

For abbreviations, see legend to Table 1.

Table 6. Comparison of anthropometric and biochemical parameters among the rs2237895 genotypes.

rs2237895	Genotype		P value
	AA	AC/CC	
WHR	0.92 ± 0.16	0.94 ± 0.08	0.39
BMI (kg/m2)	24.21 ± 2.02	25.67 ± 2.87	0.58
SBP (mmHg)	136.03 ± 14.45	134.71 ± 15.14	0.49
DBP (mmHg)	83.54 ± 11.6	84.61 ± 8.52	0.40
FPG (mM)	7.13 ± 1.18	6.85 ± 0.86	0.57
TC (mM)	4.01 ± 1.35	4.21 ± 1.54	0.22
TG (mM)	1.83 ± 0.35	2.07 ± 1.12	0.37
LDL-C (mM)	2.89 ± 0.62	2.67 ± 0.68	0.41
HDL-C (mM)	1.18 ± 1.08	1.29 ± 0.47	0.58
FINS (pM)	44.68 ± 10.54	46.05 ± 6.27	0.28
FCP (nM)	1.46 ± 0.21	1.53 ± 0.39	0.34
HOMA-β	158.0 ± 111.9	154.0 ± 107.6	0.30
HOMA-IR	1.20 ± 0.30	1.15 ± 0.68	0.36

For abbreviations, see legend to Table 1.

DISCUSSION

The Chinese Kazakh people are mostly pastoralists and semi-pastoralists and are relatively isolated from the outside world; therefore, they rarely intermarry with other groups and have low genetic heterogeneity. Most Kazakh patients with T2DM do not undergo formal

treatment; hence, this population is amenable to the exploration of the role of genetic factors in the development of T2DM, as confounding interactions between treatment and genetics are avoided.

We strictly selected Kazakh subjects according to inclusion criteria for T2DM and healthy controls. The clinical data indicated no significant differences in gender, age, and DBP between the Kazakh T2DM and control groups; however, the T2DM group showed significantly higher FPG, TC, TG, and LDL-C levels compared to the healthy controls. Previous studies indicated that 40-50% of patients with T2DM exhibited dyslipidemia. Hyperlipidemia was not only the result of insulin resistance but was also the main risk factor for impaired insulin sensitivity (Tomkin, 2010). In the present study, we found that Kazakh patients with T2DM had significantly lower FINS and FCP levels than the control group. This, combined with higher HOMA-IR and lower HOMA-β, suggests that Kazakh patients with T2DM commonly have insulin resistance and β-cell dysfunction. These results are consistent with the pathophysiological basis of T2DM and confirm the correlation between hyperlipidemia and insulin resistance.

Our results showed that there was no significant difference in the frequencies of the three genotypes (CC, CT, and TT) and two alleles (C and T) of the *KCNQ1* rs2237892 SNP between the T2DM and control groups. This finding is consistent with data from Arab populations and middle-aged Han populations in East China (Chen et al., 2010; Turki et al., 2012), but contradicts the conclusions drawn by several other studies (Yasuda et al., 2008; Hu et al., 2009; Liu et al., 2009; Qi et al., 2009; Tan et al., 2009; Rees et al., 2011; Saif-Ali et al., 2011).

In this study, we only observed a difference in the *KCNQ1* rs2237892 polymorphism in terms of gender. The frequencies of the CT and TT genotypes and T allele were significantly higher for females in the T2DM group than in the control group. Thus, the rs2237892 SNP may be a potential susceptible locus for female Kazakh patients with T2DM, with CT or TT representing susceptible genotypes and the susceptible T allele. However, no differences were revealed between the males in the T2DM and control groups. Previous studies have reported that the rs2237892 SNP showed the strongest association with T2DM, with the C allele conferring a higher risk of the disease (Hu et al., 2009), which was in contrast to our findings in the Kazakh population.

Previous studies showed that the rs2237895 SNP is closely associated with T2DM in Han Chinese, Japanese, Singaporean, and Danish subjects, and the association was significantly enhanced after adjusting for gender, age, and BMI (Unoki et al., 2008). However, the genotype and allele frequencies of the rs2237895 SNP were not significantly different between the Kazakh T2DM and healthy control groups in this study, even after stratifying the data by sex, age, and BMI. Based on these results, we determined that the *KCNQ1* rs2237895 SNP is not a susceptible site for T2DM in the Kazakh population.

In contrast to previous studies, we identified no statistically significant differences in the main anthropometric and biochemical parameters among T2DM subjects with particular rs2237892 or rs2237895 genotypes. Hu et al. (2009) found that the rs2237892 SNP was most strongly associated with T2DM in Chinese populations and, furthermore, the rs2237895 SNP was associated with both first- and second-phase insulin secretion in the control group. Our results did not confirm the association of the two SNPs with the islet β-cell dysfunction in the Kazakh population, and we also detected no significant difference in HOMA-IR among the different rs2237892 or rs2237895 SNP genotypes.

These conflicting results may arise from several phenomena. First, although more than 40 genes associated with T2DM in different races and regions have been identified

to date, the results of these genetic studies have not been highly reproducible. Second, the Chinese Kazakh population as a whole is significantly overweight and has insulin resistance, hypertension, nicotine use, and other risk factors for T2DM, and yet the prevalence of T2DM is much lower than in the Han and Uygur populations in the region. Thus, it is possible that the unique genetic background of the Kazakh population protects them from T2DM. Third, our sample size was small, which could confound our analysis. Thus, it will be necessary to include larger sample sizes in future studies to replicate these findings.

In summary, we have demonstrated that the rs2237892 SNP in *KCNQ1* may be a susceptible locus for T2DM in female Kazakh individuals. Furthermore, CT/TT are susceptible genotypes and T is a susceptible allele at this locus. However, the *KCNQ1* rs2237895 SNP does not appear to be associated with T2DM in the Chinese Kazakh population. The findings of this study will serve as a platform for further research to elucidate the mechanisms or the functionalities of the variants of the *KCNQ1* gene in the Chinese Kazakh population. Further studies are needed to investigate other potential SNPs in *KCNQ1* and to fully delineate the role of *KCNQ1* in the pathogenesis of T2DM in the Chinese Kazakh population.

Conflicts of interest

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

The authors are grateful to the staff of the Department of Endocrinology (Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology) and Departments of Endocrinology and Metabolism (First Affiliated Hospital, Shihezi University School of Medicine) for their assistance throughout this study. We also thank all the volunteers who have participated in this research. No funding was received for this study.

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