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Case Report

Association between gout and polymorphisms in SLC17A1 gene in male Han Chinese

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Abstract: Human sodium-dependent phosphate cotransporter type 1 encoded by *SLC17A1* is a urate transporter localized to the renal proximal tubular cells and candidate molecule to secret urate from renal tubular cells to urine. The *SLC17A1* locus was also found to be associated with serum urate concentration. However, evidence for association with gout was equivocal. In current study, we investigated the association of the *SLC17A1* locus with gout in male Han Chinese. This was a case-control study in a group of 400 male patients with gout and 424 gout-free male controls to genotype the single-nucleotide polymorphism rs1165196, rs1183201 and rs3799344 of *SLC17A1* gene. There were significant differences between gout and control groups in the allele frequencies at rs1165196 (T806C; Ile269Thr, odds ratio (OR) 0.758, P=0.027) and rs1183201 (OR 0.745, P=0.018). The allele frequencies of rs3799344 were not significantly associated with the development of gout (OR 0.811, P=0.064). The association was found between genotypes at rs1165196 and rs1183201 (P=0.032 and P=0.029) and serum uric acid (sUA) levels. The genotype status of rs1183201 was significantly associated with sUA using Multivariate regression analysis. However, there were no differences in the distribution of genotypes at rs1165196 (OR 1.121, P>0.05) and rs1183201 (OR 0.887, P>0.05) in patients with gout with kidney stones and without kidney stones. Our data suggest that *SLC17A1* polymorphisms were associated with the development of gout in male Han Chinese.

Keywords: Single-nucleotide polymorphism, sodium-phosphate cotransporter proteins, gout

Introduction

Hyperuricaemia is caused by either overproduction or renal under excretion of urate. In the nephron, after filtration by the glomerulus, urates are reabsorbed and secreted in the proximal tubules and 10% of glomerular filtrate is excreted in the urine. Recent investigations suggest that renal urate under excretion is the major mechanism of hyperuricaemia in the majority of patients with primary gout [1]. Every year a considerable number of people are hospitalized for gout. An improved understanding of the genetic factors that contribute to the development of this disorder will lead to better diagnosis, treatment, and prevention and will also help to stem, or even to reverse, the rise in prevalence of this disease.

Human sodium-dependent phosphate cotransporter type 1 (NPT1), a voltage-driven organic anion transporter encoded by *SLC17A1*, has been reported to localize to the apical membrane of the proximal tubule in the human kidney. It has also been identified as a urate transport protein [2, 3], probably secretory with the gout-protective allele of I269T leading to increased sodium-dependent transporter 1 activity [3, 4] and, presumably, increased secretion of uric acid. Genome-wide association scans have shown that genetic variants associate with serum urate concentration in a Caucasian sample [5, 6]. *SLC17A1* has been associated with gout in a Japanese sample set (I269T(rs1165196), odds ratio (OR)=0.55, P=0.004) [4] but with conflicting results in Caucasian sample sets. A separate study

Table 1. Demographic and clinical characteristics (Mean ± SD) of the study population

Parameter	Gout (*n*=400)	Control (*n*=424)	*p* Value
Age (year)	52.37 ± 13.32	54.33 ± 15.90	0.055
Body mass index (kg/m^2)	26.04 ± 2.99	25.33 ± 3.61	0.002
Systolic pressure (mmHg)	134.28 ± 16.59	133.17 ± 17.14	0.346
Diastolic pressure (mmHg)	85.06 ± 10.45	80.81 ± 11.26	<0.001
Blood glucose (mmol/l)	5.44 ± 1.43	5.60 ± 1.07	0.068
Uric acid (umol/l)	477.52 ± 108.30	300.48 ± 62.62	<0.001
Total cholesterol (mmol/ll)	5.06 ± 1.03	4.65 ± 0.81	<0.001
Triglycerides (mmol/l)	2.40 ± 1.97	1.44 ± 1.05	<0.001
Creatinine (umol/l)	92.82 ± 29.81	80.75 ± 12.27	<0.001
Urea nitrogen (mmol/l)	5.63 ± 2.02	5.36 ± 1.24	0.018

Data are represented as the mean ± standard deviation.

reported no evidence in Caucasian for association with gout (rs1183201, r2 with rs1165196=0.87, OR=0.97, P=0.68) [7]. And it has been reported that at rs1183201 and rs3799344 (*SLC17A1*), evidence for association with gout was observed in both the Caucasian (OR=0.67, P=3.0 × 10-6 and OR= 0.69, P=2.8 × 10-5) [8]. This equivocal evidence for association with gout in a Caucasian population is notable given the genome-wide evidence for association with serum urate concentration [6].

To clarify the global relevance of *SLC17A1*, the association needs to be confirmed by independent studies in different ethnic groups. The objective of this study was to assess the genetic association of single nucleotide polymorphism (SNP) in *SLC17A1* gene with gout in a Chinese Han male population.

Materials and methods

Study population

Gout prevalence was higher in male and even some genetic polymorphisms show gender specific effects [9]. Among all of our outpatients, only 5% was female (data not shown), not sufficient to perform the statistical analysis. Therefore, the present study focused on male gout population only.

A total of 407 male patients with gout and 438 gout-free male as control were recruited. We collected the clinical features (age, height, weight and blood pressure) from all the participants. The diagnosis of gout was based on the preliminary criteria for classification of gout of the American Rheumatism Association for use in either clinical settings or population-based epidemiology studies [10]. Normal male controls with no personal or familial history of hyperuricemia or gout or any other serious illness were recruited. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. Researches and all subjects participating in the study gave informed consent.

We measured blood glucose, urea nitrogen, creatinine, uric acid, total cholesterol, and triglycerides levels in the plasma of all the participants using an automated multichannel chemistry analyzer (PPI; Roche, Germany). Body mass index (BMI) was calculated to assess obesity. It was calculated as weight in kilograms divided by squared height in meters. Hyperuricemia in males was defined as uric acid levels >420 umol/l.

Genotype analysis

Blood samples were collected from the gout patients and healthy controls, and stored at -20°C until analyzed. Genomic DNA was extracted from peripheral blood leukocytes according to standard methods. The following three SNPs in the SCL17A1 were selected: rs1165196, rs1183201 and rs3799344. Of those, rs1165196 is a non-synonymous SNP at exon 7 with T to C changes at nucleotide 806 resulting in an Ile to Thr substitution. Polymerase chain reaction (PCR) and ligase detection reaction assay (LDR) was employed for genotyping the rs1165196, rs1183201 and rs3799344 SNPs. A PCR assay for the rs1165196 was using forward primer (5'-GTGTCATGATGTTATGTGACC-3') and reverse primer (5'-GCTATACTTAAGTCGCTTCC-3') was performed in a 10 μL of reaction volume; for genotyping the rs1183201, a PCR assay was using forward primer (5'-CTGATAGCCAAAAAACTGGA-3') and reverse primer (5'-GGATGTGCCATAGTTTGTTC-3'); and for genotyping the rs3799344, a PCR assay was using forward primer (5'-ATGCTGACCCCACCTCTGAC-3') and reverse primer (5'-GCCAGAAATTTCCATGCCTG-3'). The Probe for the rs1165196_C was using (5'-TTTTTTTTTTTTTTTTTTTTTTTTTTTTCCAGAAAAACGTAAAACTACCAG-

Table 2. Genotype distribution and relative allele frequencies of rs1165176, rs1183201 and rs3799344 polymorphism of *SLC17A1* gene in Chinese with Gout (n = 400) and controls (n = 424)

SNP		Distribution, n (%)			OR	95% CI	*p* Value
rs1165196	Genotype	C/C	C/T	T/T			
	Gout	12 (3.0)	114 (28.5)	274 (68.5)			0.078
	Control	18 (4.2)	147 (34.7)	259 (61.1)			
	Allele	C	T			C vs T	
	Gout	138 (17.2)	662 (82.8)		0.758	0.592~0.969	0.027
	Control	183 (21.6)	665 (78.4)				
rs1183201	Genotype	A/A	A/T	T/T			
	Gout	272 (68.0)	116 (29.0)	12 (3.0)			0.056
	Control	255 (60.1)	150 (35.4)	19 (4.5)			
	Allele	A	T			A vs T	
	Gout	660 (82.5)	140 (17.5)			0.583~0.951	0.018
	Control	660 (77.8)	188 (22.2)		0.745		
rs3799344	Genotype	C/C	C/T	T/T			
	Gout	234 (58.5)	144 (36.0)	22 (5.5)			0.124
	Control	218 (51.4)	179 (42.2)	27 (6.4)			
	Allele	C	T			C vs T	
	Gout	612 (76.5)	188 (23.5)		0.811	0.649~1.013	0.064
	Control	615 (72.5)	233 (27.5)				

OR, odds ratio; SNP, single nucleotide polymorphism; CI, confidence interval.

Table 3. Association of three-marker rs1165196-rs1183201-rs3799344 haplotypes with gout

Haplotype	Frequency		OR (95% CI)	*p* Value
	Case	Control		
C-T-T	127.27 (0.159)	158.80 (0.187)	0.803 [0.621~1.038]	0.093
T-A-C	599.27 (0.749)	587.63 (0.693)	1.261 [1.008~1.577]	0.042
T-A-T	59.73 (0.075)	72.37 (0.085)	0.848 [0.593~1.212]	0.365

3') and for the rs1165196_T was using (5'-TTTTTTTTTTTTTTTTTTTTTTTTTTTTCCAGAAAAACGTAAAACTACCAA-3'). The Probe for the rs1183201_A was using (5'-TTTTTTTTTTTTTTTTTTTTCATTCACCTACTGATGGACATT-3') and for the rs1183201_T was using (5'-TTTTTTTTTTTTTTTTTTTTTTTTCATTCACCTACTGATGGACATA-3'). The Probe for thers3799344_C was using (5'-TTTTTTTTTTTTTTTTTTTTTTTTTTTTCCTCTGACCCCTCCTGAGGTGTG-3') and for the rs3799344_T was using (5'-TTTTTTTTTTTTTTTTTTTTTTTTTTTTCCTCTGACCCCTCCTGAGGTGTA-3'). The PCR conditions consisted of a denaturation step at 95°C for 2 min, followed by 35 cycles of 94°C for 30 s, 53°C for 1 min, and 65°C for 30 s, followed by a final extension step at 65°C for 10 min. The specific amplified fragments were used in an LDR assay to identify the mutations associated with rs1165196, rs1183201 and rs3799344. The LDR assay was performed as follows: 10 μL of the reaction mix contained 1 μL of 1 × ligase reaction buffer, 1 μL of probes (2 pmol/μL each), 0.05 μL (2 U) of thermostable Taq DNA ligase (Friendship Biotechnology Co, Ltd, China), and 4 μL of PCR product. The ligation reaction was performed with a GeneAmp PCR System 9600 (Norwalk, CT.06859 USA) as follows: 2 min at 95°C, followed by 40 cycles of 15 s at 94°C and 25 s at 50°C. The products were separated by agarose gel electrophoresis and analyzed by an ABI PRISM 3730 DNA sequencer. Genotyping was performed using an independent external contractor (Biowing Applied Biotechnology Co. Ltd., China).

Statistical analysis

Statistical analyses were carried out using SPSS version 13.0 (Stata, College Station, TX, USA). The student's t-test was used to assess a significant difference in demographic and clinical characteristics between cases and controls. Student's t test was also used to compare the levels of uric acid clinical parameters between different genotypes. Differences

Table 4. Demographic and clinical characteristics (Mean ± SD) between TT and CC+CT in rs1165176 genotype in *SLC17A1* gene

Parameter	TT (*n*=533)	CC+CT (*n*=291)	*p* Value
Age (year)	53.15 ± 14.78	53.79 ± 14.64	0.551
Body mass index (kg/m^2)	25.67 ± 3.13	25.76 ± 3.40	0.701
Waist/Hip	0.93 ± 0.07	0.93 ± 0.07	0.554
Systolic pressure (mmHg)	133.59 ± 16.65	134.01 ± 17.38	0.738
Diastolic pressure (mmHg)	82.50 ± 10.69	83.57 ± 11.74	0.186
Blood glucose (mmol/L)	5.48 ± 1.24	5.59 ± 1.30	0.264
Uric acid (umol/L)	393.31 ± 123.99	373.81 ± 125.12	0.032
Total cholesterol (mmol/L)	4.85 ± 0.97	4.83 ± 0.91	0.692
Triglycerides (mmol/L)	1.96 ± 1.79	1.80 ± 1.29	0.172
Creatinine (μmol/L)	86.75 ± 24.28	86.36 ± 21.56	0.821
Urea nitrogen (mmol/L)	5.45 ± 1.66	5.56 ± 1.68	0.317

Data are represented as the mean ± standard deviation.

Table 5. Demographic and clinical characteristics (Mean ± SD) between AA and TT+AT in rs1183201 genotype in *SLC17A1* gene

Parameter	AA (*n*=527)	TT+AT (*n*=297)	*p* Value
Age (year)	53.65 ± 14.70	52.89 ± 14.78	0.476
Body mass index (kg/m^2)	25.64 ± 3.17	25.81 ± 3.33	0.469
Waist/Hip	0.93 ± 0.070	0.93 ± 0.069	0.563
Systolic pressure (mmHg)	133.56 ± 17.09	134.05 ± 16.57	0.689
Diastolic pressure (mmHg)	82.66 ± 10.78	83.26 ± 11.61	0.452
Blood glucose (mmol/L)	5.52 ± 1.27	5.53 ± 1.24	0.944
Uric acid (umol/L)	393.56 ± 125.60	373.76 ± 122.16	0.029
Total cholesterol (mmol/L)	4.86 ± 0.95	4.82 ± 0.95	0.517
Triglycerides (mmol/L)	1.95 ± 1.61	1.82 ± 1.68	0.268
Creatinine (μmol/L)	86.72 ± 23.75	86.42 ± 22.64	0.856
Urea nitrogen (mmol/L)	5.53 ± 1.71	5.41 ± 1.58	0.269

Data are represented as the mean ± standard deviation.

between noncontiguous variables, genotype distribution, allele frequency, and Haplotype analysis were tested by chi-square analysis using SHEsis [11, 12]. Odds ratios and 95% confidence interval (CI) were calculated when possible. Multivariate regression analysis was conducted to evaluate the interaction between serum uric acid (sUA) and various factors such as body mass index (BMI), serum triglycerides and genotypes at rs1165196, rs1183201 and rs3799344 in gout and controls. Significant differences between or among groups were indicated by a *p* value<0.05.

Results

A total of 407 male gout patients and 424 male gout-free controls were participated in this study. Genotype from 400 of 407 gout patients and 424 of 438 gout-free controls were successfully sequenced. There were 159 cases of renal calculi patients, 241 patients without renal calculi in 400 patients with primary gout. Allele frequencies for each SNP were in Hardy-Weinberg equilibrium in both the patients and the controls (data not shown). Demographic data of the study population were shown in **Table 1**. The results showed that the gout patients had significantly higher levels of abnormal Body mass index, Diastolic pressure, Uric acid, creatinine, Urea nitrogen, total cholesterol, triglycerides, and higher rate of obesity, hypertension and hyperuricemia than the gout-free controls (P<0.05) (**Table 1**).

Rs1183201 and rs1165196 were located in the intronic region of the *SLC17A1* gene. The allele frequencies of both were significantly associated with the development of gout (**Table 2**), rs1183201 had stronger effect (OR 0.745, 95% CI=0.583~0.951, P=0.018) than rs1165196 (OR 0.758, 95% CI=0.592~0.969, P=0.027). However, Genotype frequencies of these two SNPs found no correlation with the development of gout (P=0.056, 0.078). The allele frequencies and Genotype frequencies of rs3799344 were not significantly associated with the development of gout (OR 0.811, 95% CI=0.649~1.013, P=0.064; 0.124). Because haplotypes were multi-allelic, we analyzed the association between haplotypes and gout in order to study how haplotype alterations affected the morbidity of gout. For example, whether it is risky or protective and it's associative in population. Analysis of three-marker haplotypes (rs1165196-rs1183201-rs3799344; **Table 3**) revealed the consistent evidence for

Table 6. Demographic and clinical characteristics (Mean ± SD) between CC and TT+CT in rs3799344 genotype in *SLC17A1* gene

Parameter	CC (*n*=452)	TT+CT (*n*=372)	*p* Value
Age (year)	53.98 ± 14.90	52.64 ± 14.50	0.195
Body mass index (kg/m^2)	25.59 ± 3.18	25.84 ± 3.28	0.278
Waist/Hip	0.93 ± 0.071	0.93 ± 0.068	0.434
Systolic pressure (mmHg)	133.56 ± 16.86	133.96 ± 16.96	0.732
Diastolic pressure (mmHg)	82.82 ± 10.71	82.94 ± 11.52	0.875
Blood glucose (mmol/L)	5.47 ± 1.25	5.60 ± 1.27	0.168
Uric acid (μmol/L)	394.12 ± 128.27	377.07 ± 119.62	0.051
Total cholesterol (mmol/L)	4.87 ± 0.97	4.83 ± 0.92	0.542
Triglycerides (mmol/L)	1.95 ± 1.60	1.85 ± 1.67	0.348
Creatinine (μmol/L)	87.80 ± 26.16	85.17 ± 19.30	0.108
Urea nitrogen (mmol/L)	5.53 ± 1.78	5.44 ± 1.52	0.431

Data are represented as the mean ± standard deviation.

Table 7. Multiple regression analysis of the association rs1165196, rs1183201 and rs3799344 polymorphism in *SLC17A1* and other factors with sUA levels in gout and controls

Variable	Regression coefficient	95% CI	*p* Value
(Intercept)	256.932	177.104 to 336.761	
rs1165196	0.037		0.337
rs1183201	0.079		0.016
rs3799344	0.033		0.472
Age	-0.141	-1.741 to -0.650	<0.001
BMI	0.114	1.822 to 6.679	<0.001
Triglycerides	0.266	15.267 to 25.253	<0.001

BMI, body mass index; sUA, serum uric acid.

association to come from the T-A-C haplotype (OR 1.261, 95% CI=1.078~1.803, P=0.042), with significant association in a Chinese Han male population.

Then, we investigated the association of the SNPs and clinical characteristics in gout and controls. Comparison between TT group and CC+CT group of rs1165196 genotype of *SLC17A1* gene, no statistical differences were found in age, body mass index, waist to hip ratio, blood pressure, blood glucose, total cholesterol, triglyceride, creatinine and urea nitrogen in two groups (P>0.05), Blood uric acid in TT group was higher than that in CC+CT group (393.31 ± 123.99 vs. 373.81 ± 125.12), the difference was statistically significant (P<0.05) (**Table 4**). Comparison between AA group and TT+AT group in rs1183201 genotype of *SLC17A1* gene, no statistical differences were found in age, body mass index, waist to hip ratio, blood pressure, blood glucose, total cholesterol, triglyceride, creatinine and urea nitrogen in two groups (P>0.05), Blood uric acid in AA group was higher than that in TT+AT group (393.56 ± 125.60 vs. 373.76 ± 122.16), the difference was statistically significant (P<0.05) (**Table 5**). Comparison between CC group and TT+CT group in rs3799344 genotype of *SLC17A1* gene, no statistical differences were found in age, body mass index, waist to hip ratio, blood pressure, blood glucose, blood uric acid, total cholesterol, triglyceride, creatinine and urea nitrogen in two groups (P>0.05) (**Table 6**).

Some medical factors such as obesity and dyslipidaemia have been indicated to be associated with sUA levels. Therefore, we conducted a Multivariate regression analysis to examine the interaction between sUA and *SLC17A1* polymorphisms together with age, BMI and serum triglyceride levels. Age, BMI, serum triglycerides and the genotype status of rs1183201 were significantly associated with sUA (P<0.001, P<0.001, P<0.001 and P=0.016) (**Table 7**).

There were 159 cases of renal calculi patients, 241 patients without renal calculi in patients with primary gout. The age in group with kidney stone was greater than that in group without renal stone, the difference was statistically significant (P<0.05), uric acid level in group with renal calculi was higher than that in group without renal calculi, but the difference was not statistically significant (P>0.05), body mass index, waist to hip ratio, systolic blood pressure, diastolic blood pressure, fasting blood glucose, serum uric acid, total cholesterol, triglyceride, serum creatinine and urea nitrogen in two groups had no significant difference (P>0.05) (**Table 8**). The allele frequencies and genotype frequencies of the rs1165196, rs1183201 and rs3799344 genotypes of *SLC17A1* gene were

Table 8. Demographic and clinical characteristics (Mean ± SD) in gout group with kidney stones (S) (n=241) and gout group without kidney stones (G) (n=159)

Parameter	G (*n*=241)	S (*n*=159)	*p* Value
Age (year)	51.15 ± 13.68	54.21 ± 12.56	0.022
Body mass index (kg/m^2)	25.92 ± 3.06	26.23 ± 2.88	0.299
Waist to Hip ratio	0.92 ± 0.06	0.92 ± 0.05	0.516
Systolic pressure (mmHg)	134.03 ± 16.92	134.67 ± 16.16	0.702
Diastolic pressure (mmHg)	84.52 ± 10.50	85.92 ± 10.37	0.189
Blood glucose (mmol/L)	5.47 ±1.50	5.40 ± 1.32	0.650
Uric acid (umol/L)	471.47 ± 113.70	486.69 ± 99.21	0.158
Total cholesterol (mmol/L)	5.03 ± 1.05	5.11 ± 1.02	0.443
Triglycerides (mmol/L)	2.46 ± 2.13	2.29 ± 1.70	0.376
Creatinine (μmol/L)	91.77 ± 31.31	94.42 ± 27.41	0.372
Urea nitrogen (mmol/L)	5.52 ± 1.99	5.81 ± 2.05	0.156

Data are represented as the mean ± standard deviation.

not significantly associated with the development of renal stones in patients with primary gout (P>0.05) (**Table 9**). Analysis of SLC17A1 rs1165196-rs1183201-rs3799344 gene haplotypes showed that C-T-T, T-A-C and T-A-T haplotypes (OR 1.207, 95% CI=0.823~1.772; OR 1.182, 95% CI=0.694~2.013 and OR 0.848, 95% CI=0.593~1.212) in Chinese Han population were not associated with the pathogenesis of kidney stones in patients with primary gout (P>0.05) (**Table 10**).

Discussion

Polymorphisms in the *SLC17A1* gene, which codes for NPT1, a sodium-dependent phosphate co-transporter, have also been shown to associate with gout [4]. It has also been shown that NPT1 mediates the transport of *p*-aminohippuric acid (PAH) and also accepts uric acid as one of the substrates [2]. Human NPT1 carrying an SNP mutation, Thr269Ile, known to increase the risk of gout, exhibited 32% lower urate transport activity compared to the wild type protein, leading to the conclusion that NPT1 is the long searched for transporter responsible for renal urate excretion [13]. Therefore, NPT1 was suggested to be responsible for tubular urate secretion in human kidney. *SLC17A1* is one of the genetic factors for the development of gout. Dehghan *et al.* [14] have reported the association between rs1165196 (T806C) and sUA using a genome-wide association study. The role of *SLC17A1* has been previously evaluated in gout in a Japanese sample set [4], with the nonsynonymous variant I269T (rs1165196) having the strongest evidence for association (OR= 0.55, P=0.004, minor allele (I269T) protective) and in a Caucasian population [8] with the variant rs1183201 having the strongest evidence for association (OR=0.67, P=3.0 × 10-6). Gout with uric acid under excretion is associated with transporter gene SNP related mainly to tubular reabsorption, whereas uric acid normoexcretion is associated only with tubular secretion SNP. This finding supports the concept of distinctive mechanisms to account for hyperuricemia in patients with gout with reduced or normal uric acid excretion [15]. And the study showed that NPT1 is a urate exporter located in the renal proximal tubule in humans, andthat its common gain-of-function variant, rs1165196, causes renal under excretion gout, a major subtype of gout [16].

Here, we provided evidence for a role of the *SLC17A1* locus (rs1183201 (OR 0.745, 95% CI=0.583~0.951, P=0.018); rs1165196 (OR 0.758, 95% CI=0.592~0.969, P=0.027)) in gout in a male Han Chinese population. The haplotype data (**Table 3**) were consistent with the presence of at least one genetic variant influencing the risk of gout at the *SLC17A1* locus. This was the first report that has indicated the association between the SNPs in the *SLC17A1* gene and the development of gout in a male Han Chinese population. The rs1165196 polymorphism leads to an Ile to Thr substitution at amino acid 269. Given that I269T has been shown to affect the function of *SLC17A1*, with the protective variant (I269T, minor allele of rs1165196) leading to increased activity in Xenopus oocytes and, presumably, increased renal elimination of urate [3], it was therefore possible that rs1165196 is an etiological variant. But rs1165196 was in strong LD with rs1183201 -the maximally associated variant in our study in Chinese samples (r2=0.96). The association was found between genotypes at

Table 9. Genotype distribution and relative allele frequencies of rs1165176, rs1183201 and rs3799344 polymorphism of *SLC17A1* gene in Chinese in gout group with kidney stones (S) (*n* = 241) and gout group without kidney stones (G) (*n* = 159)

SNP		Distribution, n (%)			OR	95% CI	*p* Value
rs1165196	Genotype	C/C	C/T	T/T			
	S	8 (5.0)	42 (26.4)	109 (68.6)			0.133
	G	4 (1.7)	72 (29.9)	165 (68.5)			
	Allele	C	T			C vs T	
	S	58 (18.2)	260 (81.8)		1.121	0.773~1.627	0.548
	G	80 (16.6)	402 (83.4)				
rs1183201	Genotype	A/A	A/T	T/T			
	S	108 (67.9)	43 (27.0)	8 (5.0)			0.137
	G	164 (68.0)	73 (30.3)	4 (1.7)			
	Allele	A	T			A vs T	
	S	259 (81.4)	59 (18.6)		0.887	0.612~1.284	0.524
	G	401 (83.2)	81 (16.8)				
rs3799344	Genotype	C/C	C/T	T/T			
	S	89 (56.0)	58 (36.5)	12 (7.5)			0.314
	G	145 (60.2)	86 (35.7)	10 (4.1)			
	Allele	C	T			C vs T	
	S	236 (74.2)	82 (25.8)		0.811	0.583~1.130	0.216
	G	376 (78.0)	106 (22.0)				

OR, odds ratio; SNP, single nucleotide polymorphism; CI, confidence interval.

Table 10. Association of three-marker rs1165196-rs1183201-rs3799344 haplotypes with gout group with kidney stones (S) and gout group without kidney stones (G)

Haplotype	Frequency		OR (95% CI)	*p* Value
	S	G		
C-T-T	55.84 (17.6)	71.43 (14.8)	1.207 [0.823~1.772]	0.335
T-A-C	232.84 (73.2)	366.43 (76.0)	1.182 [0.694~2.013]	0.538
T-A-T	59.73 (0.075)	72.37 (0.085)	0.848 [0.593~1.212]	0.365

rs1165196 and rs1183201 (P=0.032; 0.029) and sUA levels in gout and controls. The rs1183201 genotypes of *SLC17A1* gene had correlation with serum uric acid levels using multivariate regression analysis in our study. Ostensibly, this observation argued that rs1183201 (or a variant in strong LD) was also an etiological variant within *SLC17A1* in a male Han Chinese population. But we also found no association between two SNPs in the *SLC17A1* gene and the development of kidney stones in Chinese patients with primary gout.

In conclusion, the present study indicated that *SLC17A1* polymorphisms including T806C were associated with the development of gout in a male Han Chinese population. A more in-depth investigation of these loci and functional experiments are required to unravel the exact mechanism by which this region is pathologically involved in gout.

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Disclosure of conflict of interest

None.

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