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Original Article

The contribution of the *LOC105371267* and *MRPS30-DT* genetic polymorphisms to IgA nephropathy in the Chinese Han population

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Abstract: Background: IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide. Genetic factors are reported to play an essential role in IgAN progression. This study was designed to investigate the association between *LOC105371267* and *MRPS30-DT* and IgAN risk among the Chinese Han population. Methods: Six SNPs were genotyped. A logistic regression model was used to calculate the effects of the candidate SNPs on IgAN. The SNP-SNP interaction was analyzed using multifactor dimensionality reduction. Results: We observed that only *LOC105371267* had a relationship with IgAN. The results indicated an association between the genotype "CC" and a decreased IgAN risk (OR=0.44, *P*=0.014). The stratification analysis of the patients over 35 years old showed that rs3931698 contributes to IgAN susceptibility in the "GT" genotype (OR=1.78, *P*=0.038), while rs8044565 showed a significantly decreased risk-effect with IgAN ("T", OR=0.59, *P*=0.006; "CC", OR=0.15, *P*=0.015; "CC-CT", OR=0.59, *P*=0.023; Log-additive, OR=0.56, *P*=0.005). rs8044565 was correlated with a decreased susceptibility of IgAN in males ("CC", OR=0.27, *P*=0.006) and in patients with a Lee's grade ≥III ("CC", OR=0.46, *P*=0.046). We found rs8044565 is related to systolic blood pressure and urinary casts and rs3852740 has a relationship with the serum C3 and hemoglobin levels (*P*<0.05). Conclusion: The present study demonstrated that the SNPs in long non-coding RNAs might be related to IgAN.

Keywords: IgA nephropathy, *LOC105371267*, *MRPS30-DT*, polymorphisms

Introduction

With the development of modern society, especially changes in dietary habits, the increased morbidity and mortality of chronic kidney disease has attracted attention. Immunoglobulin A nephropathy (IgAN) is an autoimmune disease, accounting for 45.3%-54.3% of primary glomerulonephritis, and is a leading cause of end-stage renal disease (ESRD) in China [1, 2]. IgAN is characterized by a single histopathological criterion of pre-dominant IgA deposits in kidney biopsies; however, renal biopsies are invasive and have the limitation of assessing disease activity only at the time of the biopsy, which could lead to inconclusive findings and decisions [3, 4]. Recently, it has been recognized that genetic factors play a crucial role in the development of IgAN, and genetic differences may serve as potential diagnostic indicators [5-7].

Research reveals that greater than 70% of the genome is transcribed, and that a vast majority of transcribed DNA encodes long non-coding RNAs (lncRNAs) [8, 9]. lncRNAs are an important class of non-coding RNA characterized by a length longer than 200 nt. Accumulating evidence suggests that lncRNAs have an essential role in diverse pathological settings, including cancer, cardiovascular disease, and kidney disease [9, 10]. Recent studies have reported a relationship between lncRNAs and various kidney diseases [11-13], but few have addressed IgAN [14, 15]. Guo et al. used high-throughput RNA sequencing and qRT-PCR to test the exo-

somes isolated from the plasma of IgAN patients and a healthy first-degree relative. The results revealed that exosomal lncRNA-G21551 is downregulated in IgAN patients, indicating its potential to serve as a non-invasive biomarker for IgAN [14]. In the study of Zuo et al., peripheral blood mononuclear cells were collected from both IgAN patients and healthy controls to identify differentially expressed lncRNAs and mRNAs using microarray analyses and quantitative polymerase chain reactions. Their results demonstrate that differentially expressed lncRNAs and mRNAs may have a role in the development of IgAN [15]. However, there is no genetic polymorphism research on IgAN. Thus, we designed this study to investigate the association between single nucleotide polymorphisms (SNPs) and IgAN.

LOC105371267, located on chromosome 16, is a lncRNA involved in the p53 network that is not well studied. It was reported that p53 upregulation in renal resident cells may be linked to the pathogenesis of progressive IgAN [16], but the role of *LOC105371267* in IgAN susceptibility remains unclear. Additionally, *MRPS30-DT* on chromosome 5 is broadly expressed in breast, kidney, and other tissues [17]. Until now, no data have been found on the relationship between *MRP30-DT* and IgAN.

Therefore, in this study, we conducted a case-control study to identify the association between IgAN susceptibility and six SNPs in *LOC105371267* and *MRP30-DT* in the Chinese Han population. The study aimed to identify the potential role of these SNPs in IgAN.

Methods

Study participants

Our study included 836 unrelated people, including 413 IgAN patients and 423 geographically ethnicity-matched healthy subjects who were recruited from the Xi'an Hospital of Traditional Chinese Medicine. All the patients met the diagnostic criteria as confirmed by renal biopsies, and patients with other autoimmune diseases or secondary IgAN were excluded [18]. The healthy subjects were recruited from the physical examination center during the same period. The participants' clinical information was collected, including their ages, genders, serum albumin (ALB) levels, creatinine (CREA) levels, urine red blood cell (URBC) counts, hemoglobin (HB) levels, serum uric acid (UA) levels, fibrinogen (FIB) levels, and pathological grades (Lee's classification).

We designed this protocol in compliance with the Ethics Committee of the Xi'an Hospital of Traditional Chinese Medicine and the guidelines of the Declaration of Helsinki. All the participants were provided with and signed the written informed consent forms.

Selection and genotyping of SNPs

We identified six SNPs in *LOC105371267* and *MRP30-DT* with a minor allele frequency (MAF) >0.05 in the 1000 Genomes Projects (http://www.internationalgenome.org/). Fasting peripheral blood from all the participants was collected in anticoagulant tubes and stored at -80°C. We extracted the DNA using whole blood genomic DNA extraction kits (GoldMag, China) in accordance with the provided manufacture's protocol, and the DNA content was measured using spectrometry (NanoDrop 2000 spectrophotometer, Thermo Scientific, USA). An SNP MassEXTEND assay was designed by Agena MassARRAY Assay Design Software (version 3.0, Agena Bioscience, USA). Moreover, Agena MassARRAY RS100 was used to determine the SNP genotyping. The data were analyzed using Agena Typer Software (version 4.0, Agena Bioscience, USA).

Bioinformatics analysis

The current study analyzed and predicted the possible functional effects of these candidate SNPs using the online software HaploReg v4.1 (https://pubsbroad institute.org/mamma ls/haploreg/haploreg.php) [19, 20] and SNP info Web Server (https://snpin fo.niehs.nih.gov/snpinfo/index.html) [21].

Statistical analysis

SPSS software (version 20.0) was used for the data analysis. Independent sample T-tests or χ^2 tests were used to examine the differences in the basic parameters between the cases and the controls. The Hardy-Weinberg equilibrium (HWE) was tested using χ^2 tests for each SNP selected in the current study. The IgAN risk associated with the genotype was estimated using odds ratios (ORs) with 95% confidence intervals (CIs) for five different genetic models. The differences in the clinical characteristics

Table 1. Basic characteristic of the IgAN cases and the healthy controls in this study

Characteristics	Controls (n=423)	Cases (n=413)	*P*
Age, years (mean ± SD)	33.34±10.11	33.21±12.07	0.861
>35 years old	165 (39%)	155 (38%)	
≤35 years old	258 (61%)	258 (62%)	
Gender			0.942
Male	275 (65%)	267 (65%)	
Female	148 (35%)	146 (35%)	
Pathological grade			
≥III	423 (100%)	263 (64%)	
<III	423 (100%)	136 (33%)	
Clinical index			
Urine RBC (μL)	26.17±141.94	195.42±371.96	<0.001
Urine casts (μL)	0.38±0.58	4.93±19.14	<0.001
ALB (g/L)	46.95±2.97	35.95±9.50	<0.001
CREA (μmol/L)	67.24±15.51	154.03±173.05	<0.001
UA (μmol/L)	340.83±94.75	383.88±114.60	<0.001
HB (g/L)	150 87±17.89	126.49±23.98	<0.001
FIB (g)	3.03±0.24	3.78±1.28	<0.001

RBC, Red blood cell; ALB, Serum albumin; CREA, Creatinine; UA, Serum uric acid; HB, Hemoglobin; FIB, Fibrinogen.

among the different genotypes were analyzed using ANOVA tests. The SNP-SNP interactions associated with the risk of IgAN were analyzed using multifactor dimensionality reduction (MDR) (version 3.0.2). For all the tests, a two-tailed *P*-value <0.05 was considered statistically significant.

Results

Basic characteristics of the participants

The current study included 413 IgAN patients (267 males and 146 females) and 423 healthy controls (275 males and 148 females). The mean ages of the cases and controls were (33.21±12.07) and (33.34±10.11) years old, and there were no significant differences in terms of age or gender between the case and control groups (*P*=0.861, *P*=0.942, respectively). The demographic and clinical characteristics are listed in **Table 1**, including age, gender, pathological grade, URBC, urine casts, serum ALB, CREA, serum uric acid (UA), HB, and fibrinogen (FIB). Significant differences were observed in the URBC, urine casts, ALB, CREA, UA, HB, and FIB between the two groups (all *P*<0.001). The genotypes of the 6 SNPs in the case group and the control group were shown in Supplementary Table 1.

The association between genetic polymorphisms and IgAN risk

The basic information of the SNPs in *LOC105371267* and *MRPS30-DT* is presented in **Table 2**. All the genetic polymorphisms were complied with HWE (*P*>0.05). Significantly in **Table 3**, rs8044565 in *LOC105371267* showed a decreased risk for IgAN adjusted for age and gender (CC vs TT, OR=0.43, 95% CI=0.23-0.84, *P*=0.012; Recessive model, OR=0.43, 95% CI=0.23-0.82, *P*=0.011). However, other SNPs in *LOC105371267* and *MRP30-DT* showed no significant association with IgAN risk.

Stratification analysis of the SNPs with IgAN risk

Next, we did a stratified analysis of selected SNPs with IgAN risk. The results shown in **Table 4** indicate that in the subgroup of age >35 years, rs3931698 in *LOC105371267* was significantly associated with an increased risk of IgAN (GT vs TT, OR=1.78, 95% CI=1.03-3.07, *P*=0.038), while rs8044565 in *LOC105371267* showed a decreased risk of IgAN (T vs C, OR=0.59, 95% CI=0.40-0.86, *P*=0.006; CC vs TT, OR=0.15, 95% CI=0.03-0.69, *P*=0.015; Dominant model, OR=0.59, 95% CI=0.97-0.93, *P*=0.023; Recessive model, OR=0.17, 95% CI=0.04-0.08, *P*=0.025; Log-additive, OR=0.56, 95% CI=0.38-0.84, *P*=0.005).

Using the gender stratification shown in **Table 5**, we observed that in males, rs8044565 in *LOC105371267* was associated with a decreased IgAN risk (CC vs TT, OR=0.27, 95% CI=0.11-0.69, *P*=0.006; Recessive model, OR=0.27, 95% CI=0.11-0.70, *P*=0.007). In addition, using the stratification of Lee's grade shown in **Table 6**, rs8044565 in *LOC105371267* was correlated with a decreased IgAN risk (CC vs TT, OR=0.46, 95% CI=0.21-0.98, *P*=0.046; Recessive, OR=0.44, 95% CI=0.21-0.95, *P*=0.036).

Genotypes and clinical characteristics

Additionally, we analyzed the relationship between the different genotypes of the SNPs in *LOC105371267* and *MRPS30-DT* and the cli-

Table 2. Basic information for *Loc105371267* SNPs

SNP ID	Gene	Chr: Position	Role	Alleles (A/B)	MAF		*P-value* for HWE	Haploreg 4.1
					Cases	Controls		
rs3931698	LOC105371267	Chr16: 53070825	Intron	G/T	0.144	0.139	1	Enhancer histone marks; DNAse; Motifs changed
rs8044565	LOC105371267	Chr16: 53073990	Intron	C/T	0.230	0.261	0.450	Motifs changed
rs3852740	LOC105371267	Chr16: 53078171	Intron	G/C	0.212	0.217	0.668	Promoter histone marks; Enhancer histone marks; DNAse; Proteins bound; Motifs changed
rs111577197	LOC105371267	Chr16: 53083155	Intron	T/C	0.195	0.193	0.438	Enhancer histone marks; Motifs changed
rs16901963	MRPS30-DT	Chr5: 44783102	Intron	T/A	0.390	0.391	0.307	Motifs changed; Selected eQTL hits
rs2118763	MRPS30-DT	Chr5: 44787546	Intron	T/C	0.057	0.067	0.702	Motifs changed

SNP, Single nucleotide polymorphisms, MAF, minor allele frequency, HWE, Hardy-Weinberg equilibrium.

Table 3. Association analysis between the SNPs and the IgAN risk

SNP ID	Gene	Model	Genotype	Case	Control	Without adjusted		Adjusted by age and gender	
						OR (95% CI)	P^a	OR (95% CI)	P^b
rs8044565	*LOC105371267*	Genotype	TT	233	234	1		1	
			CC	14	32	0.44 (0.23-0.84)	0.014	0.43 (0.23-0.84)	0.012
			CT	159	157	1.02 (0.76-1.35)	0.907	1.02 (0.76-1.35)	0.912
		Dominant	TT	173	189	1		1	
			CC-CT	233	234	0.91 (0.70-1.21)	0.548	0.92 (0.70-1.21)	0.540
		Recessive	CT-TT	14	32	1		1	
			CC	392	391	0.44 (0.23-0.83)	0.012	0.43 (0.23-0.82)	0.011
		Log-additive	-	-	-	0.84 (0.67-1.06)	0.139	0.84 (0.67-1.06)	0.133

CI, confidence interval; OR, odds ratio; SNP, single nucleotide polymorphism. The *P* a-values were calculated using an unconditional logistic regression analysis without adjustments for age and gender. The *P* b-values were calculated using an unconditional logistic regression analysis with adjustments for age and gender. $P<0.05$ indicates statistical significance.

Table 4. The SNPs of *LOC105371267* associated with the IgAN risk in the age subgroup tests

SNP ID	Model	Allele/ genotype	Case	Control	OR (95% CI)	*P*	Case	Control	OR (95% CI)	*P*
Age, years			>35				≤35			
rs3931698	Allele	G	49	39	1.00		70	78	1.00	
		T	261	291	1.40 (0.89-2.20)	0.143	446	436	0.88 (0.62-1.24)	0.462
	Genotype	TT	110	131	1.00		191	182	1.00	
		GG	4	5	1.04 (0.27-4.05)	0.951	3	3	0.93 (0.19-4.70)	0.945
		GT	41	29	1.78 (1.03-3.07)	0.038	64	72	0.86 (0.58-1.29)	0.469
	Dominant	TT	110	131	1.00		191	182	1.00	
		GG-GT	45	34	1.67 (1.00-2.81)	0.052	67	75	0.87 (0.59-1.28)	0.473
	Recessive	GT-TT	151	160	1.00		255	254	1.00	
		GG	4	5	0.91 (0.24-3.51)	0.892	3	3	0.97 (0.19-4.87)	0.972
	Log-additive	-	-	-	1.44 (0.92-2.25)	0.106	-	-	0.88 (0.61-1.27)	0.498
rs8044565	Allele	C	54	89	1.00		377	384	1.00	
		T	248	241	0.59 (0.40-0.86)	0.006	133	132	1.03 (0.78-1.34)	0.856
	Genotype	TT	99	87	1.00		134	147	1.00	
		CC	2	11	0.15 (0.03-0.69)	0.015	12	21	0.58 (0.27-1.23)	0.157
		CT	50	67	0.66 (0.41-1.06)	0.087	109	90	1.34 (0.93-1.94)	0.118
	Dominant	TT	99	87	1.00		134	147	1.00	
		CC-CT	52	78	0.59 (0.37-0.93)	0.023	121	111	1.19 (0.84-1.69)	0.327
	Recessive	CT-TT	149	154	1.00		243	237	1.00	
		CC	2	11	0.17 (0.04-0.80)	0.025	12	21	0.52 (0.25-1.08)	0.078
	Log-additive	-	-	-	0.56 (0.38-0.84)	0.005	-	-	1.01 (0.76-1.34)	0.934

CI, confidence interval; OR, odds ratio; SNP, single nucleotide polymorphism. $P<0.05$ indicates statistical significance.

nical characteristics, including systolic blood pressure (SBP), diastolic blood pressure (DBP), urinary casts, serum C3, CREA, serum UA, HB, and the urine beta 2 microglobulin (β2-MG) levels. As shown in **Table 7**, we observed that in *LOC105371267* rs8044565, the "TC" genotype patients (91.80±19.89 mmHg) had higher DBP levels than the TT (89.82±20.93 mmHg) and CC (77.64±26.73 mmHg) genotype patients, and the TT genotype patients (18.46±41.23 μL) had significantly higher urinary cast levels than the TC (5.57±21.28 μL) and CC (3.70±15.28 μL) genotype patients. Meanwhile, for rs3852740 in *LOC105371267*, the GG genotype patients (1.22±.041 g/L) had higher serum C3 levels than the CG (1.05±0.25 g/L) and CC (1.04±0.25 g/L) genotype patients, but the GG genotype patients (137.45± 18.06 g/L) had higher HB levels than the CG (128.92±23.78 g/L) and CC (124.33±24.22

Table 5. The association between the SNPs and the IgAN risk using gender stratification tests

SNP ID	Model	Allele/ genotype	Case	Control	OR (95% CI)	*P*	Case	Control	OR (95% CI)	*P*
Gender			Male				Female			
rs8044565	Allele	C	116	149	1.00		71	72	1.00	
		T	406	401	0.77 (0.58-1.02)	0.065	219	224	1.01 (0.69-1.47)	0.964
	Genotype	TT	151	147	1.00		82	87	1.00	
		CC	6	21	0.27 (0.11-0.69)	0.006	8	11	0.77 (0.30-2.02)	0.599
		CT	104	107	0.94 (0.66-1.34)	0.739	55	50	1.17 (0.71-1.90)	0.533
	Dominant	TT	151	147	1.00		82	87	1.00	
		CC-CT	110	128	0.83 (0.59-1.17)	0.292	63	61	1.10 (0.69-1.74)	0.696
	Recessive	CT-TT	255	254	1.00		137	137	1.00	
		CC	6	21	0.27 (0.11-0.70)	0.007	8	11	0.73 (0.28-1.87)	0.509
	Log-additive	-	-	-	0.75 (1.56-1.00)	0.052	-	-	1.01 (0.70-1.46)	0.962

CI, confidence interval; OR, odds ratio; SNP, single nucleotide polymorphism. *P*<0.05 indicates statistical significance.

Table 6. The correlation between the SNPs and the IgAN susceptibility stratified by pathological grade

SNP ID	Model	Allele/ genotype	Case	Control	OR (95% CI)	*P*	Case	Control	OR (95% CI)	*P*
Pathological grade			≥III				<III			
rs8044565	Allele	C	122	221	1.00		61	221	1.00	
		T	396	625	0.87 (0.68-1.12)	0.288	207	625	0.83 (0.60-1.15)	0.270
	Genotype	TT	146	234	1.00		78	234	1.00	
		CC	9	32	0.46 (0.21-0.98)	0.046	5	32	0.45 (0.17-1.20)	0.239
		CT	104	157	1.07 (0.77-1.48)	0.679	51	157	0.99 (0.66-1.50)	0.981
	Dominant	TT	146	234	1.00		78	234	1.00	
		CC-CT	113	189	0.97 (0.70-1.32)	0.833	56	166	0.90 (0.61-1.33)	0.595
	Recessive	CT-TT	250	391	1.00		129	391	1.00	
		CC	9	32	0.44 (0.21-0.95)	0.036	5	32	0.45 (0.17-1.18)	0.106
	Log-additive	-	-	-	0.88 (0.68-1.13)	0.312	-	-	0.84 (0.61-1.15)	0.275

P values were calculated by logistic regression adjusted by age and gender. *P*<0.05 indicates statistical significance.

Table 7. The correlation between the clinical characteristics and the SNP genotypes

SNP	SBP (mmHg)	DBP (mmHg)	Urinary Casts (μL)	Serum C3 (g/L)	CREA (μmol/L)	UA (μmol/L)	HB (g/L)	Urine β2-MG (μg/L)
rs8044565								
CC	121.55±33.54	77.64±26.73	3.70±15.28	1.06±0.28	92.97±63.68	354.50±140.62	124.86±23.23	884.47±999.78
TC	138.35±26.75	91.80±19.89	5.57±21.28	1.04±0.22	155.22±178.35	391.51±115.08	125.77±23.93	620.08±893.88
TT	139.64±30.48	89.82±20.93	18.46±41.23	1.05±0.25	152.62±164.61	379.13±113.05	127.57±23.89	584.34±900.57
P	0.080	0.048	0.023	0.836	0.410	0.381	0.738	0.505
rs3852740								
GG	140.30±34.47	90.21±22.33	1.56±2.67	1.22±.041	123.61±94.53	361.96±89.4	137.45±18.06	439.54±759.32
CG	140.14±30.86	90.38±20.13	4.52±15.76	1.05±0.25	155.20±182.82	379.67±100.28	128.92±23.78	477.98±743.99
CC	137.73±27.92	138.65±29.20	5.41±21.38	1.04±0.25	155.82±172.82	387.99±123.47	124.33±24.22	694.13±974.74
P	0.721	0.886	0.658	0.011	0.723	0.546	0.022	0.096

SBP, systolic blood pressure; DBP, diastolic blood pressure; CREA, creatinine; UA, Serum uric acid; HB, Hemoglobin; β2-MG, beta 2 microglobulin. The *P* values were calculated using Kruskal-Wallis H tests. *P*<0.05 indicates statistical significance.

g/L) genotype patients. However, other SNPs in *LOC105371267* and *MRP30-DT* showed no significant correlations with the characteristics of IgAN.

Table 8. MDR analyses of the SNP-SNP interactions and the IgAN risks

Model	Training Bal. Acc	Testing Bal. Acc	OR (95% CI)	Testing χ^2 value	*P* value	CVC
rs8044565	0.522	0.482	1.36 (0.93-2.01)	2.506	0.113	8/10
rs8044565, rs3852740	0.536	0.454	1.35 (1.01-1.82)	3.975	0.046	7/10
rs8044565, rs3852740, rs111577197	0.550	0.464	1.50 (1.12-2.01)	7.570	0.006	9/10

MDR, multifactor dimensionality reduction; Bal. Acc., balanced accuracy; CVC, cross-validation consistency; OR, odds ratio; 95% CI, 95% confidence interval. The *P* values were calculated using χ^2 tests. *P*<0.05 indicates statistical significance.

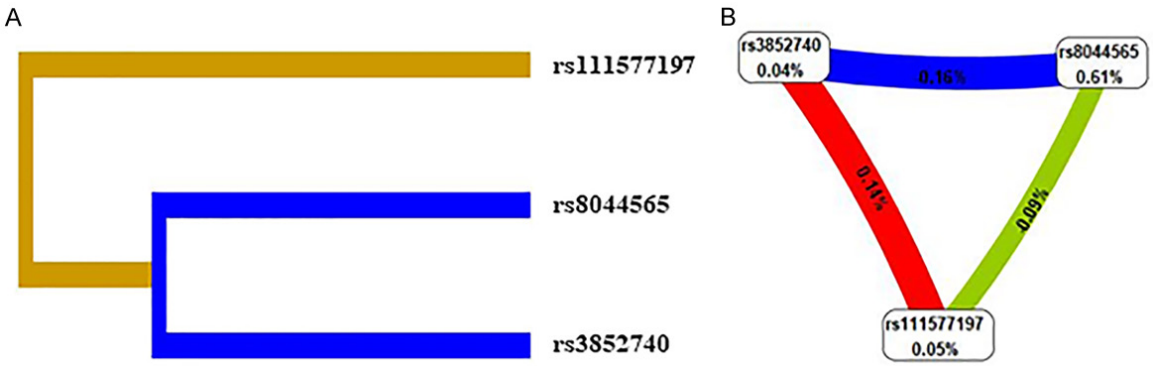

Figure 1. An SNP-SNP interaction dendrogram (A) and Fruchterman-Reingold (B). The dendrogram and Fruchterman-Reingold include a spectrum of colors that represent a continuum from synergy to redundancy. Orange represents a relatively high degree of synergy (positive information gain), and blue represents redundancy (negative information gain).

SNP-SNP interactions

We used an MDR analysis to assess the effect of the SNP-SNP interactions among the four selected SNPs in *LOC105371267* (**Table 8**). In total, we found a three-locus mode including rs8044565, rs3852740, and rs111577197 were the best model (cross-validation consistency =9/10, testing balanced accuracy =0.464, *P*=0.006). The interactions between the loci are presented in a dendrogram and the Fruchterman-Reingold in **Figure 1A** and **1B**, respectively.

Discussion

IgAN is a complex autoimmune disease with a pathogenesis that needs clarification. Accumulating evidence indicates that genetic and environmental factors have an essential role in the development of IgAN. Previous studies revealed that some genetic variations, such as *FCRL3*, *DRB-1* and *DEFA* [22-24], are significantly associated with the risk of IgAN, but few associations are reported with lncRNAs, which recently have attracted attention for their functions in gene regulation [25]. More importantly, it was reported that lncRNAs are associated with IgAN; however, there is no data demonstrating the genetic polymorphisms that influence IgAN.

We designed this case-control study to determine the association between the genetic polymorphisms in two lncRNAs and the susceptibility to IgAN. The results show that only *LOC105371267* has an association with IgAN, and the rs8044565 variant in *LOC105371267* might serve as a potential protective factor for IgAN overall. Interestingly, our subsequent stratified analysis showed that the *LOC105371267* rs3931698 variant are associated with a susceptibility to IgAN in the subgroup of age >35 years, while the *LOC105371267* rs8044565 variant reduced the risk of IgAN. We also found that rs8044565 decreased the risk of IgAN in males and was significantly associated with the Lee's grade. In view of the complicated pathogenic factors of IgAN, SNP-SNP interaction studies may help discover the risk factors for IgAN [26]. Accordingly, we analyzed the potential SNP-SNP interactions in *LOC105371267* using MDR. The analysis indicated a strong interaction between rs8044565, rs3852740,

and rs111577197 regarding the association with IgAN. To the best of our knowledge, this is the first demonstration of the effects of the relationships between these SNPs in lncRNA and the IgAN risk.

LOC105371267, located on chromosome 16, is a p53-regulated lncRNA that does not have a clear association with IgAN risk. In recent years, evidence has emerged showing that the dysfunction of the p53 network is associated with the development of autoimmune diseases [27-29]. Thus, it is important to determine the association between *LOC105371267* and IgAN. In the current study, we first investigated the association between four polymorphisms in *LOC105371267* with IgAN risk among the Chinese Han population. The results show that rs8044565 in *LOC105371267* is significantly associated with a reduced IgAN risk in the different genetic models. Therefore, it may serve an important protective role against IgAN, but this needs to be further verified.

Given the current aging society in China, age in IgAN patients is an important factor to consider. A previous cohort study in 2019 indicated that the mean age at the diagnosis of IgAN was 32.9 years old [3]. Thus, to determine the genetic effect of age in IgAN, we did an analysis stratified by age at 35 years old, which showed that the genotype "GT" in *LOC105371267* rs3931698 contributes to IgAN susceptibility (OR=1.78, 95% CI=1.03-3.07, *P*=0.038) in the group aged >35 years, while *LOC105371267* rs8044565 is significantly associated with a reduced IgAN risk in the same subgroup. At the same time, the genotype "CC" in rs8044565 showed a decreased risk-effect with IgAN (OR=0.27, 95% CI=0.11-0.69, *P*=0.006). This suggests that rs8044565 in *LOC105371267* might have a protective effect in the group of males who were older than 35 years.

Several studies show that SNPs have a strong susceptibility to IgAN according to the Lee's grade [30-32]. In the current study, we observed that the genotype "CC" (OR=0.46, 95% CI=0.21-0.98, *P*=0.046) in *LOC105371267* rs8044565 is significantly related to a reduced IgAN risk under the stratification of Lee's grade >III. The clinical characteristics can be regarded as indicators for IgAN [33]. Thus, we determined the correlation between the SNPs and the clinical characteristics of IgAN. We observed that *LOC105371267* rs8044565 is related to diastolic blood pressure and urinary casts, but *LOC105371267* rs3852740 is related to the serum C3 and hemoglobin levels. We speculate that the SNPs in *LOC105371267* may correlate with the clinical indicators, but this needs to be verified by investigating additional indicators in further studies.

Several intrinsic limitations to our study should be considered. First, the selection bias in this case-control study was its hospital-based design, and it may not be representative of the general population. Second, environmental exposure was not available, which did not allow us to further analyze the potential interactions of the gene-environment on the IgAN risk. Importantly, further functional assays in our present study provide scientific evidence about the association of *LOC105371267* with IgAN in future studies.

Conclusion

To summarize, this study investigated the association of the SNPs in lncRNA *LOC105371267* and *MRPS30-DT* with the risk of IgAN. The results revealed that only the *LOC105371267* variants are significantly associated with the IgAN risk, and rs8044565 may be a protective factor, but this needs to be further verified using larger sample studies. Notably, our study is the first to determine the relationship between lncRNA and IgAN risk. Finally, new insight on the molecular mechanism in the development of IgAN is provided.

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Disclosure of conflict of interest

None.

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Supplementary Table 1. The genotypes of 6 SNPs in the case group and the control group

serial number	type	rs111577197	rs16901963	rs3852740	rs3931698	rs8044565	rs2118763
1	cases	CC	TA	CC	GG	TT	CT
2	cases	TC	TA	CC	TT	TT	CC
3	cases	TC	AA	CC	GT	TT	CC
4	cases		AA	CC	TT	TC	CT
5	cases	CC	AA	CC	TT	TC	CC
6	cases	CC	TA	CC	TT	TT	CC
7	cases	CC	TA	CC	TT	TC	CC
8	cases	TC	AA	CC	TT	CC	CC
9	cases	CC	TA	CG	GT	TT	CC
10	cases	TC	AA	CC	TT	TC	CC
11	cases	TC	AA	CG	TT	TC	CT
12	cases	CC	TA	GG	TT	TC	CC
13	cases	CC	TA	CG	TT	TT	CC
14	cases	CC	TA	CC	TT	TC	CT
15	cases	CC	TT	CC	TT	TC	CC
16	cases	CC	AA	CG	TT		CT
17	cases	TT	TA	CG	TT	TC	CC
18	cases	TC	AA	CC	TT	TC	CC
19	cases	TC	TA	CC	GT	TC	CC
20	cases	TT	TA	CC	TT	TC	CT
21	cases	TC	AA	CC	GG	TT	CC
22	cases	CC	AA	GG	TT	TT	CT
23	cases	TC	AA	CC	TT	TT	CT
24	cases	CC	TA	CC	GT	TT	CC
25	cases	TC	TA	CC	GT	TT	CC
26	cases	TC	TA	CG	GT		CC
27	cases	CC	AA	CC	GT	TT	CC
28	cases	TC	TA	CC	TT	TC	CC
29	cases	TC	TA	CC	TT	TC	CC
30	cases	CC	TA	CG	GT	TT	CC
31	cases	CC	TT	CC	TT	TT	CC
32	cases	CC	TA	CG	GT	TT	CC
33	cases	CC	AA	CG	TT	TT	CC
34	cases	TC	TA	CC	GT	TC	CC
35	cases	CC	TA	CC	GT	TT	CC
36	cases	TC	TT	CG	TT	TC	CC
37	cases	CC	AA	CC	GT	TT	CC
38	cases	TC	TA	CG	TT	TT	CC
39	cases	TT	TA	CG	TT	TC	CC
40	cases	CC	AA	CC	TT	TC	CC
41	cases	TC	TT	CC	GT	TC	CC
42	cases	TC	AA	CC	TT	TC	CC
43	cases	CC	AA	CG	TT	TT	CC
44	cases	CC	TA	CG	TT	TC	CC
45	cases	CC	TA	CC	TT	TT	CC
46	cases	CC	AA	CC	TT	TT	CC
47	cases	TC	TA	CC	GT	TT	CC
48	cases	TC	TA	CC	TT	TC	CT

49	cases	CC	TA	CC	TT	TC	CC
50	cases	CC	AA	CG	GT	TT	CT
51	cases	TC	TT	CC	TT	TT	CC
52	cases	TC	TA	CC	TT	TT	CC
53	cases	CC	TA	CC	TT	TT	CC
54	cases	CC	TT	CC	TT	TC	CC
55	cases	TC	AA	CC	GT	TC	CT
56	cases	CC	TA	CG	TT	TT	CC
57	cases	CC	AA	GG	TT	TT	CT
58	cases	CC	AA	CC	TT	TC	CC
59	cases	CC	AA	CC	GT		CC
60	cases	TC	AA	CC	TT	TC	CC
61	cases	CC	TT	CC	GT	TT	CC
62	cases	TC	TT	CC	TT	TT	CC
63	cases	TC	TA	CG	TT	TC	CC
64	cases	CC	TA	CC	GT	TT	CC
65	cases	CC	TA	CG	TT	TT	CT
66	cases	CC	AA	CG	TT	TC	CT
67	cases	TT	TA	CG	TT	TT	CC
68	cases	CC	TA	CC	GT	TC	CC
69	cases	CC	TA	CG	TT	TC	CC
70	cases	CC	AA	CG	TT	TT	CC
71	cases	TC	TT	CG	TT	TC	CC
72	cases	CC	TT	CC	TT	TC	CC
73	cases	CC	TA	CC	TT	TC	CC
74	cases	TC	TT	CC	TT	TT	CC
75	cases	CC	TA	CC	TT	TT	CT
76	cases	CC	TT	CC	GT	TT	CC
77	cases	CC	TT	CG	GT	TT	CC
78	cases	CC	AA	GG	TT	TC	CC
79	cases	TC	TA	CC	TT	CC	CT
80	cases	CC	TA	CC	TT	TC	CC
81	cases	CC	TA	CG	TT	TT	CC
82	cases	CC	TA	CC	TT	TC	CC
83	cases	CC	TT	CG	TT	TT	CC
84	cases	TC	TA	CG	GT	TT	CC
85	cases	TC	AA	CG	GT	TT	CC
86	cases	CC	AA	GG	GT	TT	CC
87	cases	CC	TA	CG	TT	TT	CC
88	cases	CC	TA	GG	TT	TT	CC
89	cases	TC	AA	CC	TT	CC	CC
90	cases	TC	TA	CC	TT	TC	CC
91	cases	TC	TA	CG	TT	TC	CC
92	cases	CC	TA	CC	TT	TC	CC
93	cases	CC	TA	CC	TT	TC	CC
94	cases	CC	AA	GG	TT	TC	CC
95	cases	CC	TT	GG	TT	TC	CC
96	cases	CC	TA	CC	TT	TT	CC
97	cases	CC	AA	CC	TT	TT	CT
98	cases	CC	TA	CG	TT	CC	CC

99	cases	CC	TA	CG	TT	TC	CC
100	cases	TT	TT	CC	TT	TT	CC
101	cases	TC	TA	CC	TT	TT	CT
102	cases	TC	TA	CC	TT	TT	CT
103	cases	TC	TA	CC	TT	TC	CC
104	cases	TC	AA	CG	TT	TT	CC
105	cases	TC	AA	CC	TT	CC	CC
106	cases	CC	TA	CG	TT	TT	CT
107	cases	CC	AA	CG	TT	TT	CC
108	cases	CC	AA	CC	TT	TC	CC
109	cases	CC	TA	CC	TT	TC	CC
110	cases	CC	AA	CG	TT	TT	CC
111	cases	CC	TA	CG	TT	TC	CC
112	cases	TC	TA	CG	TT	TC	CC
113	cases	TC	AA	CC	TT	TT	CC
114	cases	CC	TA	CC	GT	TC	CC
115	cases	CC	TA	CC	TT	TC	CC
116	cases	CC	TT	GG	TT	TT	CC
117	cases	CC	TT	CC	TT	TT	CC
118	cases	TC	AA	CC	GT	TT	CC
119	cases	CC	TT	CG	TT	TC	CC
120	cases	TC	AA	CC	GT	TT	CC
121	cases	CC	AA	CC	GT	TT	CC
122	cases	CC	TT	CC	GT	TC	CC
123	cases	TC	AA	CG	TT	TT	CC
124	cases	TT	AA	CC	TT	CC	CC
125	cases	TC	TT	CC	TT	TC	CC
126	cases	CC	AA	CC	TT	TC	CC
127	cases	TC	AA	CC	TT	CC	CC
128	cases	CC	AA	CC	GG	TT	CC
129	cases	CC	TT	CG	TT	CC	CC
130	cases	TC	TA	CG	TT	TT	CC
131	cases	TC	AA	CC	TT	TT	CC
132	cases	CC	AA	CC	TT	TT	CC
133	cases	CC	AA	CG	TT	TC	CC
134	cases	CC	AA	CG	TT	TT	CT
135	cases	CC	AA	CC	TT	TT	CC
136	cases	CC	AA	CC	TT	TC	CT
137	cases	TC	TT	CG	TT	TC	CC
138	cases	CC	AA	CC	TT	TC	CC
139	cases	CC	AA	CC	GT	TT	CT
140	cases	CC	TA	CC	TT	TT	CC
141	cases	CC	TA	CG	TT	TC	CC
142	cases	TC	TA	CC	TT	TT	CC
143	cases	TC	TA	CC	TT		CC
144	cases	TC	TT	CC	GT	TC	CC
145	cases	CC	TA	CC	TT	TC	CC
146	cases	CC	AA	CG	TT	TT	CT
147	cases	CC	TA	CC	TT	TC	CC
148	cases	CC	TA	CC	GT	TC	CC

149	cases	TC	TA	CC	TT	TT	CC
150	cases	CC	TT	CC	GT	TT	CC
151	cases	CC	AA	CC	GT	TT	CT
152	cases	CC	AA	CG	TT	TT	CC
153	cases	CC	TA	GG	TT	TC	CC
154	cases	CC	TA	CC	GT	TT	CC
155	cases	CC	TT	CC	GT	TT	CC
156	cases	CC	AA	CC	TT	TC	CC
157	cases	CC	AA	CG	TT	CC	CC
158	cases	CC	AA	CC	TT	TT	CT
159	cases	CC	TA	GG	TT	TT	CC
160	cases	TC	TA	CC	TT	TT	CC
161	cases	CC	AA	GG	GT	TT	CC
162	cases	CC	AA	CC	GT		CC
163	cases	CC	TA	CC	TT	TC	CC
164	cases	CC	TA	CC	TT	TT	CC
165	cases	CC	TA	CG	TT	TT	CC
166	cases	CC	AA	CC	GT	TT	CT
167	cases	TC	TA	CC	TT	TC	CC
168	cases	TC	TT	CC	TT	TC	CC
169	cases	CC	TA	CC	TT	TT	CT
170	cases	CC	AA	CC	TT	TT	CC
171	cases	TC	TT	CC	GT	TT	CC
172	cases	CC	TA	CC	TT	TT	CC
173	cases	CC	AA	CG	GT	TT	CC
174	cases	CC	TA	GG	GT	TT	CC
175	cases	CC	AA	CG	TT	TC	CC
176	cases	CC	AA	CC	TT	TC	CT
177	cases	CC	TA	CC	TT	TC	CC
178	cases	CC	AA	CC	TT	TC	CT
179	cases	CC	TA	CC	TT	TC	CC
180	cases	TT	TA	CC	GT	TT	CC
181	cases	CC	TA	CC	TT	TC	CC
182	cases	TC	TA	CC	TT	TT	CC
183	cases	CC	AA	CG	TT	TT	CT
184	cases	TC	TA	CC	GT	TT	CC
185	cases	TC	TA	CC	GT	TT	CC
186	cases	CC	TA	CC	TT	TT	CC
187	cases	TC	TT	CC	TT	TC	CC
188	cases	TT	TA	CC	TT	TT	CC
189	cases	TC	TA	CG	TT	TC	CC
190	cases	TC	TT	CC	TT	TT	CC
191	cases	CC	TA	CG	TT	TT	CC
192	cases	CC	TA	CC	TT	TT	CC
193	cases	TC	TA	CC	GG	TT	CT
194	cases	CC	AA	CC	GT	TT	CC
195	cases	CC	TA	CC	GT	TC	CC
196	cases	CC	TA	CG	GT	TT	CC
197	cases	CC	TA	CC	TT	TT	CC

198	cases	CC	TA	CC	GT	TC	CC
199	cases	CC	TA	CG	TT	TT	CC
200	cases	TC	AA	CC	TT	TT	CC
201	cases	TC	TT	CG	GT	TT	CC
202	cases	CC	TA	CC	TT	TC	CC
203	cases	CC	TA	CC	TT	TT	CC
204	cases	CC	AA	CC	GT	TC	CC
205	cases	CC	AA	CC	TT	TT	CC
206	cases	CC	TA	CC	TT	TC	CC
207	cases	CC	AA	CC	TT	TT	CC
208	cases	TC	TA	CC	TT	TT	CC
209	cases	TC	AA	CG	TT	TT	CC
210	cases	CC	AA	CC	TT	TC	CC
211	cases	CC	AA	CG	TT	TC	CC
212	cases	CC	TT	CG	TT	TC	CC
213	cases	CC	TA	CG	TT	TT	CC
214	cases	TC	TA	CC	TT	TC	CC
215	cases	CC	TA	CG	TT	TT	CC
216	cases	CC	TA	CC	TT	TC	CC
217	cases	CC	AA	CC	TT	TC	CC
218	cases	CC	AA	CG	TT	TC	CC
219	cases	TC	TA	CC	TT	TC	CC
220	cases	CC	AA	GG	TT	TT	CC
221	cases	CC	TT	CG	TT	TT	CC
222	cases	CC	TA	CC	TT	TC	CC
223	cases	TC	TA	CG	TT	TT	CC
224	cases	CC	AA	CC	TT	TC	CT
225	cases	CC	TA	CG	TT	TT	CC
226	cases	CC	TA	CC	TT	TT	CC
227	cases	TC	TA	CC	TT	TT	CC
228	cases	CC	AA	CG	TT	TC	CC
229	cases	TC	TT	CC	TT	TC	CC
230	cases	TC	TA	CG	TT	TT	CC
231	cases	CC	AA	CC	GT	TT	CC
232	cases	TC	TA	CC	TT	TT	CC
233	cases	TC	TT	CG	GT	TT	CC
234	cases	CC	TT	CC	GT	TC	CC
235	cases	TC	TA	CG	TT	TT	CC
236	cases	CC	TA	CC	GT	TT	CC
237	cases	CC	AA	CC	TT	TT	CT
238	cases	CC	TA	CC	TT	TT	CC
239	cases	TC	TA	CC	TT		CC
240	cases	CC	TA	CC	GT	TT	CC
241	cases	CC	TT	CG	GT	TT	CC
242	cases	CC	TA	CC	TT	TT	CC
243	cases	TC	AA	CC	TT	TT	CC
244	cases	CC	TA	CC	TT	CC	CC
245	cases	TC	AA	CG	TT	TC	CC
246	cases	TC	TA	CC	GT	TC	CT
247	cases	CC	TA	CC	GT	TT	CC

248	cases	TC	AA	CC	TT	TT	CC
249	cases	CC	TA	CG	GT	TT	CC
250	cases	TC	TA	CC	TT	TC	CC
251	cases	CC	AA	CC	TT	TT	CC
252	cases	CC	TA	GG	TT	TT	CC
253	cases	CC	TT	CG	TT	TC	CC
254	cases	CC	AA	CG	GT	TT	CC
255	cases	CC	TA	GG	TT	TC	CC
256	cases	TC	AA	CG	TT	TC	CC
257	cases	CC	TA	CC	TT	TC	CC
258	cases	CC	AA	CG	GT	TC	CC
259	cases	CC	AA	CC	TT	TT	CC
260	cases	CC	TT	CC	TT	TT	CC
261	cases	CC	TA	CG	GT	TT	CC
262	cases	TC	AA	CC	TT	TC	CC
263	cases	CC	AA	CC	TT	TC	CC
264	cases	CC	AA	CC	GT	TC	CC
265	cases	CC	AA	CG	TT	TC	CC
266	cases	TC	AA	CC	GT	TT	CC
267	cases	CC	TA	CC	TT	TT	CC
268	cases	CC	TA	CC	TT	TT	CC
269	cases	CC	AA	CC	GG	TT	CC
270	cases	TC	TA	CC	TT	TT	CC
271	cases	TC	TA	CC	TT	TT	CT
272	cases	CC	AA	CG	GT	TT	CC
273	cases	CC	AA	CC	TT	TT	CC
274	cases	CC	TA	CG	GT	TT	CC
275	cases	CC	TA	CG	GT	TT	CC
276	cases	CC	TA	CC	GG	TT	CC
277	cases	TC	AA	CG	TT	TC	CC
278	cases	TT	TT	CC	TT	TC	CC
279	cases	CC	TA	CC	TT	TC	CC
280	cases	CC	TA	CG	TT	TT	CC
281	cases	TC	AA	CC	GT	TC	CC
282	cases	CC	TT	CC	TT	TC	CC
283	cases	TC	TT	CC	TT	TC	CC
284	cases	TC	AA	CC	TT	TC	CT
285	cases	CC	TA	CC	TT	CC	CC
286	cases	CC	TA	CC	GT	TC	CC
287	cases	CC	TA	CC	TT	TC	CC
288	cases	CC	TA	CC	GT	TT	CC
289	cases	CC	TA	CC	GT	TT	CC
290	cases	TC	TA	CC	GT	TT	CC
291	cases	TC	TA	CG	TT	TC	CC
292	cases	CC	TA	CC	GT	TT	CC
293	cases	CC	TA	CC	GT	TT	CC
294	cases	TC	TA	CG	GT	TT	CC
295	cases	CC	TA	CG	TT	TT	CC
296	cases	TC	AA	CC	TT	CC	CT

297	cases	CC	TA	CC	TT	TT	CC
298	cases	CC	TA	CC	TT	TT	CC
299	cases	CC	AA	CC	TT	TC	CC
300	cases	CC	AA	CG	GT	TT	CC
301	cases	CC	AA	CC	GT	TT	CC
302	cases	CC	AA	CC	TT	TC	CC
303	cases	TC	AA	CC	GT	TC	CC
304	cases	CC	TA	CG	GT	TT	CC
305	cases	CC	AA	CG	TT	TT	CC
306	cases	CC	TA	CG	TT	TC	CC
307	cases	TC	TA	CC	TT	TC	CC
308	cases	CC	AA	CG	TT	TT	CC
309	cases	TC	TA	CG	GT	TT	CC
310	cases	TC	TA	CC	TT	CC	CC
311	cases	CC	AA	CG	TT	TT	CC
312	cases	CC	TT	CC	TT	TT	CC
313	cases	CC	AA	CC	TT	TC	CC
314	cases	TC	TA	CC	TT	TC	CC
315	cases	CC	AA	CC	TT	TT	CC
316	cases	TC	TT	CC	TT	TC	CC
317	cases	CC	TA	CG	TT	TT	CC
318	cases	CC	TA	CG	TT	TT	CC
319	cases	CC	AA	CG	TT	TC	CC
320	cases	CC	TA	CG	TT	TT	CT
321	cases	CC	TT	CG	GT	TC	CC
322	cases	CC	TT	CG	TT	TC	CC
323	cases	CC	TA	CG	TT	TT	CC
324	cases	TT	TA	CC	TT	TT	CC
325	cases	CC	AA	CC	TT	TC	CT
326	cases	TC	AA	CG	TT	TT	CC
327	cases	CC	AA	CG	TT	TT	CC
328	cases	CC	TA	CC	TT	TT	CC
329	cases	TC	TA	CG	GT	TT	CC
330	cases	TC	TA	CC	TT	TT	CC
331	cases	TC	AA	CC	GT	TT	CC
332	cases	TC	TA	CG	TT	TC	CC
333	cases	CC	TA	CG	TT	TT	CC
334	cases	CC	TA	CG	TT	TC	CC
335	cases	CC	AA	CC	TT	TT	CT
336	cases	TC	TA	CC	GT	TC	CC
337	cases	CC	TA	CG	TT	TC	CT
338	cases	TC	AA	CC	TT	TT	CT
339	cases	CC	AA	CG	TT	TT	CC
340	cases	TC	TA	CG	TT	TC	CC
341	cases	TC	AA	CC	GT	TT	CC
342	cases	CC	AA	CG	TT	TC	CC
343	cases	CC	TA	CC	TT	TT	CC
344	cases	TC	TA	CG	TT	TT	CC
345	cases	TC	AA	CC	GT	TC	CC

346	cases	TC	TA	CG	GT	TT	CC
347	cases	CC	AA	CC	TT	TC	CC
348	cases	TC	AA	CG	TT	TT	CC
349	cases	CC	TT	CC	TT	TC	CC
350	cases	CC	TA	CC	TT	TT	CC
351	cases	CC	TT	CG	TT	TT	CC
352	cases	TC	TA	CC	GT	TT	CC
353	cases	TC	AA	CC	TT	TT	CC
354	cases	CC	AA	CG	TT	TC	CC
355	cases	CC	TA	CC	TT	TT	CT
356	cases	TC	TA	CG	GT	TT	CC
357	cases	TC	TA	CG	TT	TT	CC
358	cases	CC	TA	GG	TT	TT	CC
359	cases	CC	TA	CC	GT	TT	CC
360	cases	CC	TA	CC	GT	TT	CC
361	cases	CC	TA	CC	TT	TC	CC
362	cases	CC	TA	GG	TT	TC	CC
363	cases	CC	TT	CC	TT	TT	CC
364	cases	TC	TA	CC	TT	TC	CT
365	cases	CC	TA	CG	TT	TC	CC
366	cases	CC	AA	CC	TT	TT	CC
367	cases	TC	AA	CC	TT	TT	CT
368	cases	CC	TA	CC	TT	TT	CC
369	cases	CC	TT	CG	GT	TT	CC
370	cases	TC	TA	CC	TT	TT	CC
371	cases	CC	AA	CC	TT	TT	CC
372	cases	TC	TT	CC	TT	TC	CC
373	cases	CC	TA	CG	TT	TT	CC
374	cases	CC	TT	CG	TT	TC	CC
375	cases	TT	AA	CC	GT	TC	CC
376	cases	CC	TA	CG	GT	TT	CC
377	cases	TT	AA	CC	GG	TT	CC
378	cases	CC	AA	CG	TT	TT	CC
379	cases	CC	TA	GG	TT	TT	CC
380	cases	CC	TA	CC	GT	TC	CC
381	cases		TA	CC	TT	TT	CC
382	cases	CC	AA	CC	TT	TC	CC
383	cases	CC	AA	CG	TT	TC	CC
384	cases	CC	AA	CC	TT	TT	CC
385	cases	CC	TT	GG	TT	TT	CC
386	cases	CC	TA	CC	TT	TC	CC
387	cases	CC	AA	CC	GT	TT	CC
388	cases	CC	TT	CC	GT	TC	CC
389	cases	TC	TA	CC	GT	TT	CC
390	cases	CC	TT	CC	TT	TT	CC
391	cases	TC	AA	CC	GT	TC	CC
392	cases	CC	TA	CG	TT	TC	CC
393	cases	CC	TT	CG	TT	TT	CC
394	cases	TC	TT	CC	TT	TC	CC

395	cases	TT	AA	CC	GT	TT	CC
396	cases	TC	TT	CC	TT	CC	CC
397	cases	CC	TA	CG	GT	TT	CC
398	cases	CC	TA	CG	GT	TT	CC
399	cases	TC	AA	CC	TT	TT	CC
400	cases	CC	TA	CC	TT	TC	CC
401	cases	TC	TA	CC	TT		CC
402	cases	TC	AA	CC	TT	TT	CT
403	cases	CC	TA	CG	TT	TT	CC
404	cases	CC	AA	CG	TT	TC	CC
405	cases	CC	TA	CC	TT	TC	CC
406	cases	CC	AA	CC	GT	TT	CC
407	cases	CC	AA	CC	TT	TT	CC
408	cases	CC	TA	CG	TT	TT	CC
409	cases	TC	AA	CC	TT	TC	CC
410	cases	TC	TA	CG	TT	TT	CC
411	cases	TT	AA	CC	TT	TC	CC
412	cases	CC	TA	CG	TT	TT	CC
413	cases	CC	AA	CC	TT	TT	CC
414	Controls	CC	TA	GG	TT	TC	CC
415	Controls	CC	TA	CC	GG	TT	CC
416	Controls	TC	AA	CG	TT	TC	CC
417	Controls	CC	AA	CG	TT	TC	CC
418	Controls	TC	AA	CC	GT	TT	CC
419	Controls	CC	TT	CG	TT	TT	CC
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421	Controls	CC	TA	CC	TT	TC	CC
422	Controls	CC	TA	CG	GT	TC	CC
423	Controls	CC	TA	CG	TT	TC	CC
424	Controls	TT	TA	CC	TT	CC	CC
425	Controls	TC	TA	CC	GT	TT	CC
426	Controls	CC	TA	CG	GT	TT	CC
427	Controls	CC	TT	CC	TT	TT	CC
428	Controls	CC	TT	CC	TT	TT	CC
429	Controls	CC	TA	CC	TT	TC	CC
430	Controls	TC	TA	CC	GT	TT	CC
431	Controls	CC	AA	CC	TT	TT	CC
432	Controls	CC	TA	CG	TT	TT	CC
433	Controls	CC	AA	CG	TT	TC	CC
434	Controls	CC	AA	CG	TT	TC	CC
435	Controls	TC	TA	CG	GT	TT	CC
436	Controls	TC	TA	CC	TT	TC	CC
437	Controls	CC	TA	CC	GG	TT	CC
438	Controls	CC	TA	GG	TT	TT	CC
439	Controls	TC	TT	CG	TT	TT	CC
440	Controls	CC	TA	CC	GG	TT	CC
441	Controls	TC	TA	CC	TT	TC	CC
442	Controls	TC	AA	CC	TT	CC	CC
443	Controls	CC	AA	CC	GT	TT	CC

444	Controls	CC	TA	CC	TT	TT	CC
445	Controls	TT	TA	CC	TT	TC	CC
446	Controls	CC	AA	CC	TT	TC	CT
447	Controls	CC	TT	GG	TT	TT	CC
448	Controls	CC	AA	CC	GT	TT	CC
449	Controls	CC	AA	CC	TT	TC	CC
450	Controls	CC	AA	CC	GT	TC	CC
451	Controls	TT	TA	CC	TT	TT	CC
452	Controls	CC	TA	CG	TT	TT	CC
453	Controls	CC	AA	CG	TT	TT	CC
454	Controls	TC	TA	CC	GT	TT	CC
455	Controls	CC	TA	CC	TT	TT	CC
456	Controls	CC	AA	CC	TT	CC	CC
457	Controls	TT	TA	CC	TT	TC	CC
458	Controls	TC	TA	CC	TT	TT	CC
459	Controls	TC	AA	CC	TT	TT	CC
460	Controls	TC	AA	CC	TT	TC	CC
461	Controls	CC	TT	CG	TT	TC	CC
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469	Controls	CC	TA	CC	TT	TT	CC
470	Controls	TC	TA	CC	TT	TC	CC
471	Controls	TC	TA	CC	TT	CC	CC
472	Controls	TC	TT	CG	TT	TT	CC
473	Controls	CC	AA	CC	GT	TT	CC
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480	Controls	TC	TA	CC	GT	TT	CC
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482	Controls	CC	AA	CG	TT	CC	CC
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484	Controls	CC	TA	CC	TT	TT	CC
485	Controls	TC	TT	CC	TT	TC	CC
486	Controls	CC	TT	CG	TT	TC	CC
487	Controls	TC	TT	CC	TT	TT	CC
488	Controls	CC	AA	CG	TT	CC	CC
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534	Controls	TT	TA	CC	TT	TT	CT
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539	Controls	TC	AA	CC	TT	TT	CC
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541	Controls	CC	TA	CG	TT	CC	CC

542	Controls	CC	TT	CC	GT	TT	CC
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547	Controls	TC	TA	CG	TT	TC	CC
548	Controls	CC	AA	CG	TT	TT	CC
549	Controls	TC	TA	CC	TT	TC	CC
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551	Controls	CC	AA	CG	TT	TT	CC
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582	Controls	CC	AA	CC	GT	TT	CC
583	Controls	TT	TT	CC	GT	TT	CC
584	Controls	TC	AA	CG	GT	TT	CT
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586	Controls	TC	TA	CC	GT	TC	CC
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596	Controls	CC	TA	CC	TT	TC	CC
597	Controls	CC	AA	CG	TT	TT	CC
598	Controls	CC	AA	CC	TT	TC	CC
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627	Controls	TC	TA	CC	TT	TT	CC
628	Controls	TC	AA	CC	TT	TC	CT
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630	Controls	CC	AA	CG	TT	TC	CC
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635	Controls	TC	TA	CC	TT	TC	CC
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637	Controls	CC	AA	CG	TT	TT	CC
638	Controls	CC	TT	CC	TT	TT	CC
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640	Controls	CC	AA	CG	TT	TC	CC
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643	Controls	CC	TA	CC	TT	TC	CC
644	Controls	TT	AA	CC	TT	TT	CC
645	Controls	TC	TT	CC	TT	TT	CC
646	Controls	CC	TA	CC	TT	TT	CC
647	Controls	TT	TA	CC	TT	TT	CT
648	Controls	TC	AA	CC	TT	TT	CC
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650	Controls	CC	AA	CG	TT	TC	CC
651	Controls	TC	TA	CC	TT	TT	CC
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653	Controls	TC	AA	CC	TT	CC	CT
654	Controls	CC	TT	GG	GT	TT	CC
655	Controls	TC	AA	CG	TT	TT	CC
656	Controls	CC	AA	CG	TT	TT	CC
657	Controls	CC	TA	CG	TT	TC	CC
658	Controls	TT	AA	CC	TT	TC	CT
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660	Controls	CC	TT	CC	TT	TT	CC
661	Controls	TC	TA	CC	GT	TT	CC
662	Controls	CC	TA	CC	TT	TT	CC
663	Controls	CC	AA	CG	GT	TC	CC
664	Controls	CC	TT	CC	TT	TT	CC
665	Controls	TC	AA	CC	TT	TT	CC
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694	Controls	TC	TA	CG	GT	TT	CC
695	Controls	CC	AA	CC	TT	TC	CC
696	Controls	CC	TA	CC	GT	TC	CC
697	Controls	CC	TT	CG	TT	TT	CC
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706	Controls	TC	AA	CC	TT	TT	CT
707	Controls	CC	TA	CG	TT	TT	CC
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710	Controls	TC	TT	CC	TT	TT	CC
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714	Controls	CC	TT	CC		TT	CC
715	Controls	TC	TA	CG	TT	TC	CC
716	Controls	CC	AA	CG	TT	TT	CT
717	Controls	CC	TA	CC	GG	TT	CT
718	Controls	TC	AA	CC	TT	TC	CC
719	Controls	CC	TA	CC	TT	TC	CC
720	Controls	CC	TA	CC	TT	TT	CC
721	Controls	TC	TA	CG	GT	TC	CT
722	Controls	CC	TA	CG	TT	TC	CC
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724	Controls	CC	AA	CC	TT	TT	CC
725	Controls	CC	AA	CG	TT	CC	CT
726	Controls	CC	TA	CG	TT	TT	CC
727	Controls	CC	TT	CC	GT	TC	CC
728	Controls	CC	AA	CC	GT	TC	CC
729	Controls	TC	AA	CG	TT	TC	CC
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731	Controls	CC	TA	CG	TT	TC	CC
732	Controls	CC	TA	CG	TT	TC	CC
733	Controls	TC	TA	CC	TT	TC	CT
734	Controls	CC	TA	CC	TT	TT	CC
735	Controls	CC	TA	CG	TT	TT	CC
736	Controls	CC	AA	CC	TT	TT	CC
737	Controls	TC	TA	CG	TT	TC	CC

738	Controls	CC	TA	CG	TT	TT	CC
739	Controls	CC	TT	CC	TT	TC	CC
740	Controls	TC	AA	CC	TT	TT	CC
741	Controls	CC	TA	GG	TT	TT	CT
742	Controls	TC	TA	CG	TT	TT	CC
743	Controls	TC	TA	CC	GT	TT	CC
744	Controls	CC	AA	CC	GT	TC	CT
745	Controls	CC	AA	CC	GT	TT	CC
746	Controls	CC	TA	CG	GT	TT	CC
747	Controls	CC	TT	CG	GT	TT	CC
748	Controls	CC	TA	CG	TT	TT	CC
749	Controls	CC	AA	GG	TT	TC	CC
750	Controls	CC	TA	CC	GT	TC	CC
751	Controls	CC	TA	CC	GT	TT	CC
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757	Controls	CC	TT	CC	TT	TC	CC
758	Controls	CC	TT	CC	TT	TC	CC
759	Controls	TC	TT	CG	TT	TT	CC
760	Controls	CC	TA	CC	GT	TC	CC
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771	Controls	CC	TA	CG	TT	TT	CT
772	Controls	CC	AA	CC	TT	TC	CC
773	Controls	CC	TA	CG	TT	TT	CC
774	Controls	TC	TA	CC	TT	TT	CC
775	Controls	CC	AA	CG	TT	TT	CC
776	Controls	CC	AA	CC	TT	TC	CC
777	Controls	CC	TT	CC	TT	TC	CC
778	Controls	CC	TA	CG	GT	TT	CC
779	Controls	CC	AA	CC	GT	TT	CC
780	Controls	CC	AA	CC	TT	TT	CC
781	Controls	CC	TA	CG	GT	TT	CC
782	Controls	CC	AA	GG	TT	TT	CC
783	Controls	CC	TA	CC	TT	CC	CC
784	Controls	TC	TT	CC	GT	TT	CC
785	Controls	CC	AA	CC	TT	CC	CC
786	Controls	TC	TA	CC	TT	TT	CC
787	Controls	CC	AA	CG	TT	TT	CC

788	Controls	TC	AA	CC	GT	TT	TT
789	Controls	CC	TA	CG	TT	TT	CC
790	Controls	TT	AA	CC	TT	TC	CC
791	Controls	CC	TT	CG	GT	TT	CC
792	Controls	CC	TA	CG	TT	TT	CT
793	Controls	CC	TA	CC	GG	TT	CC
794	Controls	CC	AA	CG	GT	TC	TT
795	Controls	CC	AA	CC	TT	TC	CC
796	Controls	CC	TT	CG	GT	TC	CC
797	Controls	CC	TA	CG	TT	TT	CC
798	Controls	CC	AA	CG	GT	TT	CT
799	Controls	TC	AA	CG	TT	TC	CC
800	Controls	CC	AA	CC	TT	TC	CT
801	Controls	CC	AA	CC	TT	CC	CT
802	Controls	TT	TA	CC	GT	TT	CC
803	Controls	TC	TA	CC	TT	TT	CC
804	Controls	CC	TT	CC	TT	TC	CC
805	Controls	TC	TT	CC	GT	TT	CC
806	Controls	CC	TA	CC	TT	TT	CC
807	Controls	CC	AA	CC	TT	TT	CC
808	Controls	CC	TA	CC	TT	TT	CC
809	Controls	CC	TA	CG	GT	TT	CC
810	Controls	TC	AA	CC	TT	TC	CC
811	Controls	CC	AA	CG	TT	TC	CC
812	Controls	CC	TA	CG	TT	TT	CC
813	Controls	CC	TA	CC	GT	TT	CT
814	Controls	CC	TA	CG	TT	TT	CC
815	Controls	TC	TA	CC	TT	TT	CC
816	Controls	TC	TA	CG	GT	TT	CC
817	Controls	CC	TT	CG	TT	TT	CC
818	Controls	TC	AA	CC	TT	TT	CC
819	Controls	CC	TA	CC	TT	CC	CC
820	Controls	CC	TT	CG	TT	TT	CC
821	Controls	CC	TT	CC	TT	TT	CC
822	Controls	CC	TA	CG	GT	TT	CC
823	Controls	CC	AA	CC	TT	TT	CC
824	Controls	CC	AA	GG	TT	TT	CT
825	Controls	CC	AA	CG	TT	TT	CC
826	Controls	TC	TA	CG	TT	TC	CC
827	Controls	CC	TA	CC	TT	TT	CC
828	Controls	TC	TA	CG	TT	TT	CC
829	Controls	TC	AA	CC	TT	TC	CC
830	Controls	CC	TT	CC	TT	TT	CC
831	Controls	CC	TA	CG	TT	TC	CC
832	Controls	CC	TA	CC	GT	TT	CC
833	Controls	CC	AA	CG	TT	TT	CC
834	Controls	TC	TA	CC	TT	TC	CC
835	Controls	CC	AA	CG	TT	TT	CC
836	Controls	CC	TA	CC	TT	TT	CC