J Assist Reprod Genet (2015) 32:1643–1649
DOI 10.1007/s10815-015-0548-5

GENETICS

Analysis of the correlation of *CATSPER* single nucleotide polymorphisms (SNPs) with idiopathic asthenospermia

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Received: 7 May 2015 / Accepted: 23 July 2015 / Published online: 8 September 2015

Abstract
Purpose Idiopathic asthenospermia is the most common type of male infertility. Although the mechanisms causing asthenospermia are complex, recent studies have indicated an important role of cation channel of sperm (*CATSPER*) gene downregulation or abnormality in the etiology of idiopathic asthenospermia.
Methods In the present study, 192 patients with idiopathic asthenospermia and 288 healthy controls were enrolled, and a flight mass spectrometry using Sequenom's MassArray biochip system was applied for genotyping 16 *CATSPER* gene SNPs reported in the human single nucleotide polymorphism (SNP) database.
Results Our results indicated a correlation between *CATSPER1* SNPs and idiopathic asthenospermia. In particular, the exonal SNP rs1893316 in *CATSPER1* significantly correlated with idiopathic asthenospermia risk and is a potential important factor in determining an individual's genetic susceptibility to idiopathic asthenospermia.
Conclusion These finding will help to further elucidate the role of *CATSPER1* in idiopathic asthenospermia pathogenesis.

Keywords Cation channel of sperm (CATSPER) · Single nucleotide polymorphisms (SNPs) · Idiopathic asthenospermia

Capsule The exonal SNP rs1893316 in *CATSPER1* significantly correlated with idiopathic asthenospermia risk and is a potential important factor in determining an individual's genetic susceptibility to idiopathic asthenospermia.

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Introduction

Approximately 40 % of all infertility cases are attributed to male factors. Many male infertility cases only manifest as reduced sperm concentration or decreased sperm motility and are therefore diagnosed as idiopathic oligozoospermia or asthenospermia due to the lack of a clear clinical cause [1]. As the most common type of male infertility, idiopathic asthenospermia has recently become a research focus in the field.

The etiology of asthenospermia involves many factors, including infection, abnormal semen liquefaction, abnormal immunity, endocrine dysfunction, abnormal sperm structure, chromosomal abnormalities, and varicocele. The mechanisms causing asthenospermia are complex, as they can involve abnormal sperm structure and/or motility or defects in energy metabolism closely associated with sperm motility or abnormal signal transduction pathways [2]. Recent studies have identified specialized Ca^{2+} channel proteins expressed in the sperm flagellum that are involved in sperm hyperactivation [3] and affect sperm motility, egg-penetration ability, and fertilizability [4]. These proteins belong to the cation channel of sperm (CATSPER) protein family, which includes four members, CATSPER1–4. The CATSPERs are testicular germ cell-specific ionic channels localized to the main section of the

sperm flagellum. CATSPER1 and 2 primarily localize to the flagellum's plasma membrane and regulate its whip-like movement [5, 6]. Moreover, several techniques, including immunoprecipitation, in situ hybridization, and Southern blotting, have revealed that CATSPER3 and 4 also localize to the main section of the sperm flagellum and play important roles in male fertility [7]. Nikpoor et al. [8] used reverse transcription polymerase chain reaction (RT-PCR) to study the testis and found that asthenospermia patients displayed significantly reduced *CATSPER1* expression compared to infertile patients with normal sperm motility. Animal model experiments showed that intraperitoneal selenium injection upregulated *CATSPER* gene expression in both aging and adult mice and improved their sperm motility and survival rate [9], further suggesting the causative role for decreased *CATSPER1* expression or abnormality in idiopathic asthenospermia pathogenesis.

A single nucleotide polymorphism (SNP) refers to a DNA sequence polymorphism resulting from a single nucleotide mutation at the genome level [10]. SNPs are the most widely distributed and abundant type of genetic polymorphism. It became the third-generation genetic marker, after the first-generation restriction fragment length polymorphism (RFLP) and the second-generation microsatellite (i.e., simple tandem repeat markers). These genomic sequence variations may lead to individual differences in phenotypes, disease susceptibility (especially complex diseases), and responses to environmental factors or drugs. Therefore, SNPs serve as important genetics tools and are also important in functional genomics research. However, few studies to date have focused on the relationship between *CATSPER* SNPs and idiopathic asthenospermia, which was the aim of this study.

Materials and methods

Subjects, sample collection, and testing

All volunteers were informed of the objectives and gave informed written consent before beginning the study. All experimental manipulations and protocols were approved by the Ethics Committee of Nanfang Hospital, Southern Medical University (NFEC-200 909-K1). This study was performed in accordance with the principles of the Declaration of Helsinki.

All samples from the Department of Andrology, Nanfang Hospital, Southern Medical University, Guangzhou, China, were collected and analyzed between February 2012 and January 2014. A total of 192 idiopathic asthenoteratozoospermic patients with low sperm motility (rapid forward progressive motile sperm, grade A <25 %, and forward progressive motile sperm, grade A+B< 50 %), who had failed to accomplish pregnancy in more than 1 year of unprotected sexual intercourse were enrolled in our study. Exclusion criteria were performed as described previously [11]. Partners of these infertile men enrolled in our study were healthy women who were not suffering from diseases, such as severe reproductive system infection and sexual hormone disturbance [11]. A total of 288 ethnically matched volunteers with normal sperm motility were enrolled and served as controls. All the subjects enrolled in our study were Han Chinese.

Semen samples were collected after 2–7 days sexual abstinence duration through masturbation. Semen parameters were measured with SQA-V equipment (TECHNOPATH, Ballina, Ireland) according to the World Health Organization laboratory manual for the examination and processing of human semen (fifth edition). WHO criteria for sperm morphology were applied to all patients, and the percentage of sperm with normal morphology was assessed.

Genotype determination

Genomic DNA was extracted from sperm using a DNA extraction kit (BioTeke Corporation, Beijing, China) according to the manufacturer's instructions. Assay Design 4.1 software (Sequenom, San Diego, CA, USA) was used to design the primers. SNP genotyping was performed using iPLEX genotyping assays on a MassARRAY platform (MassARRAY Workstation Version3.3, Sequenom). The DNA sample quality threshold was set at 90 %.

Fluorescence quantitative PCR

Total RNA of sperm was extracted using Trizol (Invitrogen, USA). Reverse transcription was performed with 1 μg of RNA after quantification. Quantitative PCR was conducted using the SYBR-Green dye (Toyobo) method with 100 ng of cDNA in a 20 μL system. The primer sequences are shown as follows: *CATSPER1*-F (5′-AAGAGGTGGCGAGTGAAG-3′), *CATSPER1*-R (5′-GCAGGTAATGGAACAGGAG-3′); GAPDH-F (5′-GGTATCGTGGAAGGACTC-3′), GAPDH-R (5′-GTAGAGGCAGGGATGATG-3′). The reaction conditions were as follows: 95 °C for 5 min; followed by 40 cycles of 95 °C for 30 s, 55 °C for 30 s, and 72 °C for 30 s. All reactions were run in triplicate, and quantitative analysis was performed by comparing the $2^{-\Delta\Delta Ct}$ values.

Western blot analysis

Sperm was homogenized in ice-cold CHAPS buffer (20 mM Hepes, pH 7.4, 140 mM NaCl, 10 mM CHAPS, 2 mM EDTA, 1 mM EGTA, and Complete protease inhibitor cocktail) and incubated on the thermoshaker for 30 min at 4 °C. The lysates were then subjected to 15 % SDS-PAGE, and proteins were transferred to a nitrocellulose membrane (Roche Biosciences, Germany). The membrane was blocked with 5 % nonfat milk powder in Tris-buffered saline (TBS; 10 mM Tris-HCl, pH 7.2, 150 mM NaCl) for 4 h. After being washed three times with TBS with 0.1 % Tween 20 (TBS-T), the membrane was

then incubated with Anti-CATSPER1 (Abcam, China, 1:500) or GAPDH (Novus Biologicals, 1:1000) antibodies for 2 h. Antibodies binding was visualized by a colorimetric reaction catalyzed by peroxidase-conjugated goat anti-rabbit antibody (1:10,000 dilution in TBS; Promega).

Statistical analysis

The measurement data were presented as mean±standard deviation, and the count data were expressed as percentages (%). The 16 SNPs were verified with Hardy-Weinberg equilibrium (HWE). Univariate analysis of each SNP and subsequent multivariate analysis of significant SNPs were performed using unconditional logistic regression. Linkage disequilibrium and haplotype analysis were performed with HaploView 4.2 (Daly Lab at the Broad Institute, Cambridge, MA, USA). Some data were adjusted for confounding factors, including age, semen volume, and sperm concentration. A value of $p<0.05$ was considered statistically significant.

Results

Demographic and semen parameter comparisons between the two groups

We recruited a total of 251 patients in this study and enrolled 192 eligible subjects for subsequent experiments. Our analysis of demographic and clinical characteristics showed that there was no significant difference in age or sperm concentration between the two groups ($p>0.05$). However, differences in semen volume, fast progressive motility, and normal morphology were statistically significant between the groups ($p<0.05$, Table 1).

Distribution of genotypes in the two groups

To investigate the correlation between idiopathic asthenospermia and *CATSPER* SNPs, we genotyped all of the samples for the following 16 known *CATSPER* SNPs: *CATSPER1*: rs1893316, rs1203998, rs2845570, rs35484336, rs3814747, rs3814748, and rs3829937; *CATSPER2*: rs8042868 and rs3853543; *CATSPER3*: rs3896260 and rs17167765; and *CATSPER4*: rs41284333, rs11247866, rs12138368, rs9970046, and rs17163674, using Sequenom's MassARRAY time of flight mass spectrometry. The results are shown in Table 2. While rs3853543 (*C*> *G*) and rs35484336 (*A*> *G*) were inconsistent with the HWE in the patient group, rs3896260 (*G*> *T*), rs12138368 (*G*> *T*), and rs35484336 (*A*> *G*) were inconsistent with HWE in the control group. In other words, with the exception of these four sites (rs3853543 (*C*> *G*), rs3896260 (*G*> *T*), rs12138368 (*G*> *T*), and rs35484336 (*A*> *G*)), the remaining loci satisfied HWE ($p>0.05$), indicating that the cohort of subjects in both groups of this study was representative. Therefore, our study was feasible.

Correlation of CATPSER SNPs with asthenospermia

We studied the correlation of the 16 SNPs with asthenospermia using univariate logistic regression analysis. Our results indicated that only rs1893316 (*C*> *T*) was significant and the risk of asthenospermia in individuals with the mutant genotype was 1.60 [95 % confidence interval (CI) 1.11–2.32] times of that of wild-type individuals. We observed similar results after adjustment for confounding variables, including age, semen volume, and sperm concentration. The other 15 SNPs showed no significant correlation with asthenospermia risk (Table 3).

Correlation between rs1893316 and CATSPER1 expression

The mutant genotype of rs1893316 has been reported to increase the risk of asthenospermia. However, its exact role in asthenospermia development requires extensive investigation. SNP rs1893316 is a synonymous SNP and does not alter the CATSPER1 protein structure, which does not affect protein function. However, SNP rs1893316 is located in the first exon of the *CATSPER1* gene, which usually contains CpG islands or regulator binding sites. The SNP rs1893316 mutation alters the nucleotide sequence, which may destroy the binding sites of some regulators, thereby affecting transcription. We collected and grouped clinical samples according to the SNP rs1893316 genotype and determined CATSPER1 *mRNA* and protein expression by RT-PCR assay and Western blotting analysis, respectively. We found that CATSPER1 *mRNA* and protein expression was significantly lower in patients with the TT genotype than in controls and

Table 1 Comparison of demographic characteristics and semen parameters between patient and control groups

Variables	Patients	Control	*t* value	*P* value
Age (years)	30.3±5.9	29.4±5.3	−1.620	0.106
Volume (mL)	2.9±1.3	3.2±1.3	2.164	0.031
Concentration (M/mL)	90.1±67.3	100.3±59.2	1.756	0.080
Fast progressive motility (%)	17.6±10.0	45.8±9.9	30.341	<0.001
Normal morphology (%)	4.7±1.7	13.4±5.1	26.864	<0.001

Table 2 Genotype distribution in patient and control groups

SNP	Patients *N* (%)	Control *N* (%)	$\chi^2_{patient}$	$P_{patient}$	$\chi^2_{control}$	$P_{control}$
rs1893316 (*C*> *T*)						
CC	100 (52.1)	183 (63.5)	0.242	0.622	1.366	0.243
CT	79 (41.1)	89 (30.9)				
TT	13 (6.8)	16 (5.7)				
rs1203998 (*G*> *A*)						
GG	50 (25.6)	92 (31.9)	3.390	0.065	0.006	0.941
GA	108 (55.4)	141 (49.0)				
AA	34 (19.0)	55 (19.1)				
rs2845570 (*G*> *T*)						
GG	78 (40.6)	131 (45.6)	0.205	0.651	1.894	0.169
GT	91 (47.4)	118 (41.1)				
TT	23 (12.0)	38 (13.3)				
rs3814747 (*A*> *G*)						
AA	159 (82.8)	235 (81.6)	1.243	0.265	3.644	0.056
AG	30 (15.6)	47 (16.3)				
GG	3 (1.6)	6 (2.1)				
rs3814748 (*A*> *G*)						
AA	3 (1.6)	6 (2.1)	1.787	0.181	2.127	0.145
AG	28 (14.6)	52 (18.1)				
GG	161 (83.8)	230 (79.8)				
rs3829937 (*C*> *T*)						
CC	156 (81.3)	219 (76.0)	0.650	0.420	1.678	0.195
CT	33 (17.2)	67 (23.3)				
TT	3 (1.5)	2 (0.7)				
rs8042868 (*C*> *T*)						
CC	102 (53.1)	169 (58.7)	0.722	0.395	0.638	0.425
CT	79 (41.1)	100 (34.7)				
TT	11 (5.8)	19 (6.6)				
rs17167765 (*C*> *T*)						
CC	156 (81.3)	240 (83.3)	2.055	0.152	0.674	0.412
CT	36 (18.7)	47 (16.3)				
TT	0 (0.0)	1 (0.4)				
rs41284333 (*A*> *G*)						
AA	188 (97.9)	278 (96.5)	0.021	0.884	0.090	0.764
AG	4 (2.1)	10 (3.5)				
GG	0 (0.0)	0 (0.0)				
rs11247866 (*A*> *G*)						
AA	186 (96.9)	274 (95.1)	0.048	0.826	3.495	0.062
AG	6 (3.1)	13 (4.5)				
GG	0 (0.0)	1 (0.4)				
rs9970046 (*A*> *G*)						
AA	69 (35.9)	95 (33.1)	0.021	0.885	0.341	0.560
AG	93 (48.4)	136 (47.4)				
GG	30 (15.7)	56 (19.5)				
rs17163674 (*C*> *T*)						
CC	164 (85.4)	237 (82.3)	0.689	0.407	0.934	0.334
CT	26 (13.5)	50 (17.4)				
TT	2 (1.1)	1 (0.3)				

patients with the CC and CT genotypes, while there were no significant differences in CATSPER1 *mRNA* and protein expression between controls and patients with the CC and CT genotypes (Fig. 1). The results demonstrate that SNP rs1893316 correlates with idiopathic asthenospermia, and it may be involved in the development of idiopathic asthenospermia by downregulating CATSPER1 expression at both the transcriptional and translation levels.

Haplotype analysis of CATSPER SNPs

Finally, we analyzed linkage disequilibrium and haplotype using the HaploView software, and we found that among seven *CATSPER1* SNPs (rs1893316, rs1203998, rs2845570, rs35484336, rs3814747, rs3814748, and rs3829937), rs3814747 and rs3814748 displayed linkage disequilibrium (D'=0.953, r^2=0.877) (Fig. 2). However, the frequency of AG and GA haplotypes was 0.894 (p=0.549) and 0.095 (p= 0.322), respectively, showing no statistically significant difference. The remaining *CATSPER1* SNPs did not exhibit linkage disequilibrium. Among the five *CATSPER4* SNPs (rs41284333, rs11247866, rs12138368, rs9970046, and rs17163674), rs41284333 and rs11247866 displayed linkage disequilibrium (D'=1, r^2=0.733) (Fig. 2), and the frequency of AG and GG haplotypes was 0.980 (p=0.448) and 0.015 (p=0.379), respectively, which was not statistically significant. The remaining *CATSPER4* SNPs did not show linkage disequilibrium.

Discussion

Recent studies have shown that the main sperm flagellar segment and acrosome contain a specific protein family known as cation channels of sperm (CATSPERs), which can mediate Ca^{2+} flow and thereby regulate sperm motility and hyperactivation. They play important roles in the acrosome reaction and capacitation [2, 7].

Studies have found that CATSPER1 is closely associated with sperm motility. *CATSPER1* knockout mice exhibit poor sperm motility and lack the sperm's fast progressive linear motility, powerful whip-like movement, and cAMP-induced Ca^{2+} flow [4]. In addition, *CATSPER1* knockout sperm failed to show whip-like movement even after capacitation [12]; they also lost the ability to penetrate the zona pellucida as well as the Ca^{2+} flux in the sperm flagellum [13], suggesting that CATSPER channels not only regulate sperm movement but also function in sperm hyperactivation and the acrosome reaction [7, 14]. In addition, clinical studies have shown that decreased sperm motility in certain idiopathic infertility patients was associated with abnormal *CATSPER1* expression due to mutations [8, 15]. Furthermore, Wang et al. [16] have found that CATSPER1 downregulation in epididymal

Table 3 Correlation of different *CATSPER* SNPs with asthenospermia

CATSPER	Patient		Control		OR (95%CI)	OR[§] (95%CI)
	N	%	*N*	%		
rs1893316 (*C*> *T*)						
CC	100	52.1	183	63.5	1.60 (1.11–2.32)*	1.62 (1.02–2.60)*
CT/TT	92	47.9	105	36.5		
rs1203998 (*G*> *A*)						
GG	50	26.0	92	31.9	1.33 (0.89–2.00)	1.36 (0.77–2.40)
GA/AA	142	74.0	196	68.1		
rs2845570 (*G*> *T*)						
GG	78	40.6	131	45.6	1.23 (0.85–1.78)	1.50 (0.90–2.49)
GT/TT	192	59.4	156	54.4		
rs3814747 (*A*> *G*)						
AA	159	82.8	235	81.6	0.92 (0.57–1.49)	1.22 (0.69–2.19)
AG/GG	33	17.2	53	18.4		
rs3814748 (*A*> *G*)						
AA	3	1.6	6	2.1	1.34 (0.33–5.43)	0.96 (0.20–4.57)
AG/GG	189	98.4	282	97.9		
rs3829937 (*C*> *T*)						
CC	156	81.2	219	76.0	0.73 (0.47–1.15)	1.03 (0.58–1.81)
CT/TT	36	18.8	69	24.0		
rs8042868 (*C*> *T*)						
CC	102	53.1	169	58.7	1.25 (0.87–1.81)	1.27 (0.87–1.87)
CT/TT	90	46.9	119	41.3		
rs17167765 (*C*> *T*)						
CC	156	81.2	240	83.3	1.15 (0.72–1.86)	1.07 (0.64–1.79)
CT/TT	36	18.8	48	16.7		
rs41284333 (*A*> *G*)						
AA	188	97.9	278	96.5	0.59 (0.18–1.91)	0.47 (0.05–4.22)
AG/GG	4	2.1	10	3.5		
rs11247866 (*A*> *G*)						
AA	186	96.9	274	95.5	0.68 (0.25–1.82)	1.21 (0.19–7.62)
AG/GG	6	3.1	13	4.5		
rs9970046 (*A*> *G*)						
AA	69	35.9	95	33.1	0.88 (0.60–1.30)	0.95 (0.62–1.44)
AG/GG	123	64.1	192	66.9		
rs17163674 (*C*> *T*)						
CC	164	85.4	237	82.3	0.79 (0.48–1.31)	0.73 (0.43–1.26)
CT/TT	28	14.6	51	17.7		

[§] Logistic regression analysis, adjusted for confounders such as age, semen volume, and sperm concentration

*$p<0.05$

spermatozoa contributes to asthenozoospermia pathogenesis, whereas Sheng-Jing-San treatment induces upregulation of the channel and improves sperm motility in a rat model of asthenozoospermia.

There have been recent studies on the correlation of gene SNPs with idiopathic asthenospermia. For example, Buldreghini et al. [17] reported that the T allele encoding for aspartic acid in eNOS (Glu298Asp) may contribute to poor sperm motility. Tronchon et al. [18] found that the frequency of the 2308 *TNF* A allele increased in patients with low sperm counts of testicular origin [$p=0.002$; odds ratio (OR)=2.93] or with normal production count but altered sperm motility ($p=0.003$; OR=2.32) compared to patients with normal sperm count and quality (morphology and motility). However, studies have rarely focused on the relationship between *CATSPER* SNPs and idiopathic asthenospermia. Although Visser et al.

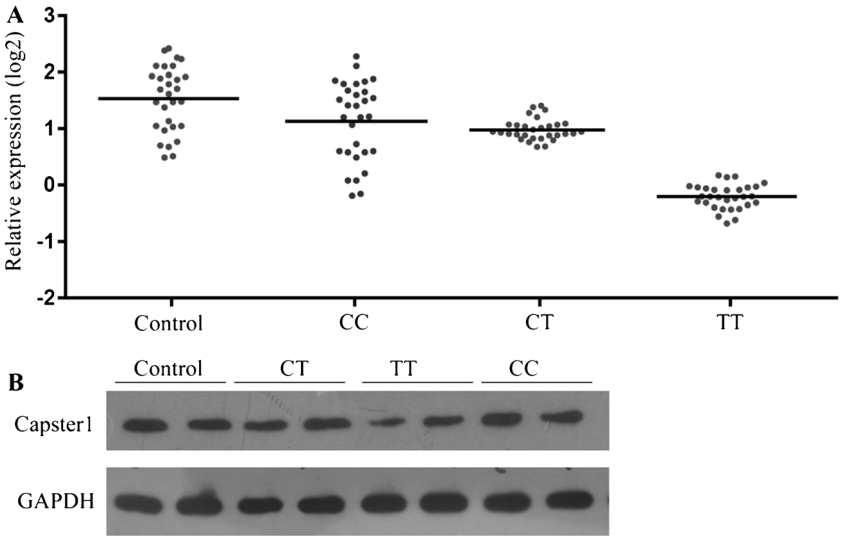

Fig. 1 CATSPER1 expression. **a** Real-time qPCR analysis showed expression of CATSPER1 in normal tissue samples and idiopathic asthenospermia tissue samples, and they were significantly different (p <0.01). **b** Western blot analysis showed expression of CATSPER1 in normal tissue samples and idiopathic asthenospermia tissue samples

[19] reported relevant investigations, they only presented sequencing data and did not perform correlation analysis of a larger sample.

Therefore, we conducted an in-depth study on the basis of the previous study by Visser et al. [19] to analyze the 16 *CATSPER* SNPs selected from the human SNP database. We performed flight mass spectrometry using Sequenom's MassArray biochip system for a case-control study of 192 patients with idiopathic asthenospermia and 288 healthy controls. Our results demonstrated a correlation between *CATSPER1* SNPs and idiopathic asthenospermia; in particular, the exonal *CATSPER1* rs1893316 SNP significantly correlated with the risk of idiopathic asthenospermia and may be an important factor in determining genetic susceptibility to idiopathic asthenospermia. As a synonymous SNP, rs1893316 does not alter CATSPER1 protein structure. Therefore, we speculated that rs1893316 does not affect the amino acid structure to correlate with idiopathic asthenospermia. However, rs1893316, which is located in the first exon of the *CATSPER1* gene, may contribute to idiopathic asthenospermia by affecting transcription. We evaluated the association of rs1893316 with CATSPER1 *mRNA* and protein expression and found that both were significantly lower in patients with the TT genotype than controls and patients with the CC and CT genotypes. However, we did not detect any significant differences in CATSPER1 *mRNA* and protein expression between controls and patients with the CC and CT genotypes. These results demonstrate that rs1893316 is associated with idiopathic asthenospermia. By using denaturing high-performance liquid chromatography (DHPLC) and bidirectional sequence analysis in two consanguineous Iranian families segregating autosomal-recessive male infertility, Avenarius et al. [20] found two separate insertion mutations (c.539-540insT and c.948-949insATGGC) in *CATSPER1* that are predicted to lead to frameshifts and premature stop codons (p.Lys180LysfsX8 and p.Asp317MetfsX18). Hildebrand et al.

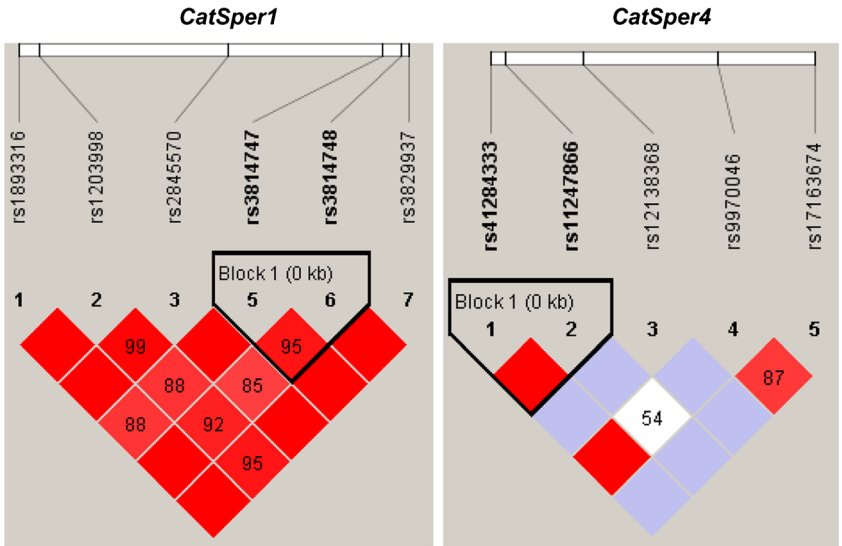

Fig. 2 *CATSPER* haploblocks in the Chinese population in relation to idiopathic asthenospermia-associated single nucleotide polymorphisms (SNPs). HaploView V4.2 was used to define linkage disequilibrium (LD) blocks represented by the *triangular lines* based on the current genotyping data from the Chinese population. *Squares* indicate pair-wise r^2 values on a red-scale with D'=1 (*red*) through to D'=0 (*white*)

[21] thought that mutations in the CATSPER channel genes should be considered a potential cause in cases of recessively inherited male infertility and deafness-infertility syndrome (DIS), and CATSPER mutations may also be associated with sporadic cases of male infertility. Bhilawadikar et al. [22] found that the levels of Tektin 2 and CatSper 2 were significantly lower in spermatozoa of oligoasthenozoospermic men as compared to normozoospermic controls; the levels were also lower in immotile fraction as compared to motile fraction of spermatozoa obtained from normozoospermic individuals, and the levels of Tektin 2 and CatSper 2 were higher in individuals demonstrating sperm motility >60 % as compared to sperm motility <30 %. It is thought that *CATSPER1* downregulation or abnormality may affect sperm motility and thereby induce the development of idiopathic oligozoospermia. Therefore, the clinical detection of *CATSPER1* mutations, SNPs, or expression may facilitate of idiopathic oligozoospermia diagnosis and therapy.

In this study, we examined 16 *CATSPER1* SNPs, which did not cover all SNP loci. It is currently thought that four CATSPER family members may directly or indirectly form a functional tetramer. Further studies to investigate other idiopathic oligozoospermia-associated SNPs are necessary. Subsequent linkage disequilibrium and haplotype analysis using HaploView software detected linkage disequilibrium in rs3814747 of *CATSPER1* and in rs3814748, rs41284333, and rs11247866 of *CATSPER4,* but the difference in haplotypes between groups was not statistically significant.

In summary, there were several SNPs in the *CATSPER* genes among the subjects in this study, but only the *CATSPER1* SNP rs1893316 significantly correlated with the pathogenesis of idiopathic asthenospermia. This finding will help us to further decipher the role of CATSPER1 in idiopathic asthenospermia pathogenesis.

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