Candidate Gene of NOS3, MMP3, AGT, and AGT1R and Pathway Analyses for Platelet Reactivity and Clinical Outcomes of Repeat Revascularization After First PCI in Chinese Patients

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Abstract

Purpose

Major disadvantages of the percutaneous coronary intervention (PCI) are the high occurrence of repeat revascularization due to restenosis and disease progression. The current study aimed to identify indicators that can predict the risk of repeat revascularization.

Methods

A total of 143 patients who underwent PCI and had genetic test results were enrolled. We retrospectively reviewed their medical records after the first PCI. P2Y12 reaction units (PRU) test results were obtained by VerifyNow; 372 SNPs of NOS3, MMP3, AGT, and AGT1R gene and 380 genes related to platelet activation-related processes and clopidogrel activity were selected for analysis. Repeat revascularization and in-stent restenosis (ISR) were used as clinical outcomes, and PRU and ADP aggregation rates were used as platelet function outcomes in analysis.

Results

After the first PCI, the incidence of repeat revascularization at 18, 30, and 42 months was 14.1% (20/142), 17.5% (24/137), and 39.7% (31/78), respectively. In the candidate gene analysis, Rs 78830 (NOS3) was associated with both ADP aggregation rate and 18- and 30-month ISR, and rs 62275847 (AGTR1) was associated with both ADP aggregation rate and 30-month ISR. In the pathway, gene-set analysis, the linkage rs471683 and rs7785386 of GNAI1|GNAT3 were associated with PRU and ADP aggregation rate, 18-months and 30-months ISR, and repeat revascularization within 30 months. Rs1715389 of GNAI1|GNAT3 were associated with both PRU and ADP aggregation rate, 18-months and 30-months ISR, and repeat revascularization within 30 months. Rs7313458 of ITPR2 were associated with PRU and ADP aggregation rate, 18-months and 30-months ISR, and repeat revascularization within 18 months.

Conclusions

The genetic polymorphisms of rs78830(NOS3), rs62275874 (AGTR1), linkage rs471683 and rs7785386 (GNAI1|GNAT3), rs1715389(GNAI1|GNAT3), and rs7313458 (ITPR2) may lead to an increased risk of in-stent restenosis and revascularization after the first PCI in Chinese patients by affecting the efficacy of clopidogrel. The above six SNP may be used as potential genetic biomarkers for high risk of in-stent restenosis and revascularization after the first PCI in Chinese patients.

1. Introduction

Over the past few years, an exponential increase in percutaneous coronary intervention (PCI) as the common form of myocardial revascularization has led to a significant improvement in the clinical management of coronary artery disease (CAD) patients (1, 2). Despite advances in stent technology, restenosis continues to be the most frequent cause of target lesion failure following PCI. In-stent restenosis (ISR) has been reported to occur in 32–55% of patients undergoing angioplasty and in 17–41% of patients receiving the bare metal stents (BMS) era.(3) Restenosis-related complications include stable angina, unstable angina, acute coronary syndrome, acute myocardial infarction, and even death. Revascularization procedures for ISR could also be hindered by complications from access site bleeding, stent under-expansion, incomplete revascularization, coronary artery dissection, and stent thrombosis(4).

Some extrinsic and intrinsic factors may contribute to ISR. Numerous studies have examined the risk predictors of ISR. Following characteristics have been associated with ISR: age, female gender, diabetes, chronic kidney disease, and multivessel CAD; the lesions' characteristics include smaller reference artery diameter, ostial lesion, and initial plaque burden(5–7). Furthermore, the efficacy of clopidogrel as the necessary antiplatelet therapy after PCI is also a relevant factor that should not be ignored. Clopidogrel, with or without aspirin, has been proven to reduce the occurrence of ISR(8). However, there is interindividual variability in response to clopidogrel, and a substantial number of ISR still occur despite clopidogrel treatment, even among those treated with dual-antiplatelet agents(9).

Previous studies reported that genetic polymorphisms, such as P2RY12(10), PON1(11), ABCB1(12), and CES1(13), especially the reduced function of CYP2C19(14), were associated with interindividual variability in response to clopidogrel. Still, the polymorphisms of these genes do not account for all the individual differences.

Our previous meta-analysis revealed that the polymorphism of NOS3, MMP3, AGT, and A1TR might increase ISR risk after PCI based on the studies on the relationship between polymorphism and clinical outcomes (15). However, to the best of our knowledge, no studies investigated the relationship between the polymorphism of these four genes and clopidogrel response. Furthermore, gene set analysis was mainly developed to analyze large-scale genomic data, which facilitates the interpretation of experimental results and helps to identify key biological findings(16, 17). Candidate gene and gene set analysis has been widely used to determine a cumulative effect on platelet function by modifying basic platelet parameters, altering the expression or activity of key platelet receptors, and influencing downstream effector pathways utilized by these receptors(18, 19).

The present study focused on candidate gene association studies and gene set analysis to further explore the effect of NOS3, MMP3, AGT, and AGT1R as candidate genes on platelet function and repeat revascularization.

2. Methods

2.1 Subjects, Design, and Procedures

This study was a retrospective cohort review from medical records of CAD patients who took antiplatelet drugs and underwent genetic testing at Peking University First Hospital. All patients were enrolled in a previous study, which was approved by the ethics committee of Peking University First Hospital (NO. 2013 [634]). The protocol of this study was approved by the Ethics Committee of the Medical University of Peking University First Hospital and was in accordance with the Declaration of Helsinki (ethics approval number: 2017 scientific research ethics No. 81).

In this study, we screened patients according to the following inclusion criteria: (1) PCI or (2) patients who received dual antiplatelet therapy consisting of 100 mg of aspirin daily and 75 mg of clopidogrel for at least 1 year after the first PCI; however, if the endpoint occurred within 1 year, patients must have used dual antiplatelet therapy during the period from the first PCI to repeat revascularization. The exclusion criteria were: (1) patients with cancer, viral hepatitis, and other related diseases or (2) incomplete records of the PCI operation. According to the above criteria, a total of 168 patients were enrolled between April 2015 and June 2016. Written informed consent was obtained from all participating patients.

Information was collected from a medical record review, including hospital inpatient, outpatient visits and telephone contact records with patients or their families. Sociodemographic variables, medical history, therapeutic procedures, smoking status (i.e., current smoker vs. former/no smoker at admission), clinical events, stent implantation, laboratory results, genomics results, and follow-up information were reviewed.

The independent variables in the present study were: (1) clinical variables, such as the age when the first PCI was conducted, gender, diabetes mellitus (DM), hypertension, chronic kidney disease (CKD), smoking status, and the time (days) from the first PCI to the repeat revascularization, including target vessel revascularization (TVR), target lesion revascularization (TLR), and non-target vessel revascularization (NTVR), either by repeated PCI or coronary artery bypass graft (CABG). The repeat revascularizations due to incomplete initial revascularization were excluded; (2) variables on genetic results; and (3) variables on the platelet aggregation by VerifyNow.

The outcomes of this study consisted of two following parts: the first part was platelet function, including PRU and ADP aggregation rate; the second part was the repeat revascularization after the first PCI, either by repeated PCI or CABG. Follow-ups at 18, 30, and 42 months were used to evaluate the relationship between revascularization and potential indicators.

2.2 Platelet function measurements

In 71 out of 143 enrolled patients, the platelet function testing was performed by VerifyNow measurements. Platelet function was detected after the clopidogrel efficiency reached homeostasis (clopidogrel 75 mg daily for more than 7 days, 300 mg loading dose and 75 mg daily for 5 days, or 600 mg loading dose with 75 mg for 3 days) (20,21).

The platelet activity was assessed using the VerifyNow® P2Y12 (VN-P2Y12) assay (Accumetrics, San Diego, California, USA) as described by Price MJ (22). This test constitutes a whole-blood, point-of-care, light transmission-based optical detection assay that measures adenosine diphosphate (ADP)-induced platelet agglutination (23). In addition to ADP, prostaglandin E1 is incorporated into the VN-P2Y12 assay. Prostaglandin E1 suppresses the intracellular free-calcium levels and thereby reduces the contribution of activation by ADP binding to P2Y1 receptors (24).

The assay was performed according to the manufacturer's instructions within 10 to 15 mins of venipuncture. Data were directly recorded from the VerifyNow® device as percent inhibition of P2Y12 reaction units (PRU).

2.3 Candidate gene and pathway selection

Candidate genes came from a meta-analysis of the relationship between NOS3, MMP3, AGT, AGT1R, and the risk of restenosis after PCI performed by our project team members and colleagues. In this study, 372 SNPs in these four genes were selected for analysis (**Appendix Table 1**).

Pathways related to platelet activation-related processes and clopidogrel activity were selected from KEGG, BioCarta, and GeneCards. A total of 380 genes from platelet activation pathway (KEGG), platelet amyloid precursor protein pathway (BioCarta), aspirin blocks signaling pathway involved in platelet activation (BioCarta), and clopidogrel related genes (GeneCard) were analyzed in our study (**Appendix Table 2**).

2.4 Genotyping

We collected the information on genetic testing results from enrolled patients. The SNPs were measured by OmniZhongHua-8 (Omni China), a specific genomic SNPs chip for Chinese individuals launched by the Illumina Company. The chip especially covers those frequent and rare variants that are found in the Chinese population, which covers 85% of the common genetic variation in the Chinese population at $r^2 > 0.8$. The optimized 900,000 SNPs tag information was from all three stages of the HapMap and the 1000 genome project (1KGP). OmniZhongHua-8 detection was relegated to the Beijing Yi De PR Technology Development Co. Ltd. After genotyping, samples and genetic markers were subjected to a stringent quality control protocol.

IMPUTE2 (25) was used to impute genotypes for autosomal SNPs using the CHB (Han Chinese in Beijing, China) population as a reference retrieved from the 1000 Genome Project dataset (Phase 3) (26). Threshold criteria for imputed SNPs were set as pro > 0.9 and info > 0.5, where pro referred to the probability of an imputed genotype and info referred to the overall quality of an imputed SNP. There were 7,802,735 SNPs after genotyping, and only high-quality SNPs (genotyping rate > 0.95, call rate > 0.95, Hardy-Weinberg p > 0.00001) were kept for subsequent analysis.

2.5 Statistical Analysis

All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) 21.0 software (IBM, Armonk, NY) and R (http://www.R-project.org). For clinical parameters, $P < 0.05$ was considered statistically significant. The continuous and categorical variables were presented as mean ± standard deviation (SD) and frequencies and percentages, respectively. To identify independent variables affecting repeat revascularization at 18 or 30 months, the effect was evaluated and expressed as an odd ratio (OR). Multivariable logistic regression was used to analyze adjusted correlations of SNPs with repeat revascularization and PRU.

PLINK v1.07 software was used to filter relevant SNPs, which were adjusted by smoking statuses. The SNPs of candidate genes and selected pathways were performed. This analysis was repeated 10,000 times in simulated datasets. SNPs showing a significant ($p<0.05$) association with the phenotypes under analysis were selected.

3. Results

3.1 Patient Characteristics

A total of 143 patients who underwent PCI with dual antiplatelet therapy were included in this study. The baseline characteristics of included patients at the first PCI are shown in **Table 1**.

3.2 Patient Outcome

After the first PCI, the incidence of repeat revascularization at 18, 30, and 42 months was 14.1% (20/142), 17.5% (24/137), and 39.7% (31/78), respectively.

3.3 Association of SNPs with Platelet function

3.3.1 The SNPs of candidate gene variations

To analyze the association of SNPs of candidate gene and platelet function, 372 SNPs of 4 genes (15 SNPs of NOS3, 9 SNPS of MMP3, 46 SNPs of AGT, and 302 SNPs of AGT1R) were evaluated in the current study. After adjusting for smoking status, 4 and 7 SNPs were significantly related with PRU values and ADP aggregation rate, respectively (**Table 2**).

3.3.2 The SNPs of pathway gene variations

To analyze the association of SNPs of pathways and PRU or ADP aggregation rate, a total of 380 genes in four pathways (platelet activation pathway, platelet amyloid precursor protein pathway, aspirin blocks signaling pathway involved in platelet activation, and clopidogrel related gene) were analyzed in our study. After adjustment of smoking status, 363 SNPs were significantly related to PRU values, and 529 SNPs were significantly related to ADP aggregation rate (**Appendix Table 3**). Furthermore, 25 SNPs were associated with PRU value and ADP aggregation rate; details are listed in **Table 3**. Among these SNPs, the P-link values of kgp10633449 were less than 0.01 both for PRU and ADP aggregation rate, and the P-link values of PRU and ADP aggregation rate were 0.00606 and 0.003235, respectively.

3.4 Association of SNPs with the outcome

3.4.1 The SNPs of candidate gene variations

To analyze the association of SNPs of candidate genes and clinical outcomes, 372 SNPs of the four genes were analyzed. After adjusting for smoking status, 10, 20, and 8 SNPs were significantly related with repeat revascularization at 18, 30, and 42 months, respectively. Meanwhile, 24, 35, and 8 SNPs were significantly related with ISR at 18, 30, and 42 months, respectively (**Table 4**).

3.4.2 The SNPs of pathway gene variations

In addition to platelet function, 380 identical genes were used to analyze the association between SNPs and clinical outcomes. After adjusting for smoking status, 462 SNPs were significantly related with repeat revascularization within 18 months, 500 SNPs were significantly related with it within 30 months, 273 SNPs were significantly related with it within 42 months, 468 SNPs were significantly related with ISR within 18 months, 428 SNPs were significantly related with ISR within 30 months, and 363 SNPs were significantly related with ISR within 42 months. The details of the 2494 SNPs are shown in **Appendix Table 3**. There were 61 SNPs and 2 SNPs significantly associated with repeat revascularization and ISR within 18 months, 30 months, and 42 months (**Table 5**). There were three linkage SNPs (rs3788367, kgp3029439, and kgp15051272) of CABIN1. The correlation P-link values between them and repeat revascularization at 18 months, 30 months and 42 months were 0.002694, 0.0001099 and 0.007271, respectively ($P < 0.01$ for all).

3.5 Association of SNPs with Platelet function and outcomes

3.5.1 The SNPs of candidate gene variations

There were two SNPs associated with both platelet function, and clinical outcome. rs 78830 of NOS3 was associated with both ADP aggregation rate (Plink-P, 0.013) and 18- month ISR (Plink-P, 0.035) and 30-month ISR (Plink-P, 0.025), respectively. rs 62275847 of AGTR1 was associated with both ADP aggregation rate (Plink-P, 0.029) and 30-month ISR (Plink-P, 0.036).

3.5.2 The SNPs of pathway gene variations

Among the 588 SNPs associated with PRU, 21, 28, and 12 were associated with ISR at 18, 30, and 42 months, and 36, 33, and 16 SNPs were associated with re-revascularization at 18, 30, and 42 months, respectively. Of the 529 SNPs associated with ADP aggregation, 13, 15, and 8 SNPs were associated with ISR at 18, 30, and 42 months, and 16, 12, and 11 SNPs were associated with repeat revascularization at 18, 30, and 42 months, respectively (**Table S5**).

There were four SNPs of pathway gene variations associated with both platelet function and clinical outcome. The linkage rs471683 and rs7785386 of GNAI1|GNAT3 were associated with both PRU (Plink-P, 0.016), ADP aggregation rate (Plink-P, 0.002), 18-months ISR (Plink-P, 0.013), 30-months ISR (0.035), and repeat revascularization within 30 months (Plink-P, 0.030). Rs1715389 of GNAI1|GNAT3 were associated with both PRU (Plink-P, 0.019), ADP aggregation rate (Plink-P, 0.002), 18-months ISR (Plink-P, 0.016), 30-months ISR (0.046), and repeat revascularization within 30 months (Plink-P, 0.040). Rs7313458 of ITPR2 were associated with both PRU (Plink-P, 0.024), ADP aggregation rate (Plink-P, 0.036), 18-months ISR (0.043), 30-months ISR (Plink-P, 0.004), and repeat revascularization within 18 months (Plink-P, 0.009).

4. Discussion

In the current study, we selected 372 SNPs from 4 genes to analyze their association with the platelet function and clinical outcomes of dual antiplatelet therapy after the first PCI. Furthermore, we explored the relation of the polymorphisms of 380 genes in 9 platelet function pathways with platelet function and clinical outcomes in the included patients. To the best of our knowledge, this is the first study that investigated the association of polymorphism with both platelet function detected by two assays and clinical outcomes during 42 months follow-up in the Chinese cohort after PCI. We intended to capture the polymorphic variations in relation to higher thrombotic risk after PCI in Chinese.

In the candidate gene-associated SNP analysis section, two individual SNPs were significantly associated with the pharmacodynamic of clopidogrel and clinical outcomes. Their polymorphic was significantly associated with both ADP aggregation rate and ISR events during the follow-up. SNP rs7830, which is located in the NOS3 locus on chromosome 7, produces nitric oxide (NO) that is implicated in vascular smooth muscle relaxation through a cGMP-mediated signal transduction pathway. NO mediates vascular endothelial growth factor (VEGF)-induced angiogenesis in coronary vessels and promotes blood clotting through the activation of platelets (27,28). While there is good evidence on the clinical importance of NOS3 single nucleotide polymorphisms, the current knowledge is superficial in most clinical settings, and further studies are needed (29).

SNP rs7313458 is intron variant of ITPR2 (Inositol 1,4,5-Trisphosphate Receptor Type 2). The protein encoded by this gene belongs to the inositol 1,4,5-triphosphate receptor family, whose members are second messenger intracellular Ca^{2+} release channels. These proteins mediate a rise in cytoplasmic calcium in response to receptor-activated production of inositol triphosphate. In platelets, the elevation in the intracellular Ca^{2+} concentration contributes to various steps of cellular activation, such as reorganization of the actin cytoskeleton necessary for shape change (30,31), and degranulation or inside-out activation of integrin αIIbß3, indispensable for platelet aggregation (32). Polymorphism of ITPR2 in the change of platelet intracellular Ca ion concentration offers a new explanation for platelet function of individual differences. 1,4,5-inositol trisphosphate (IP3) opens Ca^{2+} channels in the platelet dense tubular system, raising intracellular Ca^{2+} levels. In addition, in our study, ITPR2 was associated with both platelet function and clinical outcomes, thus suggesting that ITPR2 gene polymorphism leads to adverse clinical outcomes by affecting platelet function. Another locus that affects both platelet function and clinical outcomes is the linkage rs471683 and rs7785386 of G protein subunit alpha i1 (GNAI1) and Protein Subunit Alpha Transducin 3 (GNAT3). Platelet G protein-coupled receptors (GPCRs) initiate and reinforce platelet activation and thrombus formation(33). Activation of platelets by GPCRs mainly produces effects through the receptors P2Y12 and P2Y1 for ADP, TP receptors for TXA2, and PAR1 and PAR4 receptors for thrombin. Therefore, genetic polymorphisms of GNAI1 and GNAT3 have the potential to influence platelet function and clinical outcome.

The present study has some limitations. First, this is a retrospective study, for which all data were obtained from the previous medical records, and the majority of clinical outcome events were obtained by telephone follow-up. Second, the small sample size makes the identified associations between genes and revascularization just a possible indication.

Declarations

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Author Contribution

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Data Availability

Availability of data and material has been described in the manuscript. Data would be provided upon request from the authors and in accordance with local regulations.

Ethics Approval

All procedures involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent

All participants provided written informed consent before enrollment in this study.

Consent for Publication

Written informed consent was obtained from all study participants.

Conflict of Interest

The authors declare no competing interest.

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Tables

Table 1 Baseline Characteristics of Participants at the first PCI.

Characteristics	N (Total)	Mean ± SD / N (%)
Age	143	65.16 ± 11.76
BMI	140	23.98 ± 6.647
Gender (Female)	143	32 (22.38)
Smoke	143	62 (43.36)
Current smokers	143	28 (19.58)
Former smokers	143	34 (23.78)
Drinker (current drinkers)	142	29 (20.42)
Diabetes	143	52 (36.36)
Hypertension	143	97 (67.83)
Hypercholesterolemia	143	95 (66.43)
Clinical indication of PCI	143	
Stable angina		14 (9.79%)
Unstable angina		46 (32.17%)
NSTEMI		11 (7.69%)
STEMI		23 (16.08%)
Unknown		49 (34.27%)

SD, Standard deviation; BMI, Body mass indes; NSTEMI, non-ST-segment elevation MI; STEMI, ST-segment elevation MI

Table 2. Results of individual polymorphisms analysis of candidate genes associated with platelet function

GeneSymbol	SNPs	Plink-P	CHR	BP	Gene type	GENO	GeneLocation
PRU							
MMP3 | MMP12	rs12808148	0.01251	11	102733163	GG/GA/AA	0/11/60	INTERGENIC
FLJ30375 | AGTR1	rs16860023	0.03416	3	147730134	GG/GA/AA	0/7/63	INTERGENIC
FLJ30375 | AGTR1	kgp6703776	0.03683	3	147731009	GG/GA/AA	0/7/64	INTERGENIC
FLJ30375 | AGTR1	rs16860017	0.03683	3	147727960	CC/CA/AA	0/7/64	INTERGENIC
ADP aggregation rate							
NOS3	rs7830	0.01349	7	150709571	AA/CA/AA	20/40/28	INTRON
AGT | CAPN9	rs3893225	0.024	1	230882946	AA/CA/AA	20/44/23	INTERGENIC
FLJ30375 | AGTR1	rs74679619	0.02574	3	147374653	AA/CA/AA	4/31/54	INTERGENIC
FLJ30375 | AGTR1	rs62275847	0.02942	3	148269641	AA/GA/GG	5/40/44	INTERGENIC
FLJ30375 | AGTR1	rs10513320	0.03527	3	147472375	AA/GA/GG	25/39/25	INTERGENIC
FLJ30375 | AGTR1	rs61710497	0.04497	3	147371594	AA/GA/GG	3/31/55	INTERGENIC
FLJ30375 | AGTR1	rs75605976	0.04797	3	147374626	AA/GA/GG	5/31/53	INTERGENIC

Table 3. Results of individual gene set-base analysis of pathway genes both associated with PRU value and ADP aggregation rate

GeneSymbol	SNP	Plink-P (PRU)	Plink-P (ADP aggregation rate)	CHR	BP	Gene type	GENO (PRU)	GENO (ADP aggregation rate)	GeneLocation
TCF4 | TXNL1	rs8097803	0.0405	0.02925	18	53805335	AA/AC/CC	0/3/68	2/6/80	INTERGENIC
GNAI1 | GNAT3	rs808956	0.02125	0.04342	7	80074216	AA/AC/CC	3/25/43	4/36/49	INTERGENIC
GNAI1 | GNAT3	rs7785386	0.01622	0.002119	7	80053909	AA/AC/CC	4/19/48	3/28/58	INTERGENIC
ITPR2	rs7313458	0.0239	0.03557	12	26763273	GG/GA/AA	7/34/30	15/44/29	INTRON
MAPK3 | CORO1A	rs6565176	0.001379	0.01754	16	30174926	AA/AG/GG	2/14/55	2/12/75	INTERGENIC
F11 | MTNR1A	rs6552971	0.03955	0.04706	4	187238388	AA/AG/GG	3/10/58	1/8/80	INTERGENIC
EDN1	rs5370	0.01436	0.01492	6	12296255	AA/AC/CC	3/23/45	6/34/49	CODING
GNAI1 | GNAT3	rs471683	0.01622	0.002119	7	80040648	AA/AG/GG	4/19/48	3/28/58	INTERGENIC
PLA2G4A | FAM5C	rs330708	0.0403	0.01392	1	187183135	AA/AG/GG	4/31/36	3/31/55	INTERGENIC
ADCY8 | EFR3A	rs273429	0.01981	0.005593	8	132479901	GG/GA/AA	8/34/29	6/42/41	INTERGENIC
CDH5	rs2344564	0.02326	0.0005299	16	66413150	GG/GA/AA	6/31/34	6/33/50	INTRON
COL4A4	rs2078635	0.03225	0.04817	2	228020491	AA/AC/CC	15/36/20	14/40/35	INTRON
EDN1	rs2071943	0.01436	0.01492	6	12295814	AA/AG/GG	3/23/45	6/34/49	INTRON
COL4A4	rs1922021	0.03246	0.04316	2	228025756	GG/GA/AA	15/35/21	15/38/36	INTRON
GNAI1 | GNAT3	rs17153898	0.01947	0.002119	7	80051323	GG/GA/AA	4/19/47	3/28/58	INTERGENIC
PRKG1	rs16913596	0.0374	0.02699	10	54023829	GG/GA/AA	12/26/33	14/44/31	INTRON
HMGCR | COL4A3BP	rs16872521	0.006834	0.04888	5	74663223	GG/GA/AA	1/9/61	1/7/80	INTERGENIC
PRKG1	rs1406477	0.02911	0.04511	10	54019620	GG/GA/AA	11/26/33	15/42/32	INTRON
PRKG1 | CSTF2T	rs10823243	0.04954	0.04699	10	53344284	AA/AC/CC	0/14/57	0/14/75	INTERGENIC
COL4A4	rs10498217	0.03879	0.009097	2	228010257	AA/AG/GG	0/12/59	0/10/79	INTRON
PLA2G4A | FAM5C	rs10494595	0.03723	0.02745	1	187239230	CC/CA/AA	6/23/42	8/34/47	INTERGENIC
ADCY2	kgp9961710	0.01535	0.02989	5	7806334	AA/AG/GG	1/14/56	2/17/69	INTRON
SLC29A1	kgp11901668	0.04204	0.03191	6	44192158	AA/AG/GG	7/31/33	14/42/33	INTRON
TMEM132E	kgp10633449	0.00606	0.003235	17	32917319	GG/GC/CC	5/23/43	7/26/56	INTRON
COL4A2	kgp10051470	0.01634	0.04435	13	110970267	GG/GA/AA	5/17/49	4/26/59	INTRON

Table 4. Results of individual polymorphisms analysis of candidate genes associated with clinical outcomes

GeneSymbol	SNPs	Plink-P	CHR	BP	Gene type	GENO	GeneLocation
Repeat revascularization within 18 months							
MMP3 | MMP12	rs522616	0.003671	11	102715048	GG/GA/AA	12/52/67	INTERGENIC
FLJ30375 | AGTR1	rs4306816	0.02121	3	148337463	GG/GA/AA	18/59/54	INTERGENIC
FLJ30375 | AGTR1	rs16859648	0.02182	3	147394647	CC/CA/AA	19/57/55	INTERGENIC
FLJ30375 | AGTR1	rs11928247	0.0224	3	147492839	GG/GA/AA	5/33/93	INTERGENIC
FLJ30375 | AGTR1	rs6777677	0.02432	3	147443667	GG/GA/AA	1/16/114	INTERGENIC
AGT	rs2148582	0.03039	1	230849799	GG/GA/AA	5/50/76	INTRON
AGT	rs2493134	0.03039	1	230849359	GG/GA/AA	5/50/76	INTRON
AGT	rs5051	0.03039	1	230849872	GG/GA/AA	5/50/76	UTR
AGT	rs699	0.03039	1	230845794	GG/GA/AA	5/50/76	CODING
FLJ30375 | AGTR1	rs2873943	0.0322	3	147403067	GG/GA/AA	17/70/44	INTERGENIC
Repeat revascularization within 30 months							
FLJ30375 | AGTR1	rs275685	0.001839	3	148347742	GG/GA/AA	0/18/71	INTERGENIC
FLJ30375 | AGTR1	rs16859648	0.007301	3	147394647	CC/CA/AA	12/42/35	INTERGENIC
FLJ30375 | AGTR1	rs4528908	0.01295	3	148085522	GG/GA/AA	12/43/33	INTERGENIC
FLJ30375 | AGTR1	rs2873943	0.01663	3	147403067	GG/GA/AA	11/45/33	INTERGENIC
FLJ30375 | AGTR1	rs4681375	0.01745	3	147496499	GG/GA/AA	22/44/23	INTERGENIC
FLJ30375 | AGTR1	rs6440539	0.01981	3	148124129	GG/GA/AA	17/43/29	INTERGENIC
FLJ30375 | AGTR1	rs6440544	0.02098	3	148170986	GG/GA/AA	14/42/33	INTERGENIC
FLJ30375 | AGTR1	rs7610743	0.0262	3	148349586	AA/AT/TT	1/26/62	INTERGENIC
FLJ30375 | AGTR1	rs16859909	0.02704	3	147626693	GG/GA/AA	5/33/51	INTERGENIC
FLJ30375 | AGTR1	rs56387025	0.03469	3	148098534	GG/GA/AA	15/44/30	INTERGENIC
FLJ30375 | AGTR1	rs1391796	0.03621	3	147505136	GG/GA/AA	10/46/33	INTERGENIC
FLJ30375 | AGTR1	rs79128431	0.03703	3	148131545	GG/GA/AA	2/35/52	INTERGENIC
NOS3 | ATG9B	rs1808593	0.03779	7	150708302	CC/CA/AA	1/33/55	INTERGENIC
NOS3	rs743506	0.03779	7	150706915	GG/GA/AA	1/33/55	INTRON
NOS3	rs743507	0.03779	7	150707488	GG/GA/AA	1/33/55	INTRON
FLJ30375 | AGTR1	rs7627412	0.04001	3	147502818	GG/GA/AA	14/45/30	INTERGENIC
FLJ30375 | AGTR1	rs6763183	0.04133	3	148048706	CC/CA/AA	20/41/28	INTERGENIC
FLJ30375 | AGTR1	rs10513322	0.04263	3	147361337	CC/CA/AA	2/29/58	INTERGENIC
FLJ30375 | AGTR1	rs66936840	0.04797	3	147322215	GG/GA/AA	3/27/59	INTERGENIC
FLJ30375 | AGTR1	rs67111729	0.04797	3	147308161	GG/GA/AA	3/27/59	INTERGENIC
Repeat revascularization within 42 months							
FLJ30375 | AGTR1	rs275685	0.00856	3	148347742	GG/GA/AA	0/8/36	INTERGENIC
FLJ30375 | AGTR1	rs7610743	0.00931	3	148349586	AA/AT/TT	0/11/33	INTERGENIC
FLJ30375 | AGTR1	rs4306816	0.02651	3	148337463	GG/GA/AA	8/19/17	INTERGENIC
FLJ30375 | AGTR1	rs16859648	0.03545	3	147394647	CC/CA/AA	7/21/16	INTERGENIC
FLJ30375 | AGTR1	rs4528908	0.04661	3	148085522	GG/GA/AA	8/20/15	INTERGENIC
FLJ30375 | AGTR1	rs6440544	0.04662	3	148170986	GG/GA/AA	8/22/14	INTERGENIC
FLJ30375 | AGTR1	rs9836223	0.04681	3	147474127	GG/GA/AA	2/17/25	INTERGENIC
FLJ30375 | AGTR1	rs2319323	0.04681	3	147475370	GG/GA/AA	2/17/25	INTERGENIC
ISR within 18 months							
FLJ30375 | AGTR1	rs4306816	0.006996	3	148337463	GG/GA/AA	18/60/60	INTERGENIC

FLJ30375 | AGTR1	rs188019	0.01121	3	148336197	GG/GA/AA	21/61/56	INTERGENIC
FLJ30375 | AGTR1	rs2029807	0.01209	3	148020990	CC/CA/AA	6/53/79	INTERGENIC
FLJ30375 | AGTR1	rs77884985	0.0164	3	148077936	GG/GA/AA	7/52/79	INTERGENIC
FLJ30375 | AGTR1	rs4374498	0.0164	3	148115945	CC/CA/AA	7/52/79	INTERGENIC
FLJ30375 | AGTR1	rs6440537	0.0164	3	148079188	GG/GA/AA	7/52/79	INTERGENIC
FLJ30375 | AGTR1	rs7615701	0.01928	3	147997618	GG/GA/AA	9/56/72	INTERGENIC
FLJ30375 | AGTR1	rs9817905	0.01946	3	147275754	GG/GA/AA	2/31/104	INTERGENIC
FLJ30375 | AGTR1	rs62274114	0.0198	3	148324431	GG/GA/AA	20/56/62	INTERGENIC
FLJ30375 | AGTR1	rs1879976	0.02016	3	148343517	GG/GA/AA	27/62/49	INTERGENIC
FLJ30375 | AGTR1	rs4355248	0.02224	3	147957721	CC/CA/AA	10/57/71	INTERGENIC
FLJ30375 | AGTR1	rs10433444	0.02998	3	148008513	GG/GA/AA	8/58/72	INTERGENIC
FLJ30375 | AGTR1	rs10935692	0.02998	3	148001131	CC/CA/AA	8/58/72	INTERGENIC
FLJ30375 | AGTR1	rs11712977	0.02998	3	148004138	GG/GA/AA	8/58/72	INTERGENIC
FLJ30375 | AGTR1	rs9873611	0.03093	3	147270026	GG/GA/AA	21/67/50	INTERGENIC
FLJ30375 | AGTR1	rs200127120	0.03187	3	148100446	CC/CA/AA	8/54/76	INTERGENIC
FLJ30375 | AGTR1	rs7610876	0.03187	3	148103369	CC/CA/AA	8/54/76	INTERGENIC
NOS3	rs7830	0.03477	7	150709571	CC/CA/AA	27/66/44	INTRON
AGT	rs2478545	0.03842	1	230844121	GG/GA/AA	12/57/69	INTRON
FLJ30375 | AGTR1	rs16859648	0.03916	3	147394647	CC/CA/AA	20/59/59	INTERGENIC
FLJ30375 | AGTR1	rs9878930	0.03928	3	147276761	GG/GA/AA	17/67/54	INTERGENIC
FLJ30375 | AGTR1	rs12629902	0.04787	3	147409986	GG/GA/AA	15/58/65	INTERGENIC
FLJ30375 | AGTR1	rs1403432	0.04865	3	148344020	GG/GA/AA	8/60/70	INTERGENIC
MMP3 | MMP12	rs522616	0.04978	11	102715048	GG/GA/AA	14/56/68	INTERGENIC
ISR within 30 months							
FLJ30375 | AGTR1	rs202136024	0.000795	3	147963041	GG/GA/AA	20/49/27	INTERGENIC
FLJ30375 | AGTR1	rs1874295	0.000879	3	147955974	CC/CA/AA	20/52/24	INTERGENIC
FLJ30375 | AGTR1	rs4355248	0.002405	3	147957721	CC/CA/AA	6/43/47	INTERGENIC
FLJ30375 | AGTR1	rs16859648	0.006205	3	147394647	CC/CA/AA	14/43/39	INTERGENIC
FLJ30375 | AGTR1	rs10804724	0.009196	3	147989624	GG/GA/AA	5/35/56	INTERGENIC
FLJ30375 | AGTR1	rs7619579	0.01037	3	147380486	AA/AT/TT	3/23/70	INTERGENIC
FLJ30375 | AGTR1	rs275685	0.01083	3	148347742	GG/GA/AA	0/20/76	INTERGENIC
FLJ30375 | AGTR1	rs62275231	0.01086	3	148047542	GG/GA/AA	7/42/47	INTERGENIC
FLJ30375 | AGTR1	rs4643674	0.01107	3	148088465	GG/GA/AA	7/42/47	INTERGENIC
FLJ30375 | AGTR1	rs4528908	0.01194	3	148085522	GG/GA/AA	13/49/33	INTERGENIC
FLJ30375 | AGTR1	rs6440544	0.01556	3	148170986	GG/GA/AA	14/49/33	INTERGENIC
FLJ30375 | AGTR1	rs7622746	0.01569	3	147390505	GG/GA/AA	4/22/70	INTERGENIC
FLJ30375 | AGTR1	rs10935703	0.01711	3	148114124	CC/CA/AA	6/41/49	INTERGENIC
FLJ30375 | AGTR1	rs13084464	0.01912	3	148195726	GG/GA/AA	9/46/41	INTERGENIC
FLJ30375 | AGTR1	rs10513333	0.02284	3	148303859	GG/GA/AA	8/44/44	INTERGENIC
NOS3	rs7830	0.02514	7	150709571	CC/CA/AA	19/47/29	INTRON
FLJ30375 | AGTR1	rs7611797	0.02575	3	147978935	GG/GA/AA	3/29/64	INTERGENIC
FLJ30375 | AGTR1	rs1456679	0.02667	3	147859661	GG/GA/AA	20/43/33	INTERGENIC
FLJ30375 | AGTR1	rs4591472	0.02667	3	147829201	CC/CA/AA	20/43/33	INTERGENIC
FLJ30375 | AGTR1	rs199534116	0.02765	3	147818301	GG/GA/AA	11/37/48	INTERGENIC

FLJ30375 | AGTR1	rs4269055	0.02765	3	147850902	GG/GA/AA	11/37/48	INTERGENIC
FLJ30375 | AGTR1	rs6770996	0.02837	3	147470053	GG/GA/AA	3/31/62	INTERGENIC
FLJ30375 | AGTR1	rs4306816	0.03066	3	148337463	GG/GA/AA	13/44/39	INTERGENIC
FLJ30375 | AGTR1	rs1156787	0.0329	3	147760244	CC/CA/AA	1/28/67	INTERGENIC
FLJ30375 | AGTR1	rs7651229	0.03316	3	147487870	GG/GA/AA	3/35/58	INTERGENIC
FLJ30375 | AGTR1	rs1841770	0.03347	3	147756686	CC/CA/AA	2/31/63	INTERGENIC
FLJ30375 | AGTR1	rs1870000	0.03558	3	147787591	GG/GA/AA	1/27/66	INTERGENIC
FLJ30375 | AGTR1	rs62275847	0.0362	3	148269641	GG/GA/AA	8/41/47	INTERGENIC
FLJ30375 | AGTR1	rs6764882	0.03805	3	147787204	GG/GA/AA	1/27/68	INTERGENIC
FLJ30375 | AGTR1	rs9848851	0.03805	3	147774712	CC/CA/AA	1/27/68	INTERGENIC
FLJ30375 | AGTR1	rs56387025	0.03986	3	148098534	GG/GA/AA	16/50/30	INTERGENIC
FLJ30375 | AGTR1	rs9825391	0.04394	3	148346933	GG/GA/AA	16/45/35	INTERGENIC
FLJ30375 | AGTR1	rs7610743	0.04932	3	148349586	AA/AT/TT	2/28/66	INTERGENIC
FLJ30375 | AGTR1	rs4681413	0.04935	3	148157911	CC/CA/AA	17/49/30	INTERGENIC
FLJ30375 | AGTR1	rs7614394	0.04992	3	147867286	GG/GA/AA	24/44/28	INTERGENIC
ISR within 42 months							
FLJ30375 | AGTR1	rs202136024	0.01152	3	147963041	GG/GA/AA	9/23/13	INTERGENIC
FLJ30375 | AGTR1	rs4355248	0.01567	3	147957721	CC/CA/AA	3/21/21	INTERGENIC
FLJ30375 | AGTR1	rs1874295	0.0168	3	147955974	CC/CA/AA	9/25/11	INTERGENIC
FLJ30375 | AGTR1	rs7610743	0.01982	3	148349586	AA/AT/TT	1/11/33	INTERGENIC
FLJ30375 | AGTR1	rs275685	0.0236	3	148347742	GG/GA/AA	0/9/36	INTERGENIC
FLJ30375 | AGTR1	rs9836223	0.03588	3	147474127	GG/GA/AA	2/17/26	INTERGENIC
FLJ30375 | AGTR1	rs2319323	0.03588	3	147475370	GG/GA/AA	2/17/26	INTERGENIC
FLJ30375 | AGTR1	rs6800835	0.04439	3	148328711	GG/GA/AA	6/20/19	INTERGENIC

Table 5. Results of individual gene set-base analysis of pathway genes associated with clinical outcome

GeneSymbol	SNP	Plink-P (within 18 months)	Plink-P (within 30 months)	Plink-P (within 42 months)	CHR	BP	Gene type	GENO (within 18 months)	GENO (within 30 months)	GENO (within 42 months)	Ge
Repeat revascularization											
TCF4	rs9966430	0.02164	0.03221	0.02041	18	53125364	AA/AC/CC	34/62/35	22/45/22	8/23/13	IN
PRKG1	rs9943368	0.01008	0.01812	0.04452	10	53015492	GG/GA/AA	27/65/39	20/47/22	11/20/13	IN
VKORC1	rs9934438	0.01287	0.03725	0.036	16	31104878	GG/GA/AA	1/19/111	1/12/76	1/4/39	IN
VKORC1 | BCKDK	rs9923231	0.01287	0.03725	0.036	16	31107689	GG/GA/AA	1/19/111	1/12/76	1/4/39	IN
TMEM132E | CCT6B	rs9916627	0.01855	0.01426	0.01529	17	33010157	AA/AG/GG	5/47/79	4/29/56	1/18/25	IN
GRM7	rs9883142	0.02919	0.009172	0.04203	3	7017919	AA/AG/GG	32/58/41	23/33/33	41962	IN
ADAMTSL1 | FAM154A	rs945442	0.004404	0.02406	0.0472	9	18927768	CC/CA/AA	21/55/55	15/38/36	40869	IN
GPI	rs8191425	0.002074	0.01412	0.03953	19	34888052	AA/AG/GG	5/40/86	4/28/57	3/15/26	IN
TMEM132E | CCT6B	rs8075272	0.01741	0.02956	0.01888	17	33042432	AA/AC/CC	21/74/36	15/46/28	8/24/12	IN
ADAMTSL1	rs7854121	0.02046	0.01539	0.04624	9	18809482	GG/GA/AA	20/62/49	11/44/34	5/22/17	IN
ADCY2	rs7714110	0.008607	0.01016	0.01915	5	7528287	GG/GA/AA	6/22/103	3/16/70	2/11/31	IN
PRKCA | CACNG5	rs758664	0.03405	0.02686	0.02619	17	64871272	GG/GA/AA	8/34/89	2/23/64	1/10/33	IN
PRKCA | CACNG5	rs740805	0.002149	0.009857	0.03978	17	64871070	AA/AG/GG	28/60/43	18/40/31	7/19/18	IN
COL4A2	rs7328731	0.009522	0.04056	0.02227	13	111056994	AA/AG/GG	0/28/103	0/21/68	0/10/34	IN
VKORC1	rs7294	0.01287	0.03725	0.036	16	31102321	AA/AG/GG	1/19/111	1/12/76	1/4/39	UT
TCF4	rs7231748	0.0162	0.0285	0.02304	18	53109035	AA/AG/GG	28/63/40	19/43/27	10/22/12	IN
P2RY1	rs701265	0.01104	0.02129	0.01015	3	152554357	GG/GA/AA	9/49/73	7/34/48	4/14/26	CC
ADCY2	rs6867567	0.006643	0.01434	0.0378	5	7519762	GG/GA/AA	17/49/65	12/30/47	8/15/21	IN
PLCB1	rs6055928	0.01601	0.006125	0.01792	20	8567151	AA/AG/GG	7/39/85	4/28/57	38320	IN
PLCB1	rs6039205	0.04566	0.04909	0.04899	20	8571934	GG/GA/AA	6/33/92	3/24/62	3/9/32	IN
TCF4 | TXNL1	rs573399	0.03726	0.002176	0.01822	18	54265847	AA/AG/GG	11/44/76	7/32/50	4/13/27	IN
MERTK | TMEM87B	rs4848973	0.01068	0.03101	0.0221	2	112790562	AA/AG/GG	1/13/117	0/11/78	0/7/37	IN
GPI	rs4806015	0.001824	0.01338	0.02928	19	34865551	AA/AG/GG	4/42/85	3/30/56	2/16/26	IN
GRM7	rs480409	0.003809	0.008568	0.03517	3	7010081	GG/GA/AA	16/58/57	13/39/37	5/21/18	IN
TCF4	rs4468713	0.02543	0.04592	0.02304	18	53104019	AA/AG/GG	26/63/42	17/45/27	10/22/12	IN
COL4A1	rs3825481	0.02632	0.0121	0.02582	13	110806852	GG/GA/AA	15/59/55	8/40/40	2/15/27	IN
ITPR1	rs3816252	0.0457	0.047	0.04348	3	4856430	GG/GA/AA	29/72/30	20/47/22	6/26/12	IN
CABIN1	rs3788367	0.002694	0.0001099	0.007271	22	24463996	AA/AG/GG	1/32/98	1/22/66	1/10/33	IN
GRLF1	rs311371	0.01023	0.01795	0.02725	19	47447158	GG/GA/AA	22/54/55	16/41/32	7/24/13	IN
VKORC1	rs2359612	0.01287	0.03725	0.036	16	31103796	GG/GA/AA	1/19/111	1/12/76	1/4/39	IN
GP1BA | SLC25A11	rs2243102	0.02244	0.004903	0.04887	17	4839149	AA/AG/GG	3/29/99	2/21/66	2/10/32	IN
TMEM132E | CCT6B	rs2215188	0.01855	0.01426	0.01529	17	33017553	AA/AG/GG	5/47/79	4/29/56	1/18/25	IN
TMEM132E | CCT6B	rs2190980	0.01687	0.04869	0.02481	17	32996753	AA/AG/GG	9/52/70	6/36/47	2/20/22	IN
ADCY2	rs2055388	0.008607	0.01016	0.01915	5	7527521	CC/CA/AA	6/22/103	3/16/70	2/11/31	IN
ADCY10	rs203782	0.0009139	0.02799	0.02774	1	167882386	AA/AG/GG	6/41/84	4/31/54	37984	IN
ADCY10	rs203777	0.0009139	0.02799	0.02774	1	167876616	AA/AG/GG	6/41/84	4/31/54	37984	IN

PRKG1	rs1865645	0.02848	0.01812	0.04452	10	52991510	AA/AG/GG	28/63/40	20/47/22	11/20/13	IN
P2RY1 | LOC100287133	rs17468698	0.02622	0.02513	0.02448	3	152831259	AA/AG/GG	0/19/112	0/13/76	0/6/38	IN
TCF4	rs1452788	0.028	0.04441	0.02954	18	53117304	GG/GA/AA	35/60/36	22/43/24	8/21/15	IN
TCF4 | TXNL1	rs12457258	0.0309	0.00162	0.01466	18	54265669	GG/GA/AA	10/45/76	6/33/50	3/14/27	IN
MERTK | TMEM87B	rs11897014	0.01388	0.0448	0.03151	2	112795908	GG/GA/AA	1/14/116	0/12/77	0/8/36	IN
PLA2G4A | FAM5C	rs11591211	0.03326	0.02318	0.046	1	187872751	CC/CA/AA	13/48/70	8/33/48	4/16/24	IN
PRKCA	rs11079667	0.02184	0.008135	0.03042	17	64725031	GG/GA/AA	20/53/58	16/36/37	8/15/21	IN
ITPR2	rs10842760	0.01335	0.004289	0.04301	12	26772311	AA/AG/GG	22/65/44	18/41/30	9/18/17	IN
STIM1	rs10835407	0.04901	0.02266	0.0188	11	3993231	GG/GA/AA	9/53/69	6/37/46	4/20/20	IN
PRKG1	rs10822496	0.01356	0.0245	0.0443	10	53013479	AA/AC/CC	23/68/40	18/48/23	10/21/13	IN
ITPR2	rs10743586	0.008208	0.01073	0.03645	12	26642577	GG/GA/AA	12/36/82	8/26/54	5/16/22	IN
STIM1	rs10742189	0.01766	0.03611	0.01824	11	3928752	CC/CA/AA	21/59/51	14/39/36	8/21/15	IN
PRKG1	rs10490978	0.03093	0.0245	0.0443	10	52994866	AA/AG/GG	26/65/40	18/48/23	10/21/13	IN
GRLF1	rs10425259	0.009649	0.01669	0.02654	19	47492475	AA/AG/GG	22/53/56	16/40/33	7/23/14	IN
CXCL12	rs1029153	0.007657	0.01525	0.02828	10	44867146	GG/GA/AA	6/37/88	5/24/60	38654	UT
ADCY2	rs10066518	0.006643	0.01434	0.0378	5	7518855	GG/GA/AA	17/49/65	12/30/47	8/15/21	IN
F2R | LOC100287744	kgp9342924	0.02785	0.04026	0.01822	5	76066861	GG/GA/AA	11/50/61	4/38/41	3/18/17	IN
PLA2G4A | FAM5C	kgp8430507	0.03224	0.001865	0.02161	1	187433648	AA/AG/GG	1/23/107	1/17/71	1/7/36	IN
ITPR1 | LOC100288535	kgp6152707	0.0192	0.007311	0.03526	3	4944138	AA/AG/GG	26/57/48	16/39/34	8/23/13	IN
RASGRP1	kgp3988187	0.02858	0.02029	0.04529	15	38816287	AA/AG/GG	12/60/59	11/37/41	4/20/20	IN
TCF4	kgp3121365	0.02358	0.0288	0.02041	18	53136122	AA/AC/CC	31/67/33	21/47/21	8/23/13	IN
CABIN1	kgp3029439	0.002694	0.0001099	0.007271	22	24472173	AA/AG/GG	1/32/98	1/22/66	1/10/33	CC
PLA2G4A | FAM5C	kgp15159942	0.03332	0.02581	0.04206	1	187899551	GG/GA/AA	13/48/70	8/33/48	4/15/25	IN
CABIN1	kgp15051272	0.002694	0.0001099	0.007271	22	24435363	AA/AG/GG	1/32/98	1/22/66	1/10/33	IN
PLCB1	kgp10950259	0.04637	0.02328	0.01505	20	8589571	GG/GA/AA	5/36/90	3/26/60	37925	IN
ISR											
P2RY1 | LOC100287133	kgp3945860	0.0268	0.02926	0.04043	3	152815451	GG/GA/AA	0/16/121	0/9/86	0/4/40	IN
ADAMTSL1	rs10811043	0.03643	0.001305	0.04403	9	18832659	AA/AG/GG	9/74/55	7/49/40	3/25/17	IN

Supplementary Files

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- AppendixTable15.xlsx