Supplementary Materials for

Remote modulation of IncRNA GCLET by risk variant at 16p13 underlying genetic susceptibility to gastric cancer

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Supplementary Materials and Methods

Study subjects
The gastric cancer GWAS for Asian populations (phs000361.v1.p1) was deposited in the Database of Genotypes and Phenotypes (dbGaP); all individuals were recruited through the Shanxi UGI Cancer Genetics Project and Linxian Nutrition Intervention Trial. The samples analyzed in the validation stages were mainly recruited from both Eastern China (Central Jiangsu Province: 1,275 cases and 1,436 controls from Nanjing-1; 1,021 cases and 1,203 controls from Nanjing-2; 550 cases and 1,155 controls from Nanjing-3; Southern Jiangsu Province: 940 cases and 1,061 controls from Yixing; Eastern Jiangsu Province: 471 cases and 652 controls from Nantong) and from Northeastern China (1,096 cases and 1,178 controls from Jilin Province). The demographic characteristics of all subjects are shown in table S9.

SNP genotyping in the replication phases
Genotyping of the gastric cancer GWAS data was conducted using Illumina Human 610-Quad BeadChips. Genotyping for rs3850997 in the replication stages was performed using TaqMan assays (Applied Biosystems). The negative control (one well with water) and blinding of technicians were used as sample genotyping quality control measures. The primers and probes for the TaqMan assays are listed in table S10.

Distributional annotation
The whole-genome genetic variants were derived from the 1000 Genomes Project (Phase 1 integrated release 3, March 2012, with 1,092 individuals). For the validity analysis, we enrolled only variants from the Asian population (CHB: Han Chinese in Beijing, China; and JPT: Japanese in Tokyo, Japan) with the following criteria of quality control: variants in autosomes, the minor allele frequency (MAF) > 0.01, call rate of genotypes > 90%, and P > 0.001 for Hardy-Weinberg Equilibrium (HWE). A total of 7,930,218 variants were retained and mapped to the four subgroup intervals (i.e., 17.7% in protein-coding genes, 10.5% in ncRNAs, 24.6% in the
In a similar manner, 21,642 cancer-related variants derived from the GWAS catalog were mapped to these intervals (i.e., 25.5% in protein-coding genes, 8.6% in ncRNAs, 31.2% in the combination, and 34.7% in intergenic regions; **fig. S1B and table S2**), of which 880 variants were initially derived from the GWAS catalog and corresponding variants with a high linkage disequilibrium (LD) of $r^2 > 0.8$. In addition, the distribution of 29 gastric cancer risk variants with higher evidence was determined using the same procedures, with 13.8% in protein-coding genes, 3.4% in ncRNAs, 62.1% in the combination, and 20.7% in intergenic regions (**fig. S1D and table S2**).

**Reanalysis of the GWAS database**

For gastric cancer GWAS data, we initially performed strict quality control, including the processes of duplicate sample detection, sex check, and relatives’ identification for individuals; the criteria were a call rate > 95%, MAF > 0.05, $P > 0.001$ for HWE, and SNPs that mapped to the hg19 version. Eventually, a total of 1,625 gastric cancer cases and 2,100 controls with 426,149 SNPs were retained for further analysis. The original findings were reanalyzed using a logistic regression model in an additive genetic model (**table S11**).

Regarding the association analysis among the European population, the germline genotypes of subjects in both The Cancer Genome Atlas (TCGA) and the Multi-Ethnic Study of Atherosclerosis (MESA, dbGaP phs000209.v12) databases were detected using an Affymetrix Human SNP Array 6.0. All subjects were identified as having a European ancestry by self-report or clustering and principal component analysis (PCA) using STRUCTURE 2.3.4 with the 1000 Genomes Project populations. Finally, we enrolled 254 gastric cancer cases from TCGA and 2,835 unrelated controls from MESA for the association analysis between candidate SNPs and gastric cancer risk.
**Patient sample collection, DNA and RNA isolation, and cDNA preparation**

A total of 331 gastric cancer tumors and 51 matched normal tissues were collected in this study. Specifically, 51 pairs of freshly frozen tumors and adjacent normal tissues were originally collected from patients among the Nanjing-1 set who underwent surgical treatment. Total DNA was isolated from frozen tissues using a Tissue DNA Kit (OMEGA), and total RNA was extracted using TRizol Reagent (Invitrogen) and a RNeasy Mini Kit (Qiagen) according the manufacturers’ protocols. In addition, 280 gastric cancer tissues were obtained from patients among the Nantong set; total RNA was isolated using a FFPE RNA Kit (OMEGA) according the manufacturers’ protocol. Then, the total RNA was reverse transcribed into cDNAs using a High-Capacity cDNA Reverse Transcription Kit (Invitrogen) according to the manufacturer’s instructions. The cDNA templates were subsequently used to quantify the expression of *GCLET* or to sequence the allele-specific expression, and the pipeline followed that reported in the study by Huang *et al.* (ref. 42).

**Cell culture and extraction of DNA and RNA**

The human gastric cancer cell lines (BGC-823, SGC-7901, and MGC-803) and gastric epithelial cell line (GES-1) were purchased from the Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences (Shanghai, China). All cells were grown in DMEM (Invitrogen) supplemented with 10% heat-inactivated FBS (Gibco), 100 U/ml penicillin and 100 μg/ml streptomycin at 37 °C in a 5% CO₂ atmosphere in a humidified incubator. None of the cells were contaminated with mycoplasma during our experiments. Total DNA and RNA were isolated from the parental and infected cells using the Tissue DNA Kit (OMEGA) and the RNeasy Mini Kit (Qiagen), respectively, according to the manufacturers’ protocols. In addition, cytoplasmic and nuclear RNA were isolated from each cell line and purified using a mirVandaTM Protein and RNA Isolation System (Ambion) according to the manufacturer’s instructions.
**Quantitative RT-PCR**

Quantitative RT-PCR (qPCR) was performed with SYBR Green reagents (Takara) using an Applied Biosystems 7900HT Real-Time PCR System. The housekeeping genes GAPDH and U6 were used as endogenous controls for GCLET, CTCF, and miR-27a-3p expression. Relative RNA expression was calculated using the comparative Ct method. The primers are presented in table S10.

**Fluorescence In Situ Hybridization (FISH)**

Both a Ribo™ Fluorescent In Situ Hybridization (FISH) Kit and Ribo™ IncRNA FISH Probe Mix (RiboBio, China) were employed to assess the FISH localization of the lncRNA in gastric cancer cells, according to the manufacturer's protocol. Briefly, the cultured cells were fixed with 4% paraformaldehyde for 10 min at room temperature, and then permeabilized with Triton X-100 for 5 min at 4 °C. Subsequently, the Cy3-labelled RNA probes and DAPI-labelled nuclei were detected. Slides were mounted and examined using a confocal fluorescence microscope (Zeiss, Germany) in the dark.

**Construction of luciferase plasmids**

For the detection of the transcriptional activity of rs3850997, the GCLET promoter (-1,000 bps relative to the TSS) was synthesized and inserted upstream of an SV40 promoter in the pGL3-basic vector between KpnI and XhoI sites, and the 1,000-bp rs3850997-containing region was synthesized through site-directed mutagenesis (T or G allele) and inserted upstream of the pGL3-basic vector containing the GCLET promoter region. Combined with these plasmids, additional pRL-SV40-Renilla vectors (as a normalized control) were cotransfected into cells with or without CTCF siRNAs.

For the identification of miRNAs for GCLET, the mature or mutant sequence of GCLET was synthesized and inserted downstream of the Renilla luciferase gene as
the 3′-UTR between XhoI and NotI sites in the psiCHECK-2 vector, which included Firefly luciferase as an internal control. The plasmids and miRNA mimics were cotransfected into gastric cancer cells.

For the determination of the miR-27a-3p target, both the complete sequence and the seed region mutant sequence in the 3′-UTR of FOXP2 were synthesized and inserted into the psiCHECK-2 vector, which was subsequently cotransfected into cells with or without miR-27a-3p mimics.

**Luciferase reporter assays**

Luciferase plasmids were cotransfected into both gastric cancer cell lines (MGC-803 and BGC-823 cultured in 24-well plates at a density of 3 × 10^5 cells/well) using Lipofectamine 2000 (Invitrogen) according to manufacturer’s instructions. After 24 h, cells were collected and analyzed for luciferase activity using a Dual-Luciferase Assay System (Promega). All data were obtained from three replicate wells and were statistically analyzed using two-tailed t tests.

**Western blot**

Using standard protocols, cells were lysed in RIPA lysis buffer supplemented with proteases inhibitors. The boiled protein samples (40 µg) were loaded onto SDS-PAGE gels, separated and then transferred onto PVDF membranes (Millipore). Membranes were blocked for 90 min with blocking buffer [TBS-T (TBS with 0.1% Tween-20) containing 5% skim milk]. Membranes were then immunoblotted overnight with primary antibodies against target genes (anti-CTCF, 2418, Cell Signaling Technology; anti-FOXP2, ab16046, Abcam) or antibodies against β-actin (13E5, Cell Signaling Technology) at a 1:1,000 dilution. After three washes with TBS-T, the blots were visualized with a HRP-conjugated secondary antibody (1:1,000 dilution, BS13278, Bioworld) and enhanced chemiluminescence reagents (Cell Signaling Technology) according to the manufacturers’ instructions.

**Electrophoretic mobility shift assay (EMSA)**
Synthetic double-stranded and 3' biotin-labeled oligonucleotides corresponding to the rs3850997 sequence were incubated with the nuclear extracts of MGC-803 and BGC-823 cells using a Light Shift Chemiluminescent EMSA Kit (Thermo Scientific) according to the manufacturer’s protocols. After a 1-h incubation at room temperature, the mixtures were separated on a 4.5% SDS-PAGE gel and transferred to a nylon membrane. Next, the signals were detected using a stabilized streptavidin-horseradish peroxidase conjugate. Unlabeled oligonucleotides were added to the reaction at 100-fold (+) or 300-fold (++) excess for competition. In addition, we conducted a super EMSA to identify specific DNA-protein products using antibodies against CTCF (2418, Cell Signaling Technology).

**Construction of overexpression plasmids and siRNAs**

For gene overexpression, the cDNAs encoding the human GCLET and CTCF genes were synthesized and subcloned into the XhoI and NotI sites of the pcDNA3.1 vector (Promega), and the XhoI and KpnI sites of the GV141 vector (Genechem). In addition, we constructed three oligonucleotides targeting using CTCF mRNA for gene knockdown. The effects of overexpression and knockdown on both MGC-803 and BGC-823 cells were determined using Western blot and qPCR; both of them showed sufficient results for gene overexpression and knockdown at 48 h after transfection. SiRNA-1 was the most efficient siRNA against CTCF and was used in subsequent experiments (fig. S11B to D).

**Cell proliferation, colony formation, cell migration, and invasion assays**

The indicated cells were trypsinized and resuspended in DMEM 48 h after transfection with negative control or GCLET overexpression vectors. For cell proliferation assays, the resuspended cells were placed in 96-well plates at a density of 1,000 cells/well, cultured with complete medium, and the cell numbers were quantified with a CCK-8 Kit (Dojindo) every 24 h after a 30-min incubation. For colony formation assays, the transfected cells were reseeded in 6-well plates (400 cells/well) containing complete medium, incubated for two weeks, fixed with
paraformaldehyde, and stained with crystal violet. The cell colonies containing more than 50 cells or > 0.5 mm in diameter were counted under a dissecting microscope. For cell migration and invasion assays, cells (7.5 × 10^4 cells/well) resuspended in serum-free medium were seeded in 8-µm Transwell inserts (Millipore) coated with or without Matrigel (BD Biosciences) in 24-well plates. The lower chambers were filled with complete DMEM as a chemoattractant. After a 24-h incubation, the cells on the upper surface of the filters were removed, and the membranes were fixed and stained with crystal violet. Invading or migrating cells were quantified by counting the numbers of cells in four microscopic fields per membrane. All assays were performed in triplicate in three independent experiments.

**Animal models**

MGC-803 cells (1 × 10^7 cells in 0.1 ml of PBS) were stably transfected with GCLET/NC lentiviral vectors (efficiency is shown in fig. S11D) and then subcutaneously injected into the right flank of male nude mice (5 weeks old, five mice per group). Tumor growth was examined every three days. After three weeks, the mice were sacrificed, and the tumor size and weight were measured. The tumors were retained for hematoxylin and eosin (HE) and immunohistochemical (IHC) staining. HE staining was utilized to select representative areas, and IHC staining was used to identify the expression of the proliferation marker Ki67 (Anti-Ki67, ab15580, Abcam). Animal studies were approved by the Institutional Animal Care and Use Committee of Nanjing Medical University (IACUC-1904029).

**Identification of targets of both GCLET and miR-27a-3p**

A systematic analysis was conducted to identify the shared targets of both GCLET and miR-27a-3p. Primarily, target prediction was performed with the following strict criteria: (a) the integrated prediction of three algorithms from TargetScan, PicTar, and miRanda for miR-27a-3p targets (405 identified); (b) cancer-associated targets (331 retained); and (c) targets with significantly lower expression in gastric cancer tissues than that in normal tissues and with an negative correlation to miR-27a-3p
expression. These targets were derived from TCGA datasets. A total of 26 candidate targets were selected (table S8).

**URLs**

GENCODE v19: https://www.gencodegenes.org/human/release_19.html

1000 Genomes project: http://www.1000genomes.org/

GWAS catalog: https://www.ebi.ac.uk/gwas/home

FM-summary: https://github.com/hailianghuang/FM-summary

RegulomeDB: http://regulome.stanford.edu/

HaploReg v4: https://pubs.broadinstitute.org/mammals/haploreg/haploreg_v4.php

Haplotter: http://haplotter.uchicago.edu/

GTEx: https://gtexportal.org/home/

LNCipedia: https://lncipedia.org/

CPAT: http://lilab.research.bcm.edu/cpat/

iSeeRNA: http://137.189.133.71/iSeeRNA/index.html

PhyloCSF: https://github.com/mlin/PhyloCSF/wiki

mfold: http://unafold.rna.albany.edu/?q=mfold

R: https://www.r-project.org/
**Supplementary Tables**

**Table S1.** The distribution of gene types based on the GENCODE v19 database

| Gene types          | Subtypes                    | Biotypes                              | Number (n = 229,917) |
|---------------------|-----------------------------|---------------------------------------|----------------------|
| Protein-coding      | protein_coding              |                                       | 81,814               |
|                     | antisense                   |                                       | 9,710                |
|                     | processed_transcript        |                                       | 28,082               |
|                     | pseudogene                  |                                       | 30,686               |
| IncRNAs             | lincRNA                     |                                       | 11,780               |
|                     | sense_intronic/overlapping  |                                       | 1,132                |
|                     | retained_intron             |                                       | 25,955               |
|                     | 3prime_overlapping_ncrna    |                                       | 25                   |
| ncRNAs (148,103)    | IG_C/D/J/V_gene            |                                       | 217                  |
|                     | Mt_rRNA/trNA                |                                       | 24                   |
|                     | nonsense_mediated_decay     |                                       | 13,052               |
|                     | non_stop_decay              |                                       | 58                   |
| Other ncRNAs        | TR_C/D/J/V_gene            |                                       | 179                  |
|                     | snoRNA, snRNA               |                                       | 3,452                |
|                     | rRNA, miRNA, misc_RNA       |                                       | 5,697                |
|                     | all IG/RNA_genes            |                                       | 18,054               |

Sense_intronic/overlapping: sense_intronic and sense_overlapping;
IG_C/D/J/V_gene: IG_C_gene, IG_D_gene, IG_J_gene, and IG_V_gene;
TR_C/D/J/V_gene: TR_C_gene, TR_D_gene, TR_J_gene, and TR_V_gene;
all IG/RNA_genes: all IG_gens and all RNA_genes.
Table S2. The frequency distribution of human genetic variants in different gene types

| Gene types         | 1000 Genomes Project | Pan-cancer GWAS Catalog | Gastric cancer risk |
|--------------------|-----------------------|-------------------------|---------------------|
|                    | n = 7,930,218 %       | n = 21,642 %            | n = 29 % P^a P^b    |
| Protein-coding genes | 1,399,941 17.7        | 5,525 25.5              | 4 13.8 0.779 0.960  |
| The combination    | 1,950,848 24.6        | 6,742 31.2              | 18 62.1 2.07E-05 5.76E-04 |
| ncRNAs             | 834,905 10.5          | 1,873 8.6               | 1 3.4 0.960 0.928   |
| Intergenic regions | 3,744,524 47.2        | 7,502 34.7              | 6 20.7 0.999 0.967  |

^a Calculated by hypergeometric test based on 1000 Genomes Project database.
^b Calculated by hypergeometric test based on Pan-cancer GWAS Catalog database.
Table S3. Association between 499 SNPs and gastric cancer risk in the GWAS stage

| Distribution-based set | SNP     | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|---------|-----|----------|--------------------|------------------|-----------------------------------|----------------------------------|------------|
| Protein-Coding         | rs4971101 | 1   | 155157635 | A/G                | 0.133/0.169      | 0.75 (0.65-0.85) 1.15E-05 0.998   |                                  | RP11-201K10.3 | Intergenic |
| Protein-Coding         | rs2070803 | 1   | 155157715 | G/A                | 0.133/0.169      | 0.75 (0.65-0.85) 1.26E-05 0.998   |                                  | RP11-201K10.3 | Intergenic |
| Protein-Coding         | rs56245197 | 3   | 67513699  | C/T                | 0.21/0.174       | 1.27 (1.13-1.42) 8.38E-05 0.996   |                                  | SUCLG2     | Intron     |
| Protein-Coding         | rs12497114 | 3   | 169799521 | T/A                | 0.171/0.137      | 1.3 (1.15-1.49) 6.59E-05 0.97     |                                  | GPR160     | Intron     |
| Protein-Coding         | rs1895321 | 5   | 159846410 | A/C                | 0.211/0.175      | 1.26 (1.12-1.42) 7.94E-05 0.992   |                                  | SLU7       | Intergenic |
| Protein-Coding         | rs9394893 | 6   | 42257161  | G/C                | 0.471/0.425      | 1.21 (1.1-1.32) 9.83E-05 0.99     |                                  | TRERF1     | Intron     |
| Protein-Coding         | rs9321547 | 6   | 136307525 | A/G                | 0.143/0.111      | 1.36 (1.18-1.56) 2.42E-05 0.99     |                                  | PDE7B      | Intron     |
| Protein-Coding         | rs1654726 | 8   | 108394551 | T/C                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1672157 | 8   | 108394572 | C/G                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1654727 | 8   | 108394639 | G/A                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1654728 | 8   | 108394663 | G/A                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1433180 | 8   | 108395312 | A/T                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1433181 | 8   | 108395511 | T/C                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1654730 | 8   | 108396003 | C/T                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1672148 | 8   | 108396035 | A/G                | 0.361/0.315      | 1.21 (1.1-1.33) 9.90E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1433183 | 8   | 108396573 | G/A                | 0.364/0.317      | 1.21 (1.1-1.34) 6.97E-05 0.997    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283707 | 8   | 108399631 | G/A                | 0.361/0.315      | 1.21 (1.1-1.33) 8.95E-05 0.998    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1315400 | 8   | 108399967 | A/G                | 0.361/0.315      | 1.21 (1.1-1.33) 8.66E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283705 | 8   | 108401111 | T/A                | 0.361/0.315      | 1.21 (1.1-1.33) 9.21E-05 0.999    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283669 | 8   | 108407422 | G/A                | 0.355/0.315      | 1.21 (1.1-1.34) 7.79E-05 0.998    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283665 | 8   | 108408926 | C/T                | 0.355/0.315      | 1.21 (1.1-1.34) 7.63E-05 1        |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283691 | 8   | 108414143 | T/C                | 0.355/0.309      | 1.22 (1.1-1.34) 6.90E-05 0.998    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283690 | 8   | 108414618 | T/C                | 0.355/0.309      | 1.21 (1.1-1.33) 9.33E-05 0.997    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283689 | 8   | 108415733 | A/G                | 0.355/0.309      | 1.22 (1.1-1.34) 6.90E-05 0.998    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283688 | 8   | 108416308 | C/T                | 0.355/0.309      | 1.22 (1.1-1.34) 6.90E-05 0.998    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs919823  | 8   | 108417005 | C/T                | 0.355/0.309      | 1.22 (1.1-1.34) 6.90E-05 0.998    |                                  | ANGPT1     | Intron     |
| Protein-Coding         | rs1283686 | 8   | 108417401 | C/T                | 0.354/0.309      | 1.21 (1.1-1.33) 9.70E-05 0.996    |                                  | ANGPT1     | Intron     |
| Distribution-based set | SNP     | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|---------|-----|----------|-------------------|-----------------|--------------------------------|---------------------------------|------------|
| Protein-Coding         | rs919822 | 8   | 108419763 | T/C               | 0.355/0.31      | 1.21 (1.1-1.33)    | 8.90E-05 0.997  | ANGPT1 | Intron |
| Protein-Coding         | rs72802160 | 10  | 23502417  | C/A               | 0.138/0.174     | 0.75 (0.66-0.85)   | 1.49E-05 0.985  | C10orf115 | Intergenic |
| Protein-Coding         | rs72802161 | 10  | 23505356  | C/A               | 0.138/0.174     | 0.75 (0.66-0.85)   | 1.41E-05 0.986  | C10orf115 | Intergenic |
| Protein-Coding         | rs17542850 | 10  | 23508781  | T/G               | 0.139/0.176     | 0.75 (0.66-0.85)   | 1.07E-05 0.99  | C10orf115 | Intergenic |
| Protein-Coding         | rs4258285 | 10  | 23515512  | T/C               | 0.141/0.177     | 0.75 (0.66-0.86)   | 1.40E-05 0.993  | C10orf115 | Intergenic |
| Protein-Coding         | rs139699574 | 10 | 23518452 | G/A               | 0.142/0.177     | 0.76 (0.67-0.86)   | 2.71E-05 0.995  | C10orf115 | Intergenic |
| Protein-Coding         | rs72802183 | 10  | 23564156  | G/A               | 0.139/0.174     | 0.76 (0.67-0.86)   | 2.93E-05 0.991  | C10orf67 | Intergenic |
| Protein-Coding         | rs72802184 | 10  | 23564964  | G/T               | 0.139/0.174     | 0.76 (0.67-0.87)   | 3.66E-05 0.992  | C10orf67 | Intergenic |
| Protein-Coding         | rs17543823 | 10  | 23569179  | G/C               | 0.14/0.174      | 0.76 (0.67-0.87)   | 4.05E-05 0.992  | C10orf67 | Intergenic |
| Protein-Coding         | rs72786797 | 10  | 23573564  | A/G               | 0.144/0.178     | 0.77 (0.68-0.87)   | 5.82E-05 0.988  | C10orf67 | Intergenic |
| Protein-Coding         | rs11597935 | 10  | 23589787  | A/C               | 0.147/0.181     | 0.77 (0.68-0.88)   | 6.86E-05 0.987  | C10orf67 | Intergenic |
| Protein-Coding         | rs72788411 | 10  | 23599728  | A/T               | 0.147/0.181     | 0.77 (0.68-0.87)   | 5.49E-05 0.986  | C10orf67 | Intergenic |
| Protein-Coding         | rs55695841 | 10  | 23606333  | C/T               | 0.146/0.181     | 0.77 (0.67-0.87)   | 4.68E-05 0.983  | C10orf67 | Intergenic |
| Protein-Coding         | rs117178402 | 10 | 23608378 | G/A               | 0.146/0.181     | 0.77 (0.67-0.87)   | 4.27E-05 0.983  | C10orf67 | Intergenic |
| Protein-Coding         | rs10828429 | 10  | 23615603  | T/C               | 0.246/0.287     | 0.8 (0.72-0.89)    | 5.96E-05 0.987  | C10orf67 | Introns |
| Protein-Coding         | rs11013394 | 10  | 23619601  | G/A               | 0.247/0.287     | 0.81 (0.73-0.89)   | 6.95E-05 0.989  | C10orf67 | Introns |
| Protein-Coding         | rs4259746 | 10  | 23622202  | G/A               | 0.248/0.289     | 0.8 (0.72-0.89)    | 4.95E-05 0.993  | C10orf67 | Introns |
| Protein-Coding         | rs3740360 | 10  | 96025491  | A/C               | 0.195/0.141     | 1.48 (1.31-1.68)   | 5.57E-10 1  | 1.48 (1.31-1.68) 6.50E-10 | PLCE1 | Introns |
| Protein-Coding         | rs17109875 | 10  | 96026575  | T/C               | 0.195/0.14      | 1.5 (1.32-1.69)    | 3.20E-10 0.993  | PLCE1 | Introns |
| Protein-Coding         | rs11187836 | 10  | 96032119  | C/T               | 0.132/0.096     | 1.43 (1.23-1.66)   | 2.33E-06 0.971  | PLCE1 | Introns |
| Protein-Coding         | rs11187837 | 10  | 96035980  | T/C               | 0.193/0.137     | 1.5 (1.33-1.71)    | 1.99E-10 0.996  | PLCE1 | Introns |
| Protein-Coding         | rs11187840 | 10  | 96050351  | A/G               | 0.198/0.143     | 1.49 (1.32-1.69)   | 3.34E-10 1  | PLCE1 | Introns |
| Protein-Coding         | rs753724 | 10  | 96051417  | G/T               | 0.199/0.143     | 1.49 (1.32-1.69)   | 2.42E-10 1  | 1.49 (1.32-1.69) 2.42E-10 | PLCE1 | Introns |
| Protein-Coding         | rs11187842 | 10  | 96052511  | C/T               | 0.199/0.143     | 1.49 (1.32-1.69)   | 2.62E-10 1  | 1.49 (1.32-1.69) 3.07E-10 | PLCE1 | Introns |
| Protein-Coding         | rs3781266 | 10  | 96052747  | A/G               | 0.199/0.143     | 1.49 (1.32-1.69)   | 2.62E-10 0.999  | PLCE1 | Introns |
| Protein-Coding         | rs3740365 | 10  | 96053239  | T/A               | 0.198/0.142     | 1.5 (1.32-1.7)     | 1.66E-10 0.999  | PLCE1 | Introns |
| Protein-Coding         | rs11220091 | 10 | 96053689  | C/T               | 0.198/0.141     | 1.5 (1.33-1.7)     | 1.61E-10 0.998  | PLCE1 | Introns |
Table S3. Continued.

| Distribution-based set | SNP         | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) \(^a\) \(^{b}\) | Info \(^{b}\) | Genotyped (45 SNPs) OR (95% CI) \(^{b}\) \(^{b}\) | Annotation \(^c\) |
|------------------------|-------------|-----|----------|-------------------|------------------|---------------------------------|----------|---------------------------------|----------------|
| Protein-Coding         | rs75017201  | 9   | 6055152  | C/T               | 0.198/0.141      | 1.5 (1.33-1.7) 1.61E-10 0.998 |         |                                 |               |
| Protein-Coding         | rs3765524   | 9   | 6058298  | C/T               | 0.267/0.206      | 1.4 (1.26-1.56) 1.62E-09 1   |         |                                 |               |
| Protein-Coding         | rs111987845 | 9   | 6060198  | C/A               | 0.198/0.141      | 1.5 (1.32-1.7) 1.83E-10 1   |         |                                 |               |
| Protein-Coding         | rs7897678   | 9   | 6060610  | C/G               | 0.268/0.206      | 1.41 (1.26-1.57) 1.09E-09 0.999 |         |                                 |               |
| Protein-Coding         | rs7914672   | 9   | 6060847  | T/A               | 0.252/0.195      | 1.39 (1.24-1.56) 1.20E-08 0.981 |         |                                 |               |
| Protein-Coding         | rs7807963   | 9   | 6060875  | A/G               | 0.268/0.206      | 1.41 (1.26-1.57) 1.09E-09 0.998 |         |                                 |               |
| Protein-Coding         | rs12217792  | 9   | 6062386  | T/C               | 0.199/0.141      | 1.51 (1.33-1.71) 9.31E-11 0.998 |         |                                 |               |
| Protein-Coding         | rs3871265   | 9   | 6063279  | T/A               | 0.268/0.206      | 1.41 (1.26-1.57) 1.11E-09 0.998 |         |                                 |               |
| Protein-Coding         | rs11187847  | 9   | 6063440  | C/G               | 0.199/0.141      | 1.51 (1.33-1.71) 9.31E-11 0.998 |         |                                 |               |
| Protein-Coding         | rs3818432   | 9   | 6064168  | C/A               | 0.253/0.192      | 1.42 (1.27-1.59) 8.77E-10 0.997 |         |                                 |               |
| Protein-Coding         | rs7099485   | 9   | 6065694  | T/C               | 0.269/0.208      | 1.4 (1.26-1.57) 1.44E-09 1   |         |                                 |               |
| Protein-Coding         | rs2274223   | 9   | 6066341  | A/G               | 0.269/0.208      | 1.4 (1.26-1.57) 1.44E-09 1   |         |                                 |               |
| Protein-Coding         | rs10509670  | 9   | 6067947  | A/G               | 0.269/0.208      | 1.4 (1.26-1.56) 1.53E-09 0.999 |         |                                 |               |
| Protein-Coding         | rs11187850  | 9   | 6068480  | A/G               | 0.253/0.193      | 1.42 (1.27-1.59) 1.09E-09 0.997 |         |                                 |               |
| Protein-Coding         | rs10509671  | 9   | 6069054  | T/G               | 0.207/0.148      | 1.52 (1.34-1.72) 2.58E-11 0.999 |         |                                 |               |
| Protein-Coding         | rs7096883   | 9   | 6069149  | G/A               | 0.199/0.142      | 1.5 (1.33-1.7) 1.22E-10 0.999 |         |                                 |               |
| Protein-Coding         | rs7096678   | 9   | 6069208  | C/T               | 0.207/0.148      | 1.52 (1.34-1.72) 2.58E-11 0.999 |         |                                 |               |
| Protein-Coding         | rs6583934   | 9   | 6069405  | T/G               | 0.268/0.208      | 1.4 (1.26-1.56) 1.60E-09 0.999 |         |                                 |               |
| Protein-Coding         | rs7100626   | 9   | 6069674  | C/A               | 0.199/0.142      | 1.5 (1.33-1.7) 1.22E-10 0.999 |         |                                 |               |
| Protein-Coding         | rs11187851  | 9   | 6069875  | G/A               | 0.207/0.148      | 1.51 (1.34-1.71) 3.24E-11 1   |         |                                 |               |
| Protein-Coding         | rs11187852  | 9   | 6070132  | G/A               | 0.199/0.142      | 1.5 (1.33-1.7) 1.54E-10 0.999 |         |                                 |               |
| Protein-Coding         | rs3781264   | 9   | 6070375  | A/G               | 0.208/0.148      | 1.51 (1.34-1.71) 3.36E-11 1   |         |                                 |               |
| Protein-Coding         | rs752140    | 9   | 6071396  | C/T               | 0.199/0.142      | 1.5 (1.33-1.7) 1.54E-10 0.999 |         |                                 |               |
| Protein-Coding         | rs11187853  | 9   | 6072228  | G/A               | 0.268/0.208      | 1.4 (1.25-1.56) 2.35E-09 0.998 |         |                                 |               |
| Protein-Coding         | rs75409190  | 9   | 6072425  | C/T               | 0.198/0.142      | 1.49 (1.32-1.69) 2.84E-10 0.998 |         |                                 |               |
| Protein-Coding         | rs6583935   | 9   | 6073325  | C/T               | 0.267/0.208      | 1.39 (1.25-1.56) 3.47E-09 0.997 |         |                                 |               |
| Protein-Coding         | rs10882422  | 9   | 6073563  | T/C               | 0.267/0.208      | 1.39 (1.25-1.55) 3.78E-09 0.996 |         |                                 |               |

\(\text{OR}\) (95% CI) \(^{b}\) is the crude odds ratio (95% confidence interval), \(\text{P}\) is the significance level, and \(\text{Info}\) is the information content of the SNP. PLCE1|Intron indicates intronic variants in the PLCE1 gene. Missense indicates missense mutations.
Table S3. Continued.

| Distribution-based set | SNP       | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation  |
|------------------------|-----------|-----|----------|--------------------|------------------|----------------------------------|---------------------------------|-------------|
| Protein-Coding         | rs7903902 | 10  | 96074157 | T/C                | 0.267/0.208      | 1.39 (1.25-1.56) 3.47E-09 0.996 | PLCE1|Intron |
| Protein-Coding         | rs7908638 | 10  | 96075433 | T/C                | 0.267/0.207      | 1.4 (1.25-1.56) 3.02E-09 0.996 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs11187856| 10  | 96076869 | G/A                | 0.202/0.144      | 1.5 (1.32-1.7) 1.73E-10 0.984 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs7094783 | 10  | 96081137 | C/T                | 0.248/0.198      | 1.34 (1.2-1.51) 4.90E-07 0.971 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs11187863| 10  | 96081457 | T/G                | 0.212/0.156      | 1.45 (1.29-1.64) 1.70E-09 0.98 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs11187864| 10  | 96082506 | C/T                | 0.206/0.151      | 1.46 (1.29-1.65) 1.97E-09 0.972 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs6583937 | 10  | 96083452 | A/G                | 0.282/0.223      | 1.37 (1.23-1.53) 1.11E-08 0.984 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs12781451| 10  | 96083920 | G/A                | 0.211/0.162      | 1.47 (1.31-1.66) 3.05E-10 0.981 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs11187866| 10  | 96085991 | C/G                | 0.212/0.156      | 1.45 (1.29-1.64) 1.85E-09 0.98 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs10882424| 10  | 96086078 | T/G                | 0.282/0.223      | 1.38 (1.23-1.53) 1.01E-08 0.984 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs11187869| 10  | 96087497 | C/T                | 0.21/0.154       | 1.46 (1.29-1.65) 9.84E-10 0.994 | NOC3L|PLCE1|Intron |
| Protein-Coding         | rs11187870| 10  | 96087866 | G/C                | 0.201/0.149      | 1.44 (1.28-1.63) 4.78E-09 0.994 | NOC3L|PLCE1|utr3   |
| Protein-Coding         | rs7074125 | 10  | 96089393 | A/G                | 0.283/0.223      | 1.38 (1.23-1.54) 8.96E-09 0.982 | NOC3L|PLCE1|Intergenic |
| Protein-Coding         | rs7096037 | 10  | 96089707 | T/A                | 0.27/0.214       | 1.36 (1.22-1.52) 3.92E-08 0.995 | NOC3L|PLCE1|Intergenic |
| Protein-Coding         | rs11187876| 10  | 96090139 | C/T                | 0.27/0.214       | 1.36 (1.22-1.52) 3.92E-08 0.995 | NOC3L|PLCE1|Intergenic |
| Protein-Coding         | rs10882430| 10  | 96090672 | A/G                | 0.27/0.214       | 1.36 (1.22-1.52) 3.69E-08 0.994 | NOC3L|PLCE1|Intergenic |
| Protein-Coding         | rs11187877| 10  | 96092121 | G/A                | 0.201/0.149      | 1.44 (1.28-1.63) 4.78E-09 0.993 | NOC3L|PLCE1|Intergenic |
| Protein-Coding         | rs11558740| 10  | 96093375 | C/T                | 0.21/0.154       | 1.46 (1.29-1.65) 9.84E-10 0.994 | NOC3L|utr3    |
| Protein-Coding         | rs11187881| 10  | 96095454 | A/G                | 0.27/0.214       | 1.36 (1.22-1.52) 3.30E-08 0.994 | NOC3L|Intron |
| Protein-Coding         | rs11187882| 10  | 96095861 | A/C                | 0.204/0.152      | 1.43 (1.26-1.61) 1.47E-08 0.977 | NOC3L|Intron |
| Protein-Coding         | rs11187883| 10  | 96096866 | T/C                | 0.201/0.149      | 1.44 (1.28-1.63) 5.02E-09 0.993 | NOC3L|Intron |
| Protein-Coding         | rs11187890| 10  | 96102758 | T/C                | 0.201/0.148      | 1.45 (1.28-1.64) 4.40E-09 0.99 | NOC3L|Intron |
| Protein-Coding         | rs11187893| 10  | 96105979 | C/G                | 0.209/0.153      | 1.46 (1.3-1.65) 9.31E-10 0.991 | NOC3L|Intron |
| Protein-Coding         | rs11187894| 10  | 96106025 | C/T                | 0.209/0.153      | 1.46 (1.3-1.65) 9.31E-10 0.991 | NOC3L|Intron |
| Protein-Coding         | rs4751153 | 10  | 131741604| A/G                | 0.406/0.361      | 1.21 (1.1-1.33) 8.16E-05 1 | 1.21 (1.1-1.33) 7.72E-05 | EBF3|Intron |
| Protein-Coding         | rs12594394| 15  | 33164777 | G/A                | 0.382/0.335      | 1.22 (1.1-1.34) 8.32E-05 1 | 1.22 (1.1-1.34) 8.14E-05 | FMN1|Intron |
| Protein-Coding         | rs4780055 | 15  | 33168360 | C/T                | 0.384/0.337      | 1.22 (1.1-1.34) 9.60E-05 0.984 | FMN1|Intron |
| Distribution-based set | SNP       | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | p* | Info* | Genotyped (45 SNPs) OR (95% CI) b | p b | Annotation |
|-------------------------|-----------|-----|----------|--------------------|-----------------|----------------------------------|----|-------|----------------------------------|-----|------------|
| Protein-Coding          | rs8026174 | 15  | 33169205 | G/A                | 0.383/0.336     | 1.22 (1.1-1.34)                  | 9.97E-05 | 0.986 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs481087  | 15  | 33172305 | T/C                | 0.383/0.337     | 1.22 (1.1-1.34)                  | 8.28E-05 | 0.997 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs579064  | 15  | 33172531 | A/G                | 0.382/0.336     | 1.21 (1.1-1.34)                  | 9.72E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs567682  | 15  | 33172627 | C/T                | 0.382/0.336     | 1.21 (1.1-1.34)                  | 9.72E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs580115  | 15  | 33172708 | G/A                | 0.382/0.336     | 1.22 (1.1-1.34)                  | 6.41E-05 | 1    | 1.21 (1.1-1.34)                  | 9.05E-05 | FMN1|Intron    |
| Protein-Coding          | rs494584  | 15  | 33173053 | C/T                | 0.382/0.336     | 1.21 (1.1-1.34)                  | 9.72E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs62001320| 15  | 33173474 | T/C                | 0.381/0.335     | 1.21 (1.1-1.34)                  | 8.93E-05 | 0.998 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs62001321| 15  | 33173482 | A/G                | 0.381/0.335     | 1.21 (1.1-1.34)                  | 8.93E-05 | 0.998 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs538535  | 15  | 33173484 | G/T                | 0.381/0.335     | 1.21 (1.1-1.34)                  | 8.93E-05 | 0.998 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs536612  | 15  | 33173707 | T/A                | 0.382/0.336     | 1.21 (1.1-1.34)                  | 9.72E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs536558  | 15  | 33173725 | T/C                | 0.382/0.336     | 1.21 (1.1-1.34)                  | 9.72E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs512644  | 15  | 33174071 | A/G                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.16E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs512752  | 15  | 33174110 | A/G                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.16E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs8030196 | 15  | 33174470 | C/T                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.91E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs8030367 | 15  | 33174548 | C/T                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.91E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs8031188 | 15  | 33174668 | A/G                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.91E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs8030557 | 15  | 33174686 | C/T                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.91E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs3110560 | 15  | 33174947 | C/T                | 0.381/0.334     | 1.22 (1.1-1.34)                  | 6.99E-05 | 0.998 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs481430  | 15  | 33175141 | C/T                | 0.38/0.334      | 1.22 (1.1-1.34)                  | 8.92E-05 | 0.997 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs477827  | 15  | 33175483 | C/T                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.91E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs692950  | 15  | 33175757 | C/T                | 0.382/0.335     | 1.22 (1.1-1.35)                  | 5.88E-05 | 0.997 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs12050715| 15  | 33176075 | G/A                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.91E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs347946  | 15  | 33176379 | G/C                | 0.381/0.335     | 1.22 (1.1-1.34)                  | 7.16E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs347941  | 15  | 33177426 | C/A                | 0.379/0.333     | 1.21 (1.1-1.34)                  | 8.95E-05 | 0.999 |                                    |     | FMN1|Intron    |
| Protein-Coding          | rs8106216 | 19  | 52294472 | G/A                | 0.045/0.067     | 0.65 (0.53-0.81)                | 8.23E-05 | 0.9 |                                    |     | FPR1|Intergenic|
| Protein-Coding          | rs3331    | 20  | 47988601 | T/C                | 0.085/0.061     | 1.44 (1.21-1.73)                | 5.91E-05 | 0.982 |                                    |     | KCNB1|utr3      |
| Protein-Coding          | rs6019774 | 20  | 47992178 | T/C                | 0.085/0.061     | 1.44 (1.2-1.72)                 | 7.00E-05 | 0.981 |                                    |     | KCNB1|Intron    |
| Distribution-based set | SNP               | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation       |
|------------------------|-------------------|-----|----------|-------------------|-----------------|----------------------------------|-------------------------------|------------------|
| Protein-Coding         | rs111355930       | 20  | 47993282 | T/C               | 0.086/0.061     | 1.45 (1.21-1.74) 4.45E-05 0.979 |                               | KCNB1|Intron           |
| Protein-Coding         | rs55678110        | 20  | 48004972 | G/A               | 0.083/0.059     | 1.45 (1.21-1.74) 6.52E-05 0.959 |                               | KCNB1|Intron           |
| Protein-Coding         | rs75260488        | 20  | 48005226 | T/C               | 0.084/0.06      | 1.44 (1.2-1.73) 8.57E-05 0.952 |                               | KCNB1|Intron           |
| The combination        | rs4971066         | 1   | 155105882| G/T               | 0.121/0.157     | 0.73 (0.63-0.83) 6.48E-06 0.955 |                               | EFNA1|Intron           |
| The combination        | rs4390169         | 1   | 155106054| A/G               | 0.101/0.136     | 0.7 (0.6-0.81) 2.07E-06 0.998 |                               | EFNA1|Intron           |
| The combination        | rs4745            | 1   | 155106227| A/T               | 0.101/0.136     | 0.7 (0.6-0.81) 2.07E-06 0.998 |                               | EFNA1|missense         |
| The combination        | rs9297            | 1   | 155106550| G/A               | 0.104/0.137     | 0.72 (0.62-0.83) 6.72E-06 1     | 0.72 (0.62-0.83) 6.72E-06 1     | EFNA1|utr3             |
| The combination        | rs12904           | 1   | 155106697| A/G               | 0.104/0.137     | 0.72 (0.62-0.83) 6.46E-06 0.999 |                               | EFNA1|utr3             |
| The combination        | rs11264333        | 1   | 155108287| A/G               | 0.104/0.138     | 0.71 (0.62-0.83) 6.17E-06 0.999 |                               | SLC50A1|Intergenic       |
| The combination        | rs4421576         | 1   | 155142210| G/A               | 0.102/0.137     | 0.7 (0.61-0.81) 2.20E-06 0.997 |                               | KRTCAP2|RP11-201K10.3|Intron |
| The combination        | rs4276914         | 1   | 155142229| A/G               | 0.102/0.137     | 0.7 (0.61-0.81) 2.20E-06 0.998 |                               | KRTCAP2|RP11-201K10.3|Intron |
| The combination        | rs4971088         | 1   | 155142883| A/G               | 0.102/0.137     | 0.7 (0.61-0.81) 2.41E-06 0.997 |                               | KRTCAP2|RP11-201K10.3|Intron |
| The combination        | rs4971089         | 1   | 155142927| G/A               | 0.105/0.141     | 0.7 (0.6-0.81) 2.29E-06 0.966 |                               | KRTCAP2|RP11-201K10.3|Intron |
| The combination        | rs4971093         | 1   | 155144300| A/G               | 0.118/0.151     | 0.74 (0.64-0.85) 1.75E-05 0.99 |                               | KRTCAP2|RP11-201K10.3|Intron |
| The combination        | rs4971059         | 1   | 155148781| A/G               | 0.121/0.154     | 0.74 (0.64-0.85) 1.53E-05 0.995 |                               | RP1-201K10.3|TRIM46|Intron           |
| The combination        | rs3814316         | 1   | 155149718| A/G               | 0.122/0.157     | 0.73 (0.64-0.84) 9.18E-06 1     | 0.73 (0.64-0.84) 7.54E-06 1     | RP1-201K10.3|TRIM46|silent           |
| The combination        | rs9426886         | 1   | 155151754| T/A               | 0.125/0.164     | 0.72 (0.63-0.82) 2.12E-06 0.972 |                               | RP1-201K10.3|TRIM46|Intron           |
| The combination        | rs76871214        | 1   | 155152205| C/T               | 0.037/0.061     | 0.58 (0.46-0.73) 2.32E-06 0.95 |                               | RP1-201K10.3|TRIM46|silent           |
| The combination        | rs4971100         | 1   | 155155731| A/G               | 0.134/0.17      | 0.75 (0.66-0.86) 1.92E-05 1     | 0.75 (0.66-0.86) 1.92E-05 1     | RP1-201K10.3|TRIM46|Intron           |
| The combination        | rs4072037         | 1   | 155162067| T/C               | 0.116/0.153     | 0.72 (0.62-0.82) 2.43E-06 1     | 0.72 (0.62-0.82) 2.23E-06 1     | MUC1|silent           |
| The combination        | rs2974937         | 1   | 155168849| T/C               | 0.115/0.153     | 0.72 (0.63-0.82) 2.71E-06 0.998 |                               | RP1-263K19.4|THBS3|Intron           |
| The combination        | rs423144         | 1   | 155169355| T/G               | 0.135/0.17      | 0.75 (0.66-0.86) 2.75E-05 0.974 |                               | RP1-263K19.4|THBS3|Intron           |
| The combination        | rs2066981         | 1   | 155172379| A/G               | 0.111/0.146     | 0.73 (0.63-0.84) 1.12E-05 0.983 |                               | RP1-263K19.4|THBS3|Intron           |
| The combination        | rs2075571         | 1   | 155174106| T/C               | 0.13/0.163      | 0.76 (0.67-0.87) 6.26E-05 0.987 |                               | RP1-263K19.4|THBS3|Intron           |
| The combination        | rs370545         | 1   | 155175390| G/A               | 0.111/0.146     | 0.73 (0.63-0.84) 1.17E-05 0.982 |                               | THBS3|Intron           |
| The combination        | rs914615         | 1   | 155175892| G/A               | 0.111/0.146     | 0.73 (0.63-0.84) 1.18E-05 0.982 |                               | THBS3|Intron           |
| The combination        | rs760077         | 1   | 155178782| T/A               | 0.1/0.135       | 0.71 (0.61-0.82) 7.08E-06 0.962 |                               | MTX1|THBS3|missense         |
| Distribution-based set | SNP | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation$^a$ |
|------------------------|-----|-----|----------|-------------------|-----------------|-------------------------------|-------------------------------|------------------|
| The combination         | rs2974395 | 1   | 155181843 | T/G               | 0.116/0.153     | 0.72 (0.63-0.83) 3.41E-06 | 0.996 | MTX1|RP11-263K19.6|Intron |
| The combination         | rs2075570 | 1   | 155182164 | T/C               | 0.116/0.154     | 0.72 (0.63-0.83) 2.87E-06 | 0.988 | MTX1|RP11-263K19.6|Intron |
| The combination         | rs11264349 | 1   | 155248113 | T/A               | 0.18/0.218       | 0.79 (0.7-0.88) 6.73E-05 | 0.972 | CLK2|HCN3|Intron |
| The combination         | rs138597847 | 1   | 155583628 | A/C               | 0.035/0.058     | 0.59 (0.47-0.74) 7.13E-06 | 0.941 | MSTO1|MSTO2P|Intron |
| The combination         | rs148001269 | 1   | 155694169 | A/G               | 0.028/0.048     | 0.57 (0.44-0.74) 1.90E-05 | 0.891 | DAP3|MSTO1|MSTO2P|Intron |
| The combination         | rs140449886 | 1   | 155734699 | T/C               | 0.016/0.034     | 0.48 (0.35-0.66) 9.28E-06 | 0.861 | GON4L|missense |
| The combination         | rs3737518 | 1   | 158597879 | G/C               | 0.059/0.038     | 1.63 (1.3-2.04) 2.11E-05 | 0.898 | SPTA1|Intron |
| The combination         | rs10432448 | 2   | 218213129 | C/T               | 0.214/0.178     | 1.27 (1.13-1.43) 9.56E-05 | 0.965 | DIRC3|Intron |
| The combination         | rs149428385 | 3   | 32031928  | C/A               | 0.032/0.017     | 1.88 (1.38-2.56) 6.29E-05 | 0.877 | OSBP10|ZNF860|missense |
| The combination         | rs12487923 | 3   | 55002066  | C/A               | 0.481/0.437     | 1.2 (1.1-1.32) 9.97E-05 | 1    | 1.2 (1.1-1.32) | 8.83E-05 | CACNA2D3|Intron |
| The combination         | rs61231973 | 5   | 168507939 | A/G               | 0.159/0.193     | 0.78 (0.69-0.88) 7.98E-05 | 0.976 | SLT3|Intron |
| The combination         | rs6917867 | 6   | 162237187 | G/A               | 0.202/0.161     | 1.31 (1.16-1.48) 1.83E-05 | 0.957 | PARK2|Intron |
| The combination         | rs836471  | 7   | 6435112  | A/G               | 0.366/0.322     | 1.22 (1.11-1.35) 7.29E-05 | 0.98  | RAC1|Intron |
| The combination         | rs836506  | 7   | 6455246  | A/G               | 0.265/0.223     | 1.26 (1.13-1.4) 4.00E-05 | 0.974 | DAGLB|Intron |
| The combination         | rs836545  | 7   | 6479410  | C/T               | 0.242/0.201     | 1.27 (1.13-1.42) 3.59E-05 | 0.976 | DAGLB|Intron |
| The combination         | rs836546  | 7   | 6479668  | G/A               | 0.241/0.199     | 1.28 (1.14-1.43) 2.18E-05 | 0.963 | DAGLB|Intron |
| The combination         | rs1802074 | 7   | 37947103 | C/T               | 0.239/0.2       | 1.25 (1.12-1.4) 6.61E-05 | 0.997 | EMDR1|SFRP4|missense |
| The combination         | rs12539011 | 7   | 141295058 | T/C               | 0.337/0.38      | 0.82 (0.74-0.9) 4.78E-05 | 1    | 0.82 (0.74-0.9) | 4.78E-05 | AGK|Intron |
| The combination         | rs55845077 | 8   | 75740061 | T/C               | 0.008/0.02      | 0.41 (0.26-0.64) 7.71E-05 | 0.816 | PI15|RP11-758M4.4|Intron |
| The combination         | rs55819117 | 8   | 75740268 | G/T               | 0.009/0.021     | 0.41 (0.27-0.64) 7.61E-05 | 0.823 | PI15|RP11-758M4.4|Intron |
| The combination         | rs17358302 | 8   | 75741263 | T/C               | 0.009/0.021     | 0.42 (0.27-0.65) 9.00E-05 | 0.822 | PI15|RP11-758M4.4|Intron |
| The combination         | rs1368632 | 8   | 75744096 | C/G               | 0.009/0.021     | 0.41 (0.27-0.64) 7.61E-05 | 0.823 | PI15|RP11-758M4.4|Intron |
| The combination         | rs1368633 | 8   | 75744457 | G/A               | 0.009/0.021     | 0.41 (0.27-0.64) 7.61E-05 | 0.823 | PI15|RP11-758M4.4|Intron |
| The combination         | rs11787260 | 8   | 75747476 | C/T               | 0.008/0.02      | 0.41 (0.26-0.64) 7.71E-05 | 0.816 | PI15|RP11-758M4.4|Intron |
| The combination         | rs1433470 | 8   | 75749982 | G/T               | 0.009/0.021     | 0.41 (0.27-0.64) 7.61E-05 | 0.823 | PI15|RP11-758M4.4|Intron |
| The combination         | rs17292788 | 8   | 75753333 | A/G               | 0.009/0.021     | 0.41 (0.27-0.64) 7.51E-05 | 0.823 | PI15|RP11-758M4.4|Intron |
| The combination         | rs67680904 | 8   | 75756759 | A/G               | 0.009/0.021     | 0.41 (0.27-0.64) 7.51E-05 | 0.822 | PI15|RP11-758M4.4|Intron |
| Distribution-based set | SNP | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) a | Genotyped (45 SNPs) OR (95% CI) b | Annotation c |
|------------------------|-----|-----|----------|-------------------|-----------------|-------------------------------|-------------------------------|-------------|
| The combination         | rs17292864 | 8   | 75757841 | C/T               | 0.008/0.02      | 0.41 (0.26-0.64) 7.62E-05 | 0.815 | PI15 | RP11-758M4.4 | Intron |
| The combination         | rs1560782 | 8   | 75767053 | A/G               | 0.008/0.02      | 0.41 (0.26-0.64) 8.96E-05 | 0.81 | PI15 | RP11-758M4.4 | Utr3 |
| The combination         | rs7084339 | 10  | 96043732 | A/G               | 0.268/0.209     | 1.39 (1.24-1.55) 5.36E-09 | 0.997 | PLCE1 | PLCE1-AS1 | Intron |
| The combination         | rs12263737| 10  | 96044913 | G/A               | 0.268/0.209     | 1.39 (1.24-1.55) 4.23E-09 | 1    | PLCE1 | PLCE1-AS1 | Intron |
| The combination         | rs10882416| 10  | 96045054 | C/T               | 0.268/0.209     | 1.39 (1.24-1.55) 4.23E-09 | 1    | PLCE1 | PLCE1-AS1 | Intron |
| The combination         | rs12220125| 10  | 96074939 | T/G               | 0.251/0.192     | 1.41 (1.26-1.58) 2.24E-09 | 0.993 | PLCE1 | RP11-76P2.4 | Intron |
| The combination         | rs11187895| 10  | 96106240 | G/C               | 0.201/0.148     | 1.45 (1.28-1.64) 3.58E-09 | 0.99 | NOC3L | missense |
| The combination         | rs11187897| 10  | 96106603 | A/G               | 0.201/0.148     | 1.45 (1.28-1.64) 3.58E-09 | 0.99 | NOC3L | Intron |
| The combination         | rs10786161| 10  | 96107671 | C/T               | 0.269/0.214     | 1.36 (1.22-1.51) 4.72E-08 | 0.992 | NOC3L | Intron |
| The combination         | rs10882435| 10  | 96107867 | A/T               | 0.209/0.153     | 1.46 (1.3-1.65) 8.60E-10 | 0.99 | NOC3L | Intron |
| The combination         | rs11187899| 10  | 96108102 | G/C               | 0.209/0.153     | 1.46 (1.3-1.65) 8.60E-10 | 0.99 | NOC3L | Intron |
| The combination         | rs11187900| 10  | 96108364 | T/G               | 0.209/0.153     | 1.46 (1.3-1.65) 8.60E-10 | 0.99 | NOC3L | Intron |
| The combination         | rs10882436| 10  | 96108800 | T/C               | 0.209/0.153     | 1.47 (1.3-1.65) 7.72E-10 | 0.99 | NOC3L | Intron |
| The combination         | rs7084988 | 10  | 96108842 | G/A               | 0.269/0.214     | 1.36 (1.22-1.51) 4.38E-08 | 0.992 | NOC3L | Intron |
| The combination         | rs7085378 | 10  | 96109325 | C/A               | 0.269/0.213     | 1.36 (1.22-1.52) 3.70E-08 | 0.991 | NOC3L | Intron |
| The combination         | rs12217597| 11  | 96110812 | T/C               | 0.209/0.152     | 1.47 (1.3-1.66) 6.04E-10 | 0.99 | NOC3L | Intron |
| The combination         | rs77687332| 11  | 22721149 | G/A               | 0.032/0.049     | 0.61 (0.47-0.78) 6.95E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs74327419| 11  | 22721358 | G/A               | 0.032/0.049     | 0.61 (0.48-0.78) 8.39E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs75530469| 11  | 22722219 | A/G               | 0.032/0.049     | 0.61 (0.48-0.78) 8.39E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs77786740| 11  | 22722323 | C/T               | 0.032/0.049     | 0.61 (0.47-0.78) 6.95E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs78429568| 11  | 22722584 | G/C               | 0.032/0.049     | 0.61 (0.47-0.78) 7.11E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs78153532| 11  | 22722757 | A/G               | 0.032/0.049     | 0.61 (0.47-0.78) 6.95E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs78740805| 11  | 22722964 | T/C               | 0.032/0.049     | 0.61 (0.48-0.78) 8.39E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs12222431| 11  | 22723471 | G/A               | 0.032/0.049     | 0.61 (0.47-0.78) 7.11E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs58813021| 11  | 22725057 | A/G               | 0.032/0.049     | 0.61 (0.47-0.78) 7.11E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs76869006| 11  | 22725228 | G/A               | 0.032/0.049     | 0.61 (0.47-0.78) 6.95E-05 | 0.99 | GAS2  | Intron |
| The combination         | rs11026743| 11  | 22726002 | A/T               | 0.032/0.049     | 0.61 (0.47-0.78) 7.11E-05 | 0.99 | GAS2  | Intron |
| Distribution-based set | SNP      | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) | Genotyped (45 SNPs) | Annotation |
|------------------------|----------|-----|----------|--------------------|------------------|------------------------|---------------------|------------|
| The combination        | rs78824250 | 11  | 22727244 | C/A                | 0.032/0.049      | 0.61 (0.47-0.78) 6.99E-05 | 0.989              |
| The combination        | rs79105453 | 11  | 22728855 | T/C                | 0.031/0.049      | 0.61 (0.47-0.78) 8.42E-05 | 0.989              |
| The combination        | rs79204070 | 11  | 22728935 | C/G                | 0.031/0.049      | 0.61 (0.47-0.78) 8.42E-05 | 0.984              |
| The combination        | rs11026745 | 11  | 22729200 | G/T                | 0.371/0.413      | 0.83 (0.75-0.91) 9.08E-05 | 1                  |
| The combination        | rs3850997 | 16  | 12043512 | T/G                | 0.37/0.413       | 0.82 (0.75-0.91) 6.44E-05 | 0.998              |
| The combination        | rs35063476 | 16  | 12044301 | G/A                | 0.146/0.18       | 0.77 (0.68-0.87) 4.45E-05 | 0.989              |
| The combination        | rs62040821 | 16  | 12044555 | C/A                | 0.146/0.18       | 0.77 (0.68-0.87) 4.52E-05 | 0.989              |
| The combination        | rs17810367 | 16  | 12044947 | G/C                | 0.146/0.18       | 0.77 (0.68-0.87) 4.52E-05 | 0.989              |
| The combination        | rs76466426 | 16  | 12045069 | T/C                | 0.36/0.402       | 0.82 (0.75-0.91) 8.23E-05 | 1                  |
| The combination        | rs7185307 | 16  | 12046899 | T/C                | 0.36/0.402       | 0.82 (0.75-0.91) 8.23E-05 | 1                  |
| The combination        | rs62037663 | 16  | 12048960 | G/A                | 0.145/0.18       | 0.76 (0.67-0.87) 3.50E-05 | 0.989              |
| The combination        | rs62037665 | 16  | 12051223 | C/T                | 0.145/0.179      | 0.77 (0.67-0.87) 3.87E-05 | 0.988              |
| The combination        | rs12445244 | 16  | 12054073 | G/C                | 0.144/0.178      | 0.77 (0.67-0.87) 4.11E-05 | 0.988              |
| The combination        | rs11570136 | 16  | 12058832 | A/T                | 0.365/0.412      | 0.81 (0.74-0.89) 2.24E-05 | 0.985              |
| The combination        | rs3862446 | 16   | 12059736 | A/G                | 0.365/0.411      | 0.82 (0.74-0.9) 3.44E-05 | 0.984              |
| The combination        | rs11570151 | 16  | 12060579 | T/C                | 0.145/0.177      | 0.78 (0.69-0.88) 1.00E-04 | 1                  |
| The combination        | rs11570152 | 16  | 12060681 | A/T                | 0.143/0.177      | 0.77 (0.68-0.87) 4.87E-05 | 0.996              |
| The combination        | rs1126889 | 16   | 12061910 | G/C                | 0.362/0.41       | 0.81 (0.73-0.89) 1.71E-05 | 0.964              |
| The combination        | rs446289  | 16  | 12070486 | T/G                | 0.044/0.064      | 0.66 (0.53-0.81) 9.81E-05 | 0.959              |
| The combination        | rs3851005 | 16   | 12071213 | T/C                | 0.287/0.338      | 0.78 (0.7-0.86) 1.66E-06 | 0.967              |
| The combination        | rs12930612 | 16  | 12072203 | A/G                | 0.29/0.339       | 0.78 (0.71-0.87) 3.51E-06 | 0.971              |
| The combination        | rs16958789 | 16  | 12075648 | A/G                | 0.29/0.339       | 0.78 (0.71-0.87) 2.71E-06 | 0.994              |
| The combination        | rs16958792 | 16  | 12075684 | A/C                | 0.29/0.339       | 0.78 (0.71-0.87) 2.84E-06 | 0.994              |
| The combination        | rs8061496  | 16  | 12076752 | G/A                | 0.291/0.339      | 0.79 (0.71-0.87) 4.16E-06 | 0.997              |
| The combination        | rs8043644  | 16  | 12077124 | T/G                | 0.291/0.339      | 0.79 (0.71-0.87) 4.16E-06 | 0.998              |
| The combination        | rs12922317 | 16  | 12077632 | G/A                | 0.291/0.339      | 0.79 (0.71-0.87) 2.76E-06 | 1                  |
| The combination        | rs11859104 | 16  | 12082052 | A/G                | 0.301/0.347      | 0.8 (0.72-0.88) 1.70E-05 | 0.97               |
| Distribution-based set | SNP           | Chr | Position  | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|--------------|-----|-----------|-------------------|------------------|------------------------------------|-------------------------------|------------|
| The combination        | rs7206479    | 16  | 12082139  | T/C               | 0.28/0.328       | 0.78 (0.71-0.87) 3.85E-06 0.986 |                               | SNX29 Intronic                  |
| The combination        | rs76445606   | 18  | 56239523  | G/A               | 0.115/0.088      | 1.36 (1.17-1.6) 9.73E-05 0.984 |                               | ALPK2 Intronic                  |
| The combination        | rs56003111   | 21  | 42792768  | C/T               | 0.183/0.147      | 1.3 (1.14-1.47) 6.98E-05 0.967 |                               | MX1 Intronic                    |
| The combination        | rs17000900   | 21  | 42798030  | C/A               | 0.185/0.15       | 1.29 (1.14-1.46) 8.22E-05 0.969 |                               | MX1 utr5                         |
| The combination        | rs5993508    | 22  | 19065430  | G/C               | 0.383/0.338      | 1.21 (1.1-1.33) 9.78E-05 0.999 |                               | DGCR2 Intronic                  |
| Intergenic regions     | rs1413953    | 1   | 71122504  | G/T               | 0.279/0.321      | 0.81 (0.73-0.9) 8.11E-05 0.977 |                               | Intergenic                       |
| Intergenic regions     | rs56859272   | 1   | 106692109 | C/A               | 0.049/0.031      | 1.62 (1.28-2.06) 6.89E-05 0.97 |                               | Intergenic                       |
| Intergenic regions     | rs1839558    | 1   | 106693366 | T/C               | 0.075/0.053      | 1.48 (1.23-1.8) 5.04E-05 0.965 |                               | Intergenic                       |
| Intergenic regions     | rs1450819    | 1   | 106694106 | C/G               | 0.076/0.054      | 1.46 (1.21-1.77) 8.59E-05 0.969 |                               | Intergenic                       |
| Intergenic regions     | rs12026453   | 1   | 106695375 | A/G               | 0.076/0.054      | 1.46 (1.21-1.77) 8.11E-05 0.977 |                               | Intergenic                       |
| Intergenic regions     | rs4378237    | 1   | 106696041 | A/G               | 0.076/0.054      | 1.46 (1.21-1.77) 8.60E-05 0.981 |                               | Intergenic                       |
| Intergenic regions     | rs11184773   | 1   | 106696126 | G/A               | 0.076/0.054      | 1.46 (1.21-1.77) 8.94E-05 0.981 |                               | Intergenic                       |
| Intergenic regions     | rs11802449   | 1   | 106697305 | A/G               | 0.076/0.054      | 1.46 (1.21-1.77) 8.94E-05 0.981 |                               | Intergenic                       |
| Intergenic regions     | rs1450817    | 1   | 106698071 | G/A               | 0.076/0.054      | 1.46 (1.21-1.77) 8.60E-05 0.981 |                               | Intergenic                       |
| Intergenic regions     | rs1450816    | 1   | 106698157 | A/G               | 0.075/0.054      | 1.46 (1.21-1.77) 9.68E-05 0.977 |                               | Intergenic                       |
| Intergenic regions     | rs12404111   | 1   | 106698237 | A/G               | 0.076/0.054      | 1.46 (1.21-1.77) 8.60E-05 0.981 |                               | Intergenic                       |
| Intergenic regions     | rs6696744    | 1   | 106698266 | T/G               | 0.076/0.054      | 1.47 (1.22-1.78) 6.90E-05 0.979 |                               | Intergenic                       |
| Intergenic regions     | rs17431569   | 1   | 106698439 | T/A               | 0.076/0.054      | 1.46 (1.21-1.77) 8.68E-05 0.981 |                               | Intergenic                       |
| Intergenic regions     | rs11184788   | 1   | 106727097 | G/A               | 0.064/0.044      | 1.5 (1.23-1.85) 9.81E-05 0.992 |                               | Intergenic                       |
| Intergenic regions     | rs4971073    | 1   | 155113104 | T/G               | 0.115/0.15       | 0.72 (0.63-0.83) 7.23E-06 0.98 |                               | Intergenic                       |
| Intergenic regions     | rs4246529    | 1   | 155115260 | C/T               | 0.104/0.138      | 0.71 (0.62-0.83) 5.76E-06 1 0.71 (0.62-0.83) 5.60E-06 | Intergenic                       |
| Intergenic regions     | rs10157801   | 1   | 155120012 | G/A               | 0.101/0.137      | 0.7 (0.6-0.81) 1.78E-06 0.986 |                               | Intergenic                       |
| Intergenic regions     | rs1179962    | 1   | 155121727 | C/T               | 0.102/0.137      | 0.7 (0.6-0.81) 2.18E-06 0.983 |                               | Intergenic                       |
| Intergenic regions     | rs7364524    | 1   | 155121922 | G/A               | 0.102/0.137      | 0.7 (0.6-0.81) 2.18E-06 0.983 |                               | Intergenic                       |
| Intergenic regions     | rs6676150    | 1   | 155123837 | G/C               | 0.082/0.114      | 0.68 (0.58-0.8) 5.36E-06 0.947 |                               | Intergenic                       |
| Intergenic regions     | rs4971076    | 1   | 155124772 | A/C               | 0.102/0.137      | 0.7 (0.6-0.81) 1.95E-06 0.982 |                               | Intergenic                       |
| Intergenic regions     | rs4971052    | 1   | 155126018 | T/C               | 0.102/0.137      | 0.7 (0.6-0.81) 1.95E-06 0.982 |                               | Intergenic                       |
### Table S3. Continued.

| Distribution-based set | SNP     | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|---------|-----|----------|--------------------|------------------|----------------------------------|--------------------------------|------------|
| Intergenic regions     | rs11264335 | 1   | 155126698 | G/A                | 0.102/0.137      | 0.7 (0.6-0.81)                  | 2.31E-06 0.978                  | Intergenic |
| Intergenic regions     | rs10908458 | 1   | 155126948 | C/T                | 0.102/0.137      | 0.7 (0.6-0.81)                  | 1.61E-06 0.982                  | Intergenic |
| Intergenic regions     | rs7535292  | 1   | 155127749 | C/T                | 0.099/0.135      | 0.69 (0.59-0.8)                 | 8.82E-07 0.986                  | Intergenic |
| Intergenic regions     | rs4971077  | 1   | 155128717 | C/T                | 0.099/0.135      | 0.69 (0.59-0.8)                 | 8.15E-07 0.987                  | Intergenic |
| Intergenic regions     | rs4971078  | 1   | 155129023 | G/A                | 0.102/0.138      | 0.69 (0.6-0.81)                 | 1.37E-06 0.983                  | Intergenic |
| Intergenic regions     | rs12112803 | 1   | 155129562 | A/G                | 0.103/0.14       | 0.69 (0.6-0.8)                  | 1.31E-06 0.955                  | Intergenic |
| Intergenic regions     | rs4971079  | 1   | 155130391 | A/G                | 0.098/0.136      | 0.68 (0.58-0.79)                | 4.22E-07 0.984                  | Intergenic |
| Intergenic regions     | rs4276913  | 1   | 155131673 | G/A                | 0.101/0.138      | 0.69 (0.6-0.8)                  | 1.11E-06 0.985                  | Intergenic |
| Intergenic regions     | rs12028043 | 1   | 155132836 | G/A                | 0.102/0.138      | 0.69 (0.6-0.8)                  | 1.03E-06 0.986                  | Intergenic |
| Intergenic regions     | rs12127609 | 1   | 155133491 | C/G                | 0.102/0.138      | 0.69 (0.6-0.8)                  | 9.10E-07 0.986                  | Intergenic |
| Intergenic regions     | rs4460629  | 1   | 155135335 | C/T                | 0.102/0.139      | 0.69 (0.6-0.8)                  | 8.21E-07 0.966                  | Intergenic |
| Intergenic regions     | rs12752585 | 1   | 155135406 | A/G                | 0.102/0.138      | 0.7 (0.6-0.81)                  | 1.51E-06 0.999                  | Intergenic |
| Intergenic regions     | rs4971085  | 1   | 155138222 | C/T                | 0.102/0.138      | 0.7 (0.6-0.81)                  | 1.51E-06 0.998                  | Intergenic |
| Intergenic regions     | rs11264337 | 1   | 155138450 | T/C                | 0.102/0.138      | 0.7 (0.6-0.81)                  | 1.51E-06 0.998                  | Intergenic |
| Intergenic regions     | rs11264338 | 1   | 155138557 | G/A                | 0.103/0.138      | 0.7 (0.6-0.81)                  | 1.84E-06 0.998                  | Intergenic |
| Intergenic regions     | rs7556304  | 1   | 155139509 | C/T                | 0.102/0.138      | 0.7 (0.6-0.81)                  | 1.51E-06 0.998                  | Intergenic |
| Intergenic regions     | rs11264339 | 1   | 155140648 | T/C                | 0.102/0.137      | 0.7 (0.61-0.81)                | 2.20E-06 0.998                  | Intergenic |
| Intergenic regions     | rs12411216 | 1   | 155164480 | C/A                | 0.116/0.154      | 0.72 (0.62-0.82)                | 2.16E-06 0.998                  | Intergenic |
| Intergenic regions     | rs2974929  | 1   | 155197268 | C/T                | 0.097/0.129      | 0.73 (0.63-0.85)               | 3.95E-05 0.961                  | non_conding_exon |
| Intergenic regions     | rs2900245  | 1   | 155197462 | T/C                | 0.116/0.154      | 0.72 (0.63-0.82)                | 2.45E-06 1                      | Intergenic |
| Intergenic regions     | rs117599624| 1    | 158417255 | C/A                | 0.052/0.032      | 1.74 (1.37-2.22)              | 6.49E-06 0.914                  | Intergenic |
| Intergenic regions     | rs117705534| 1    | 158524741 | C/T                | 0.054/0.034      | 1.66 (1.32-2.09)              | 1.66E-05 0.964                  | Intergenic |
| Intergenic regions     | rs142666726| 1    | 158560079 | C/A                | 0.036/0.02       | 1.85 (1.38-2.48)              | 3.68E-05 0.897                  | Intergenic |
| Intergenic regions     | rs537734   | 1    | 218296301 | T/C                | 0.141/0.173      | 0.76 (0.67-0.87)              | 6.72E-05 0.962                  | Intergenic |
| Intergenic regions     | rs493046   | 1    | 218303651 | C/T                | 0.153/0.187      | 0.78 (0.69-0.88)              | 9.24E-05 0.984                  | Intergenic |
| Intergenic regions     | rs482636   | 1    | 218303703 | G/T                | 0.157/0.192      | 0.77 (0.68-0.88)              | 5.99E-05 0.951                  | Intergenic |
| Intergenic regions     | rs575962   | 1    | 218304346 | T/G                | 0.153/0.186      | 0.78 (0.69-0.88)              | 9.47E-05 0.996                  | Intergenic |
| Distribution-based set | SNP     | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | P* | Info* | Genotyped (45 SNPs) OR (95% CI) | P* | Annotation |
|-------------------------|---------|-----|----------|-------------------|-----------------|----------------------------------|----|-------|---------------------------------|----|------------|
| Intergenic regions      | rs12475966 | 2   | 43342749 | G/C               | 0.247/0.209     | 1.26 (1.13-1.41)                | 3.68E-05 | 0.971 |                                |    |            |
| Intergenic regions      | rs12475994 | 2   | 43342772 | G/A               | 0.247/0.209     | 1.26 (1.13-1.41)                | 4.82E-05 | 0.971 |                                |    |            |
| Intergenic regions      | rs12475946 | 2   | 43342848 | C/T               | 0.248/0.209     | 1.27 (1.13-1.42)                | 3.32E-05 | 0.972 |                                |    | Intergenic |
| Intergenic regions      | rs62135362 | 2   | 43342942 | A/G               | 0.248/0.208     | 1.27 (1.14-1.42)                | 2.43E-05 | 0.971 |                                |    | Intergenic |
| Intergenic regions      | rs62135363 | 2   | 43343185 | A/C               | 0.249/0.21      | 1.27 (1.14-1.42)                | 2.58E-05 | 0.973 |                                |    | Intergenic |
| Intergenic regions      | rs80168958 | 2   | 43343209 | C/T               | 0.249/0.209     | 1.27 (1.14-1.42)                | 2.12E-05 | 0.972 |                                |    | Intergenic |
| Intergenic regions      | rs75494812 | 2   | 43343217 | C/T               | 0.249/0.209     | 1.27 (1.14-1.42)                | 2.12E-05 | 0.972 |                                |    | Intergenic |
| Intergenic regions      | rs78123956 | 2   | 43343222 | A/G               | 0.247/0.207     | 1.27 (1.14-1.42)                | 2.69E-05 | 0.969 |                                |    | Intergenic |
| Intergenic regions      | rs72788819 | 2   | 43343296 | G/T               | 0.249/0.21      | 1.27 (1.14-1.42)                | 2.58E-05 | 0.973 |                                |    | Intergenic |
| Intergenic regions      | rs62135364 | 2   | 43343449 | G/A               | 0.249/0.21      | 1.27 (1.13-1.41)                | 3.06E-05 | 0.974 |                                |    | Intergenic |
| Intergenic regions      | rs62135365 | 2   | 43343554 | C/G               | 0.249/0.21      | 1.27 (1.13-1.41)                | 3.06E-05 | 0.974 |                                |    | Intergenic |
| Intergenic regions      | rs62135366 | 2   | 43343572 | C/T               | 0.250/0.211     | 1.26 (1.13-1.41)                | 3.47E-05 | 0.97 |                                |    | Intergenic |
| Intergenic regions      | rs75734739 | 2   | 43343597 | A/G               | 0.250/0.21      | 1.27 (1.13-1.42)                | 3.08E-05 | 0.972 |                                |    | Intergenic |
| Intergenic regions      | rs6712537 | 2    | 43343613 | A/G               | 0.257/0.218     | 1.26 (1.12-1.4)                | 5.46E-05 | 0.965 |                                |    | Intergenic |
| Intergenic regions      | rs62135367 | 2    | 43343658 | C/G               | 0.250/0.211     | 1.26 (1.13-1.41)                | 3.71E-05 | 0.97 |                                |    | Intergenic |
| Intergenic regions      | rs6741704 | 2    | 43343806 | G/A               | 0.257/0.218     | 1.26 (1.12-1.4)                | 5.46E-05 | 0.965 |                                |    | Intergenic |
| Intergenic regions      | rs13400080 | 2    | 43343929 | A/G               | 0.250/0.211     | 1.26 (1.13-1.41)                | 4.06E-05 | 0.975 |                                |    | Intergenic |
| Intergenic regions      | rs13400166 | 2    | 43343983 | A/G               | 0.249/0.21      | 1.26 (1.13-1.41)                | 3.27E-05 | 0.975 |                                |    | Intergenic |
| Intergenic regions      | rs13388340 | 2    | 43344012 | T/C               | 0.249/0.21      | 1.27 (1.13-1.41)                | 3.06E-05 | 0.975 |                                |    | Intergenic |
| Intergenic regions      | rs13409611 | 2    | 43344176 | G/A               | 0.253/0.213     | 1.27 (1.14-1.42)                | 1.81E-05 | 0.98 |                                |    | Intergenic |
| Intergenic regions      | rs13422869 | 2    | 43344215 | T/C               | 0.255/0.215     | 1.27 (1.14-1.42)                | 2.06E-05 | 0.984 |                                |    | Intergenic |
| Intergenic regions      | rs13409474 | 2    | 43344229 | C/T               | 0.255/0.215     | 1.26 (1.13-1.41)                | 3.19E-05 | 0.982 |                                |    | Intergenic |
| Intergenic regions      | rs59576048 | 2    | 43344425 | A/G               | 0.254/0.215     | 1.26 (1.13-1.41)                | 2.93E-05 | 0.98 |                                |    | Intergenic |
| Intergenic regions      | rs10166329 | 2    | 43344553 | A/G               | 0.252/0.212     | 1.27 (1.14-1.42)                | 1.74E-05 | 0.989 |                                |    | Intergenic |
| Intergenic regions      | rs10190504 | 2    | 43344888 | C/T               | 0.264/0.223     | 1.26 (1.13-1.41)                | 2.81E-05 | 0.975 |                                |    | Intergenic |
| Intergenic regions      | rs10190773 | 2    | 43345049 | G/C               | 0.256/0.216     | 1.27 (1.14-1.41)                | 2.07E-05 | 0.989 |                                |    | Intergenic |
| Intergenic regions      | rs10169409 | 2    | 43345253 | A/G               | 0.255/0.216     | 1.26 (1.13-1.41)                | 2.98E-05 | 0.989 |                                |    | Intergenic |

Table S3. Continued.
| Distribution-based set | SNP       | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI)² | P² | Info² | Genotyped (45 SNPs) OR (95% CI)³ | P³ | Annotation³ |
|------------------------|-----------|-----|----------|-------------------|-----------------|----------------------------------|----|-------|---------------------------------|----|-------------|
| Intergenic regions     | rs56043765| 2   | 43345285 | C/A               | 0.251/0.211     | 1.27 (1.14-1.42)                  | 2.43E-05 | 0.984 |                                  |    | Intergenic |
| Intergenic regions     | rs56254138| 2   | 43345357 | T/A               | 0.255/0.215     | 1.27 (1.14-1.41)                  | 2.27E-05 | 0.989 |                                  |    | Intergenic |
| Intergenic regions     | rs55790508| 2   | 43345600 | A/G               | 0.252/0.215     | 1.25 (1.12-1.4)                  | 6.38E-05 | 0.986 |                                  |    | Intergenic |
| Intergenic regions     | rs55899636| 2   | 43345615 | C/T               | 0.252/0.215     | 1.25 (1.12-1.4)                  | 6.38E-05 | 0.986 |                                  |    | Intergenic |
| Intergenic regions     | rs56185236| 2   | 43345623 | G/A               | 0.252/0.215     | 1.25 (1.12-1.4)                  | 6.38E-05 | 0.986 |                                  |    | Intergenic |
| Intergenic regions     | rs55679540| 2   | 43345673 | G/A               | 0.243/0.205     | 1.26 (1.13-1.41)                 | 6.13E-05 | 0.968 |                                  |    | Intergenic |
| Intergenic regions     | rs56015869| 2   | 43345688 | T/C               | 0.248/0.209     | 1.27 (1.13-1.42)                 | 3.12E-05 | 0.976 |                                  |    | Intergenic |
| Intergenic regions     | rs62135402| 2   | 43345854 | G/A               | 0.255/0.216     | 1.26 (1.13-1.41)                 | 2.98E-05 | 0.99  |                                  |    | Intergenic |
| Intergenic regions     | rs13413812| 2   | 43345917 | C/G               | 0.255/0.216     | 1.26 (1.13-1.41)                 | 2.98E-05 | 0.99  |                                  |    | Intergenic |
| Intergenic regions     | rs13414085| 2   | 43346014 | G/A               | 0.255/0.215     | 1.26 (1.13-1.41)                 | 2.70E-05 | 0.989 |                                  |    | Intergenic |
| Intergenic regions     | rs13416780| 2   | 43346170 | G/A               | 0.253/0.213     | 1.26 (1.13-1.41)                 | 2.96E-05 | 0.997 |                                  |    | Intergenic |
| Intergenic regions     | rs13391171| 2   | 43346340 | A/G               | 0.255/0.216     | 1.26 (1.13-1.41)                 | 3.13E-05 | 0.99  |                                  |    | Intergenic |
| Intergenic regions     | rs6746891 | 2   | 43346511 | T/A               | 0.263/0.224     | 1.26 (1.13-1.4)                  | 3.62E-05 | 0.98  |                                  |    | Intergenic |
| Intergenic regions     | rs10209254| 2   | 43346640 | T/C               | 0.253/0.213     | 1.26 (1.13-1.41)                 | 2.60E-05 | 0.997 |                                  |    | Intergenic |
| Intergenic regions     | rs10173378| 2   | 43346789 | A/G               | 0.254/0.215     | 1.26 (1.13-1.41)                 | 2.91E-05 | 1    | 1.26 (1.13-1.4) 3.07E-05         |    | Intergenic |
| Intergenic regions     | rs10199788| 2   | 43347089 | G/A               | 0.252/0.213     | 1.26 (1.13-1.41)                 | 3.22E-05 | 0.996 |                                  |    | Intergenic |
| Intergenic regions     | rs10176003| 2   | 43347096 | A/T               | 0.252/0.213     | 1.26 (1.13-1.4)                  | 3.86E-05 | 0.996 |                                  |    | Intergenic |
| Intergenic regions     | rs10199639| 2   | 43347127 | C/G               | 0.252/0.213     | 1.26 (1.13-1.41)                 | 3.22E-05 | 0.996 |                                  |    | Intergenic |
| Intergenic regions     | rs58700409| 2   | 43347932 | C/T               | 0.258/0.22      | 1.25 (1.12-1.39)                 | 7.66E-05 | 0.978 |                                  |    | Intergenic |
| Intergenic regions     | rs12328347| 2   | 43351269 | T/G               | 0.264/0.225     | 1.24 (1.12-1.39)                 | 7.89E-05 | 0.978 |                                  |    | Intergenic |
| Intergenic regions     | rs737013  | 2   | 43352888 | A/T               | 0.264/0.224     | 1.24 (1.12-1.38)                 | 5.80E-05 | 0.992 |                                  |    | Intergenic |
| Intergenic regions     | rs13390874| 2   | 43353230 | C/T               | 0.249/0.21      | 1.26 (1.13-1.41)                 | 3.59E-05 | 0.985 |                                  |    | Intergenic |
| Intergenic regions     | rs747709  | 2   | 43353389 | G/A               | 0.264/0.223     | 1.25 (1.12-1.39)                 | 3.85E-05 | 1    | 1.25 (1.13-1.39) 3.51E-05        |    | Intergenic |
| Intergenic regions     | rs747708  | 2   | 43353424 | G/C               | 0.249/0.21      | 1.26 (1.13-1.41)                 | 3.61E-05 | 0.986 |                                  |    | Intergenic |
| Intergenic regions     | rs17030394| 2   | 43354280 | A/G               | 0.269/0.23      | 1.24 (1.12-1.38)                 | 7.68E-05 | 0.985 |                                  |    | Intergenic |
| Intergenic regions     | rs7560102 | 2   | 136785646| C/A               | 0.303/0.346     | 0.82 (0.74-0.91)                 | 9.67E-05 | 0.986 |                                  |    | Intergenic |
| Intergenic regions     | rs11903959| 2   | 225523685| G/T               | 0.414/0.464     | 0.82 (0.74-0.9)                  | 2.38E-05 | 0.987 |                                  |    | Intergenic |
| Distribution-based set | SNP          | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|-------------|-----|----------|-------------------|-----------------|-----------------------------------|---------------------------------|------------|
| Intergenic regions     | rs11884368  | 2   | 225534192| A/C               | 0.42/0.469      | 0.82 (0.75-0.9) 3.54E-05 1       | 0.82 (0.74-0.9) 2.88E-05       | Intergenic |
| Intergenic regions     | rs7604556   | 2   | 22555193 | C/G               | 0.414/0.461     | 0.83 (0.75-0.91) 9.17E-05 0.986   |                                 | Intergenic |
| Intergenic regions     | rs2396109   | 2   | 225559073| C/G               | 0.414/0.461     | 0.83 (0.75-0.91) 9.11E-05 0.979   |                                 | Intergenic |
| Intergenic regions     | rs6717108   | 2   | 225561035| C/T               | 0.421/0.468     | 0.83 (0.75-0.91) 6.32E-05 1       | 0.83 (0.75-0.91) 6.27E-05       | Intergenic |
| Intergenic regions     | rs7619231   | 3   | 27989316 | A/G               | 0.33/0.375      | 0.81 (0.73-0.9) 4.52E-05 0.978    |                                 | Intergenic |
| Intergenic regions     | rs12632457  | 3   | 28020552 | T/C               | 0.454/0.5       | 0.82 (0.75-0.91) 5.62E-05 1       | 0.82 (0.75-0.91) 5.37E-05       | Intergenic |
| Intergenic regions     | rs12489692  | 3   | 28020974 | T/C               | 0.461/0.508     | 0.82 (0.75-0.91) 5.71E-05 0.993   |                                 | Intergenic |
| Intergenic regions     | rs62295007  | 3   | 135273504| T/G               | 0.028/0.014     | 1.99 (1.42-2.79) 6.71E-05 0.935   |                                 | Intergenic |
| Intergenic regions     | rs62295008  | 3   | 135273705| G/A               | 0.028/0.014     | 1.98 (1.42-2.78) 7.09E-05 0.857   |                                 | Intergenic |
| Intergenic regions     | rs62295009  | 3   | 135274766| C/T               | 0.028/0.014     | 1.99 (1.42-2.79) 6.49E-05 0.938   |                                 | Intergenic |
| Intergenic regions     | rs9289495   | 3   | 135276133| T/C               | 0.032/0.018     | 1.83 (1.35-2.48) 9.79E-05 0.975   |                                 | Intergenic |
| Intergenic regions     | rs9289496   | 3   | 135276473| C/G               | 0.033/0.018     | 1.85 (1.37-2.51) 6.99E-05 0.978   |                                 | Intergenic |
| Intergenic regions     | rs9289497   | 3   | 135276505| C/T               | 0.033/0.018     | 1.85 (1.37-2.51) 7.05E-05 0.976   |                                 | Intergenic |
| Intergenic regions     | rs7638619   | 3   | 135278078| A/G               | 0.033/0.018     | 1.85 (1.37-2.51) 6.84E-05 0.975   |                                 | Intergenic |
| Intergenic regions     | rs7609886   | 3   | 135281406| G/A               | 0.033/0.018     | 1.85 (1.37-2.51) 6.70E-05 0.977   |                                 | Intergenic |
| Intergenic regions     | rs17720859  | 3   | 135283880| T/C               | 0.033/0.018     | 1.85 (1.37-2.51) 7.11E-05 0.974   |                                 | Intergenic |
| Intergenic regions     | rs9824873   | 3   | 183301774| T/C               | 0.344/0.3       | 1.23 (1.11-1.36) 4.83E-05 1       | 1.23 (1.11-1.36) 4.83E-05       | Intergenic |
| Intergenic regions     | rs4640595   | 3   | 183305570| T/G               | 0.328/0.286     | 1.23 (1.11-1.36) 9.32E-05 0.977   |                                 | Intergenic |
| Intergenic regions     | rs34822770  | 4   | 147472232| A/T               | 0.304/0.345     | 0.82 (0.74-0.91) 9.97E-05 0.992   |                                 | Intergenic |
| Intergenic regions     | rs1504359   | 4   | 147495449| C/T               | 0.302/0.343     | 0.82 (0.74-0.9) 7.52E-05 1        | 0.81 (0.74-0.9) 6.93E-05       | Intergenic |
| Intergenic regions     | rs11732954  | 4   | 147513675| G/A               | 0.303/0.345     | 0.81 (0.73-0.9) 5.37E-05 0.991   |                                 | Intergenic |
| Intergenic regions     | rs72731840  | 4   | 147535490| A/C               | 0.305/0.345     | 0.82 (0.74-0.9) 9.78E-05 0.992   |                                 | Intergenic |
| Intergenic regions     | rs74666125  | 4   | 183839592| C/T               | 0.11/0.082      | 1.37 (1.17-1.6) 9.42E-05 0.986   |                                 | Intergenic |
| Intergenic regions     | rs62342671  | 5   | 23246743 | C/T               | 0.101/0.132     | 0.73 (0.63-0.85) 3.90E-05 0.965   |                                 | Intergenic |
| Intergenic regions     | rs62342672  | 5   | 23246748 | G/C               | 0.108/0.138     | 0.75 (0.65-0.87) 9.12E-05 0.971   |                                 | Intergenic |
| Intergenic regions     | rs7728238   | 5   | 23253526 | C/A               | 0.11/0.141      | 0.74 (0.64-0.86) 5.17E-05 0.977   |                                 | Intergenic |
| Intergenic regions     | rs10068017  | 5   | 23254632 | C/G               | 0.112/0.144     | 0.74 (0.64-0.86) 4.35E-05 0.982   |                                 | Intergenic |
| Distribution-based set | SNP      | Chr | Position        | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|---------|-----|-----------------|--------------------|-----------------|-----------------------------------|-------------------------------|------------|
| Intergenic regions     | rs350308 | 5   | 62435983        | C/T                | 0.298/0.256     | 1.25 (1.12-1.39) | 4.09E-05                  | 0.974       | Intergenic |
| Intergenic regions     | rs28432235 | 5   | 116064442       | G/A                | 0.045/0.027     | 1.66 (1.29-2.14) | 8.95E-05                  | 0.984       | Intergenic |
| Intergenic regions     | rs1076985 | 5   | 116066910       | T/C                | 0.046/0.028     | 1.69 (1.31-2.17) | 4.67E-05                  | 0.983       | Intergenic |
| Intergenic regions     | rs10054005 | 5   | 116069411       | C/A                | 0.046/0.025     | 1.87 (1.44-2.42) | 2.54E-06                  | 0.958       | Intergenic |
| Intergenic regions     | rs10056291 | 5   | 116070510       | G/T                | 0.046/0.025     | 1.85 (1.43-2.4)  | 3.02E-06                  | 0.957       | Intergenic |
| Intergenic regions     | rs11241401 | 5   | 116072472       | C/T                | 0.047/0.026     | 1.85 (1.43-2.39) | 2.96E-06                  | 0.948       | Intergenic |
| Intergenic regions     | rs6555884  | 5   | 169510630       | C/T                | 0.199/0.164     | 1.29 (1.14-1.46) | 5.55E-05                  | 0.97        | Intergenic |
| Intergenic regions     | rs80015729 | 5   | 169510969       | G/A                | 0.668/0.045     | 1.56 (1.28-1.92) | 1.74E-05                  | 0.945       | Intergenic |
| Intergenic regions     | rs56028434 | 5   | 169514476       | C/T                | 0.067/0.044     | 1.58 (1.29-1.94) | 1.30E-05                  | 0.945       | Intergenic |
| Intergenic regions     | rs56266443 | 5   | 169514824       | C/T                | 0.067/0.044     | 1.58 (1.29-1.94) | 1.32E-05                  | 0.945       | Intergenic |
| Intergenic regions     | rs34524659 | 5   | 169515067       | G/A                | 0.165/0.128     | 1.37 (1.2-1.57)  | 5.50E-06                  | 0.968       | Intergenic |
| Intergenic regions     | rs953078   | 5   | 169515482       | C/T                | 0.048/0.028     | 1.8 (1.41-2.31)  | 3.53E-06                  | 0.921       | Intergenic |
| Intergenic regions     | rs77415591 | 5   | 169515972       | T/C                | 0.049/0.028     | 1.8 (1.41-2.31)  | 3.49E-06                  | 0.917       | Intergenic |
| Intergenic regions     | rs75696798 | 5   | 169516102       | T/C                | 0.049/0.028     | 1.8 (1.41-2.31)  | 3.49E-06                  | 0.917       | Intergenic |
| Intergenic regions     | rs113092489 | 5  | 169517335       | C/T                | 0.048/0.028     | 1.79 (1.4-2.3)   | 4.68E-06                  | 0.917       | Intergenic |
| Intergenic regions     | rs140530048 | 5  | 169517466       | C/T                | 0.048/0.028     | 1.77 (1.38-2.28) | 8.58E-06                  | 0.878       | Intergenic |
| Intergenic regions     | rs28687527 | 5   | 169519108       | G/A                | 0.048/0.028     | 1.79 (1.4-2.3)   | 4.76E-06                  | 0.914       | Intergenic |
| Intergenic regions     | rs74452850 | 5   | 169520208       | A/G                | 0.048/0.028     | 1.82 (1.42-2.33) | 2.76E-06                  | 0.917       | Intergenic |
| Intergenic regions     | rs62422302 | 6   | 131127287       | C/T                | 0.057/0.08      | 0.69 (0.57-0.83)  | 9.70E-05                  | 0.93        | Intergenic |
| Intergenic regions     | rs138655006 | 6   | 131134893       | G/A                | 0.067/0.093     | 0.68 (0.57-0.81)  | 1.58E-05                  | 0.946       | Intergenic |
| Intergenic regions     | rs1871432 | 6   | 168562760       | T/A                | 0.376/0.418     | 0.82 (0.75-0.91)  | 8.59E-05                  | 0.979       | Intergenic |
| Intergenic regions     | rs67950640 | 6   | 168563911       | C/T                | 0.376/0.418     | 0.82 (0.75-0.91)  | 9.95E-05                  | 0.98        | Intergenic |
| Intergenic regions     | rs1107046 | 6   | 168564658       | C/A                | 0.377/0.419     | 0.83 (0.75-0.91)  | 9.90E-05                  | 0.98        | Intergenic |
| Intergenic regions     | rs1107047 | 6   | 168564676       | A/G                | 0.377/0.419     | 0.83 (0.75-0.91)  | 9.89E-05                  | 0.979       | Intergenic |
| Intergenic regions     | rs9346527 | 6   | 168564920       | A/G                | 0.377/0.419     | 0.82 (0.75-0.91)  | 9.51E-05                  | 0.98        | Intergenic |
| Intergenic regions     | rs1824926 | 6   | 168565309       | T/C                | 0.377/0.419     | 0.82 (0.75-0.91)  | 9.44E-05                  | 0.979       | Intergenic |
| Intergenic regions     | rs4708443 | 6   | 168565614       | G/C                | 0.376/0.419     | 0.82 (0.75-0.91)  | 7.94E-05                  | 0.98        | Intergenic |
| Distribution-based set | SNP       | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|-----------|-----|----------|--------------------|-----------------|-----------------------------------|----------------------------------|------------|
| Intergenic regions     | rs9346660 | 6   | 168565807 | A/G               | 0.376/0.418     | 0.82 (0.75-0.91) 8.14E-05 0.98 |                                  | Intergenic |
| Intergenic regions     | rs9364410 | 6   | 168566143 | C/T               | 0.376/0.419     | 0.82 (0.75-0.9) 6.39E-05 0.982 |                                  | Intergenic |
| Intergenic regions     | rs9346662 | 6   | 168566275 | G/A               | 0.377/0.419     | 0.82 (0.75-0.91) 9.44E-05 0.982 |                                  | Intergenic |
| Intergenic regions     | rs6908443 | 6   | 168566632 | A/C               | 0.377/0.419     | 0.82 (0.75-0.9) 6.74E-05 0.985 |                                  | Intergenic |
| Intergenic regions     | rs9364413 | 6   | 168567186 | G/A               | 0.375/0.417     | 0.83 (0.75-0.91) 9.50E-05 0.988 |                                  | Intergenic |
| Intergenic regions     | rs9364227 | 6   | 168567235 | A/G               | 0.375/0.417     | 0.83 (0.75-0.91) 9.50E-05 0.988 |                                  | Intergenic |
| Intergenic regions     | rs9364228 | 6   | 168567243 | T/G               | 0.375/0.417     | 0.83 (0.75-0.91) 9.50E-05 0.988 |                                  | Intergenic |
| Intergenic regions     | rs11761083| 7   | 156044166 | A/G               | 0.055/0.035     | 1.62 (1.29-2.03) 2.73E-05 0.968 |                                  | Intergenic |
| Intergenic regions     | rs11773497| 7   | 156044392 | C/G               | 0.055/0.035     | 1.61 (1.28-2.02) 4.07E-05 0.966 |                                  | Intergenic |
| Intergenic regions     | rs12532691| 7   | 156045673 | T/A               | 0.055/0.035     | 1.61 (1.28-2.02) 4.18E-05 0.966 |                                  | Intergenic |
| Intergenic regions     | rs62482378| 7   | 156046268 | C/T               | 0.055/0.035     | 1.61 (1.28-2.02) 4.09E-05 0.966 |                                  | Intergenic |
| Intergenic regions     | rs9654739 | 7   | 156062171 | C/T               | 0.095/0.07      | 1.41 (1.19-1.67) 8.02E-05 1    | 1.41 (1.19-1.67) 8.02E-05 1   | Intergenic |
| Intergenic regions     | rs55713253| 10  | 12305358  | C/T               | 0.289/0.331     | 0.82 (0.74-0.9) 8.55E-05 0.988 |                                  | Intergenic |
| Intergenic regions     | rs11257654| 10  | 12307611  | C/T               | 0.289/0.332     | 0.81 (0.74-0.9) 4.60E-05 0.991 |                                  | Intergenic |
| Intergenic regions     | rs11595732| 10  | 23465002  | C/T               | 0.131/0.169     | 0.74 (0.64-0.84) 7.24E-06 0.958 |                                  | Intergenic |
| Intergenic regions     | rs7916519 | 10  | 23466734  | G/A               | 0.201/0.248     | 0.76 (0.68-0.85) 1.26E-06 1    | 1.26E-06 1                      | Intergenic |
| Intergenic regions     | rs12264498| 10  | 23469422  | C/T               | 0.19/0.24       | 0.73 (0.65-0.82) 1.28E-07 0.979 |                                  | Intergenic |
| Intergenic regions     | rs72802150| 10  | 23478634  | C/T               | 0.137/0.176     | 0.74 (0.65-0.84) 8.30E-06 0.956 |                                  | Intergenic |
| Intergenic regions     | rs10508658| 10  | 23529458  | G/A               | 0.143/0.178     | 0.76 (0.67-0.86) 1.84E-05 1    | 1.84E-05 1                      | Intergenic |
| Intergenic regions     | rs59254345| 10  | 23534441  | G/A               | 0.142/0.178     | 0.76 (0.66-0.86) 1.89E-05 0.998 |                                  | Intergenic |
| Intergenic regions     | rs112002725| 10  | 23536370  | T/C               | 0.142/0.178     | 0.76 (0.67-0.86) 2.08E-05 0.998 |                                  | Intergenic |
| Intergenic regions     | rs17543414| 10  | 23538351  | A/G               | 0.14/0.176      | 0.75 (0.66-0.85) 1.26E-05 0.997 |                                  | Intergenic |
| Intergenic regions     | rs4614330 | 10  | 23548299  | T/C               | 0.14/0.175      | 0.76 (0.67-0.86) 2.63E-05 0.994 |                                  | Intergenic |
| Intergenic regions     | rs56035800| 10  | 23549583  | C/T               | 0.139/0.175     | 0.76 (0.67-0.86) 2.49E-05 0.997 |                                  | Intergenic |
| Intergenic regions     | rs10826806| 10  | 30835608  | G/A               | 0.4/0.446       | 0.83 (0.75-0.91) 9.00E-05 0.996 |                                  | Intergenic |
| Intergenic regions     | rs10882861| 10  | 98751443  | C/T               | 0.222/0.261     | 0.8 (0.72-0.89) 7.72E-05 0.99  |                                  | Intergenic |
| Intergenic regions     | rs142410064| 11  | 113478766 | C/T               | 0.12/0.087      | 1.44 (1.24-1.69) 4.14E-06 0.949 |                                  | Intergenic |
| Distribution-based set | SNP          | Chr | Position   | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation |
|------------------------|--------------|-----|------------|-------------------|-----------------|-----------------------------------|-------------------------------|------------|
| Intergenic regions     | rs7959196   | 12  | 9516777   | T/C               | 0.16/0.199      | 0.78 (0.69-0.88) 4.62E-05 1     | 0.78 (0.69-0.88) 4.62E-05 1   | Intergenic |
| Intergenic regions     | rs17023235  | 12  | 95169408  | G/A               | 0.158/0.198     | 0.77 (0.69-0.87) 3.86E-05 0.993 |                              | Intergenic |
| Intergenic regions     | rs61244926  | 12  | 95169954  | G/A               | 0.159/0.198     | 0.78 (0.69-0.88) 4.49E-05 0.992 |                              | Intergenic |
| Intergenic regions     | rs73232031  | 12  | 95171478  | T/G               | 0.159/0.197     | 0.78 (0.69-0.88) 5.67E-05 0.99  |                              | Intergenic |
| Intergenic regions     | rs4761665   | 12  | 95178391  | T/C               | 0.164/0.205     | 0.77 (0.68-0.87) 3.24E-05 0.978 |                              | Intergenic |
| Intergenic regions     | rs10492261  | 12  | 115456459 | G/A               | 0.177/0.14      | 1.31 (1.15-1.48) 3.08E-05 1     | 1.31 (1.15-1.48) 3.04E-05 1   | Intergenic |
| Intergenic regions     | rs56075746  | 12  | 115457055 | G/T               | 0.177/0.139     | 1.31 (1.16-1.49) 2.18E-05 0.999 |                              | Intergenic |
| Intergenic regions     | rs55653278  | 12  | 115457113 | A/G               | 0.177/0.139     | 1.31 (1.16-1.49) 2.18E-05 0.999 |                              | Intergenic |
| Intergenic regions     | rs11067378  | 12  | 115457535 | G/A               | 0.176/0.139     | 1.31 (1.15-1.48) 3.05E-05 1     | 1.31 (1.16-1.49) 2.68E-05 1   | Intergenic |
| Intergenic regions     | rs601187    | 13  | 30725475  | G/A               | 0.389/0.435     | 0.82 (0.75-0.91) 8.61E-05 0.988 |                              | Intergenic |
| Intergenic regions     | rs148025657 | 14  | 26047244  | T/C               | 0.076/0.05      | 1.53 (1.27-1.85) 1.18E-05 0.956 |                              | Intergenic |
| Intergenic regions     | rs10852344  | 16  | 12016919  | C/T               | 0.122/0.152     | 0.76 (0.67-0.87) 8.53E-05 1     | 0.76 (0.66-0.87) 7.85E-05 1   | Intergenic |
| Intergenic regions     | rs12444127  | 16  | 12018010  | T/A               | 0.119/0.15      | 0.75 (0.66-0.87) 6.40E-05 0.978 |                              | Intergenic |
| Intergenic regions     | rs4625737   | 16  | 12018759  | G/A               | 0.119/0.149     | 0.76 (0.66-0.87) 8.39E-05 0.975 |                              | Intergenic |
| ncRNAs                 | rs28445596  | 1   | 155186729 | C/T               | 0.115/0.152     | 0.72 (0.62-0.82) 2.66E-06 0.994 |                              | GBAP1|non_conding_exon |
| ncRNAs                 | rs1057941   | 1   | 155186742 | A/G               | 0.126/0.162     | 0.73 (0.64-0.84) 6.87E-06 0.982 |                              | GBAP1|non_conding_exon |
| ncRNAs                 | rs2990220   | 1   | 155190254 | A/T               | 0.116/0.154     | 0.72 (0.63-0.83) 3.07E-06 0.987 |                              | GBAP1|Intron |
| ncRNAs                 | rs497829    | 1   | 155193532 | G/C               | 0.116/0.155     | 0.72 (0.62-0.82) 1.66E-06 0.999 |                              | GBAP1|Intron |
| ncRNAs                 | rs2049805   | 1   | 155194980 | C/T               | 0.116/0.155     | 0.72 (0.62-0.82) 1.66E-06 1     | 0.72 (0.63-0.82) 2.09E-06 1   | GBAP1|Intron |
| ncRNAs                 | rs2974931   | 1   | 155195215 | G/C               | 0.118/0.156     | 0.72 (0.63-0.83) 2.81E-06 0.983 |                              | GBAP1|Intron |
| ncRNAs                 | rs2974930   | 1   | 155196717 | G/A               | 0.116/0.154     | 0.72 (0.63-0.82) 2.45E-06 0.997 |                              | GBAP1|Intron |
| ncRNAs                 | rs117431282 | 1   | 155565760 | G/A               | 0.015/0.031     | 0.48 (0.35-0.68) 2.31E-05 0.841 |                              | DAP3P1|Intergenic |
| ncRNAs                 | rs13427419  | 2   | 34282078  | A/C               | 0.16/0.122      | 1.35 (1.19-1.54) 7.57E-06 1     | 1.36 (1.19-1.55) 6.77E-06 1   | AC009499.1|Intergenic |
| ncRNAs                 | rs1425006   | 2   | 34282880  | A/C               | 0.13/0.095      | 1.39 (1.2-1.61) 1.41E-05 0.975 |                              | AC009499.1|Intergenic |
| ncRNAs                 | rs1820327   | 2   | 34288086  | G/A               | 0.122/0.091     | 1.37 (1.18-1.59) 4.79E-05 0.994 |                              | AC009499.1|Intergenic |
| ncRNAs                 | rs1820326   | 2   | 34288170  | T/C               | 0.125/0.093     | 1.35 (1.17-1.57) 6.07E-05 0.992 |                              | AC009499.1|Intergenic |
| ncRNAs                 | rs1593293   | 2   | 34289199  | G/A               | 0.122/0.091     | 1.35 (1.17-1.57) 7.29E-05 1     | 1.35 (1.16-1.57) 8.22E-05 1   | AC009499.1|Intergenic |
| Distribution-based set | SNP      | Chr | Position | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Genotyped (45 SNPs) OR (95% CI) | Annotation^c |
|------------------------|----------|-----|----------|--------------------|------------------|------------------------------------|---------------------------------|----------------|
| ncRNAs                | rs6750420 | 2   | 34290662 | C/T                | 0.109/0.08       | 1.39 (1.18-1.63)                  | 5.65E-05 1                      | 1.4 (1.19-1.64) | 4.00E-05 | AC009499.1|Intergenic |
| ncRNAs                | rs1816151 | 2   | 34291679 | G/A                | 0.11/0.082       | 1.37 (1.17-1.61)                  | 9.74E-05 0.997                  | AC009499.1|Intergenic |
| ncRNAs                | rs13393038 | 2   | 34293353 | A/T                | 0.11/0.081       | 1.38 (1.18-1.62)                  | 6.50E-05 0.99                    | AC009499.1|Intergenic |
| ncRNAs                | rs72787456 | 2   | 34299553 | C/G                | 0.096/0.068      | 1.44 (1.21-1.71)                  | 4.76E-05 0.931                  | AC009499.1|Intergenic |
| ncRNAs                | rs9308946 | 2   | 34302827 | G/T                | 0.11/0.081       | 1.38 (1.18-1.62)                  | 7.26E-05 1                      | 1.37 (1.17-1.6) | 1.14E-04 | AC009499.1|Intergenic |
| ncRNAs                | rs6543805 | 2   | 34305367 | A/T                | 0.11/0.081       | 1.38 (1.17-1.61)                  | 8.28E-05 0.998                  | AC009499.1|Intergenic |
| ncRNAs                | rs76806892 | 2   | 136770019| C/T                | 0.223/0.265      | 0.8 (0.71-0.89)                   | 4.34E-05 0.976                  | AC093991.2|Intergenic |
| ncRNAs                | rs62277111 | 3   | 147669376| G/A                | 0.11/0.082       | 1.39 (1.19-1.63)                  | 5.67E-05 0.951                  | RP11-71N10.1|Intergenic |
| ncRNAs                | rs62277112 | 3   | 147675729| C/T                | 0.115/0.087      | 1.38 (1.18-1.61)                  | 4.78E-05 0.976                  | RP11-71N10.1|Intergenic |
| ncRNAs                | rs62277113 | 3   | 147675922| T/C                | 0.115/0.086      | 1.38 (1.18-1.61)                  | 5.20E-05 0.976                  | RP11-71N10.1|Intergenic |
| ncRNAs                | rs62277114 | 3   | 147676232| C/G                | 0.111/0.084      | 1.37 (1.17-1.61)                  | 7.89E-05 0.971                  | RP11-71N10.1|Intergenic |
| ncRNAs                | rs62277115 | 3   | 147676349| A/T                | 0.115/0.087      | 1.37 (1.17-1.6)                   | 6.38E-05 0.978                  | RP11-71N10.1|Intergenic |
| ncRNAs                | rs11711782 | 3   | 147677650| G/A                | 0.118/0.09       | 1.37 (1.17-1.59)                  | 5.88E-05 1                      | 1.37 (1.17-1.59) | 5.88E-05 | RP11-71N10.1|Intergenic |
| ncRNAs                | rs11711809 | 3   | 147677770| G/A                | 0.116/0.089      | 1.36 (1.17-1.58)                  | 8.14E-05 0.993                  | RP11-71N10.1|Intergenic |
| ncRNAs                | rs2915850 | 5   | 163739709| G/A                | 0.1/0.071        | 1.49 (1.26-1.76)                  | 3.28E-06 1                      | 1.49 (1.26-1.76) | 3.15E-06 | CTC-340A15.2|Intergenic |
| ncRNAs                | rs7780586 | 7   | 17465557 | T/G                | 0.458/0.502      | 0.82 (0.75-0.91)                  | 7.67E-05 0.979                  | AC019117.1|Intergenic |
| ncRNAs                | rs1869414 | 7   | 17476002 | A/G                | 0.457/0.5        | 0.83 (0.75-0.91)                  | 9.70E-05 0.994                  | AC019117.1|AC019117.2|Intergenic |
| ncRNAs                | rs1993246 | 7   | 17477177 | T/C                | 0.456/0.498      | 0.83 (0.75-0.91)                  | 8.66E-05 1                      | 0.83 (0.75-0.91) | 7.26E-05 | AC019117.1|AC019117.2|Intergenic |
| ncRNAs                | rs11770354 | 7   | 17477826 | C/G                | 0.459/0.503      | 0.83 (0.75-0.91)                  | 7.26E-05 0.994                  | AC019117.1|AC019117.2|Intergenic |
| ncRNAs                | rs17137682 | 7   | 17478404 | G/A                | 0.521/0.475      | 1.22 (1.11-1.34)                 | 4.17E-05 0.99                    | AC019117.1|AC019117.2|Intergenic |
| ncRNAs                | rs477587  | 7   | 17500632 | A/C                | 0.435/0.48       | 0.83 (0.75-0.91)                  | 8.48E-05 0.994                  | AC019117.1|Intergenic |
| ncRNAs                | rs3927319 | 7   | 141248158| G/A                | 0.296/0.338      | 0.81 (0.73-0.89)                  | 4.38E-05 0.993                  | RP11-74082.2|Intergenic |
| ncRNAs                | rs1560781 | 8   | 75767776 | A/G                | 0.01/0.022       | 0.43 (0.28-0.66)                 | 8.58E-05 0.824                  | RP11-758M4.4|Intergenic |
| ncRNAs                | rs11782687 | 8   | 75769122 | T/G                | 0.01/0.022       | 0.43 (0.28-0.66)                 | 8.58E-05 0.824                  | RP11-758M4.4|Intergenic |
| ncRNAs                | rs11779097 | 8   | 75769128 | G/A                | 0.01/0.022       | 0.43 (0.28-0.66)                 | 8.58E-05 0.824                  | RP11-758M4.4|Intergenic |
| ncRNAs                | rs11779867 | 8   | 75769517 | C/T                | 0.01/0.022       | 0.43 (0.28-0.66)                 | 8.58E-05 0.824                  | RP11-758M4.4|Intergenic |
| ncRNAs                | rs1433474 | 8   | 75770991 | T/C                | 0.01/0.022       | 0.43 (0.28-0.66)                 | 8.58E-05 0.824                  | RP11-758M4.4|Intergenic |
| Distribution-based set | SNP       | Chr | Position     | Allele Major/Minor | MAF Case/Control | Imputation (499 SNPs) OR (95% CI) | Imputation (499 SNPs) P | Genotyped (45 SNPs) OR (95% CI) | Genotyped (45 SNPs) P | Annotation |
|-----------------------|-----------|-----|--------------|--------------------|-----------------|-----------------------------------|--------------------------|-------------------------------|------------------------|------------|
| ncRNAs               | rs58690792 | 8   | 75772436     | A/C                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.824                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs72669224 | 8   | 75773672     | T/A                | 0.01/0.022      | 0.44 (0.29-0.66)                  | 9.68E-05                 | 0.817                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs11774767 | 8   | 75774987     | T/C                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs11784966 | 8   | 75775291     | C/T                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs11776632 | 8   | 75776814     | T/C                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs66669310 | 8   | 75776928     | A/G                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs56233308 | 8   | 7577837      | G/A                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs56338577 | 8   | 75778114     | G/T                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs66469754 | 8   | 75778445     | T/C                | 0.01/0.022      | 0.43 (0.28-0.66)                  | 8.58E-05                 | 0.822                         |                        | RP11-758M4.4| Intergenic |
| ncRNAs               | rs74471459 | 14  | 51946618     | G/A                | 0.053/0.034     | 1.59 (1.26-2.01)                 | 8.26E-05                 | 0.88                          |                        | FRMD6-AS2| Intergenic |
| ncRNAs               | rs62038793 | 16  | 11953672     | A/G                | 0.102/0.13      | 0.74 (0.64-0.86)                 | 9.50E-05                 | 0.954                         |                        | RP11-16682.8| Intergenic |

Chr, chromosome; MAF, minor allele frequency; OR, odds ratio; CI, confidence interval.

\[a\] Derived from the logistic regression analysis using the additive genetic model with adjustment of age (10-year categories), sex, and study design in the imputed GWAS set.

\[b\] Derived from the logistic regression analysis using the additive genetic model with adjustment of age (10-year categories), sex, and study design in the genotyped GWAS set.

\[c\] Annotation based on GENCODE v19 database.
**Table S4.** Results of the gene-set analysis of the association between each set and gastric cancer risk

| Sets                                | Rank | \( P^a \)    | SNPs number |
|-------------------------------------|------|---------------|-------------|
| Distribution-based set              |      |               |             |
| The combination                     | 1    | 1.14E-24      | 110         |
| Intergenic regions                  | 2    | 3.66E-18      | 198         |
| Protein-coding                      | 3    | 2.70E-17      | 138         |
| ncRNAs                             | 4    | 3.54E-15      | 53          |
| Gene-based set from the combination |      |               |             |
| PLCE1|PLCE1-AS1|RP11-76P2.4|NOC3L       | 1    | 3.53E-10 | 14  |
| KRTCAP2|RP11-201K10.3|TRIM46|MUC1      | 2    | 9.03E-07 | 11  |
| RP11-166B2.1|TNFRSF17                | 3    | 2.11E-06      | 15  |
| EFNA1                               | 4    | 2.74E-06      | 5   |
| RP11-166B2.7|SNX29                  | 5    | 2.93E-06      | 9   |
| P11-263K19.4|THBS3|MTX1|RP11-263K19.6 | 6    | 5.01E-06 | 9   |
| MSTO1|DAP3|MSTO2P          | 7    | 5.31E-06      | 2   |
| GON4L                               | 8    | 5.63E-06      | 1   |
| SLC50A1                             | 9    | 5.68E-06      | 1   |
| PARK2|AL035697              | 10   | 1.64E-05      | 1   |
| SPTA1                               | 11   | 1.71E-05      | 1   |
| DAGLB|KDELR2                | 12   | 2.10E-05      | 3   |
| PI15|RP11-758M4.4           | 13   | 3.97E-05      | 11  |
| AGK                                 | 14   | 4.64E-05      | 1   |
| OSBPL10|ZNF860              | 15   | 4.66E-05      | 1   |
| MX1|AF001610              | 16   | 6.33E-05      | 2   |
| EPDR1|SFRP4                | 17   | 6.34E-05      | 1   |
| CLK2|HCN3                 | 18   | 6.45E-05      | 1   |
| GAS2|RNA5SP338           | 19   | 6.51E-05      | 15  |
| RAC1                                | 20   | 7.01E-05      | 1   |
| SLIT3                               | 21   | 7.73E-05      | 1   |
| DIRC3                               | 22   | 8.91E-05      | 1   |
| ALPK2                               | 23   | 9.22E-05      | 1   |
| DGCR2                               | 24   | 9.54E-05      | 1   |
| CACNA2D3                            | 25   | 9.75E-05      | 1   |
Table S5. The functional annotations of 15 candidate SNPs in the *RP11-166B2.1* | *TNFRSF17* gene set

| SNPs     | Position | Located gene      | Posterior probability | RegulomeDB Functional annotation | Score | HaploReg v4 Proteins bound | eQTL | Motifs changed | Sore | Total | TagSNPs | \( r^2 > 0.8 \) |
|----------|----------|-------------------|------------------------|----------------------------------|-------|---------------------------|------|----------------|------|-------|---------|-----------------|
| rs3850997| 16:12043512 | RP11-166B2.1      | 0.940                  | Protein binding, Chromatin structure, Histone modifications | 3     | NFKB, NRSF, CTCF         | 10   | 0              | 3    | 6     | \( r^2 > 0.8 \) | rs1126889, rs35063476, rs7185307, rs11570136, rs3862446 |
| rs35063476| 16:12044301 | RP11-166B2.1      | 0.873                  | Chromatin structure, Histone modifications | 2     | LBP-1, p53               | 0    | 2              |      |       |         |                 |
| rs62040821| 16:12044555 | RP11-166B2.1      | 0.645                  | Motifs, Chromatin structure, Histone modifications | 2     | 14 altered motifs        | 1    | 3              |      |       |         |                 |
| rs17810367| 16:12044947 | RP11-166B2.1      | 0.707                  | Chromatin structure, Histone modifications | 0     | ERalpha-a, Esr2, TATA NRSF | 8    | 2              | 2    | 2     |         |                 |
| rs76466426 | 16:12045069 | RP11-166B2.1      | 0.770                  | Chromatin structure, Histone modifications | 0     | NRSF                     | 7    | 1              | 1    | 1     |         |                 |
| rs7185307 | 16:12046899 | RP11-166B2.1      | 0.908                  | Chromatin structure, Histone modifications | 0     | 7 altered motifs         | 1    | 1              |      |       |         |                 |
| rs62037663 | 16:12048960 | RP11-166B2.1      | 0.440                  | Chromatin structure, Histone modifications | 0     | SZF1-1                   | 1    | 1              |      |       |         |                 |
| rs62037665 | 16:12051223 | RP11-166B2.1      | 0.513                  | Chromatin structure, Histone modifications | 0     | 6 altered motifs         | 1    | 3              |      |       |         |                 |
| rs12445244| 16:12054073 | RP11-166B2.1      | 0.581                  | Chromatin structure, Histone modifications | 2     | Sox                      | 10   | 3              | 3    | 6     |         |                 |
| rs11570136| 16:12058832 | RP11-166B2.1      | 0.280                  | Protein binding, Chromatin structure, Histone modifications | 3     | 7 bound proteins         | 5    | 4              | 2    | 4     | \( r^2 > 0.8 \) | rs62040821, rs17810367, rs76466426, rs62037665, rs112445244, rs62037663, rs11570152 |
| rs3862446 | 16:12059736 | TNFRSF17          | 0.361                  | Motifs, Histone modifications | 1     | NRSF, Zfx                | 1    | 2              |      |       |         |                 |
| rs11570151| 16:12060579 | TNFRSF17          | 1.000                  | Protein binding, Motifs, Histone modifications | 2     | 5 altered motifs         | 2    | 4              | 2    | 4     | \( r^2 > 0.8 \) | rs62040821, rs17810367, rs62037665, rs112445244, rs62037663, rs11570152 |
| rs11570152| 16:12060681 | TNFRSF17          | 0.828                  | Protein binding, Histone modifications | 2     | Bcl6b, Dbx1, Hdα          | 1    | 3              |      |       |         |                 |
| rs1126889 | 16:12061910 | TNFRSF17          | 0.158                  | Motifs, Histone modifications | 1     | 4 altered motifs         | 1    | 2              |      |       |         |                 |
| rs4462889 | 16:12070486 | RP11-166B2.1      | 0.971                  | Protein binding, Motifs, Chromatin structure, Histone modifications | 3     | 24 bound proteins        | 9    | 3              | 3    | 6     | \( r^2 > 0.8 \) | Independent |
### Table S6. Association between rs3850997 and gastric cancer risk in a European population

| Chr | SNPs        | Position | Allele Major/Minor | Genotypes<sup>a</sup> | MAF Case/Control | \( P_{HWE} \) | Genotyped rate | Imputed info | OR (95% CI)<sup>b</sup> | \( p^b \) |
|-----|-------------|----------|---------------------|------------------------|-----------------|-----------|---------------|--------------|-----------------|--------|
| 16  | rs3850997   | 12043512 | G/T                 | 103/99/29              | 1186/1027/222   | 0.340     | 0.302         | 1.00         | 90.9% 85.9%    | 0.955 0.922 | 1.35 (1.07-1.69) 9.26E-03 |
| 16  | rs35063476  | 12044301 | A/G                 | 104/100/29             | 1194/1030/225   | 0.339     | 0.302         | 0.886        | 91.7% 86.4%    | 0.960 0.925 | 1.18 (0.97-1.45) 1.00E-01 |
| 16  | rs62040821  | 12044555 | C/A                 | 199/38/4               | 1727/289/10     | 0.095     | 0.076         | 0.751        | 94.9% 71.5%    | 0.931 0.702 | 1.28 (0.92-1.77) 1.40E-01 |
| 16  | rs17810367  | 12044947 | G/C                 | 199/38/4               | 1723/289/10     | 0.095     | 0.076         | 0.752        | 94.9% 71.3%    | 0.932 0.701 | 1.28 (0.92-1.77) 1.43E-01 |
| 16  | rs76466426  | 12045069 | T/C                 | 199/39/4               | 1723/290/10     | 0.097     | 0.077         | 0.640        | 95.3% 71.4%    | 0.932 0.702 | 1.30 (0.94-1.79) 1.15E-01 |
| 16  | rs7185307   | 12046899 | T/C                 | 148/86/20              | 1026/521/66     | 0.248     | 0.202         | 1.000        | 100.0% 56.9%  | 1.00 0.729 | 1.30 (1.04-1.61) 2.00E-02 |
| 16  | rs62037663  | 12048960 | G/A                 | 200/37/5               | 1741/290/10     | 0.097     | 0.076         | 0.751        | 95.3% 72.0%    | 0.929 0.703 | 1.31 (0.95-1.80) 1.03E-01 |
| 16  | rs62037665  | 12051223 | C/T                 | 200/34/5               | 1767/291/11     | 0.092     | 0.076         | 1.000        | 94.1% 73.0%    | 0.923 0.708 | 1.24 (0.89-1.72) 2.07E-01 |
| 16  | rs12445244  | 12054073 | G/C                 | 198/36/5              | 1738/303/10     | 0.096     | 0.079         | 0.541        | 94.1% 72.4%    | 0.921 0.711 | 1.25 (0.90-1.72) 1.85E-01 |
| 16  | rs11570136  | 12058832 | T/A                 | 109/105/29             | 1253/1130/256   | 0.335     | 0.311         | 0.964        | 95.7% 93.1%    | 0.976 0.958 | 1.12 (0.92-1.36) 2.70E-01 |
| 16  | rs3862446   | 12059736 | G/A                 | 110/105/29             | 1265/1174/280   | 0.334     | 0.319         | 0.757        | 96.1% 95.9%    | 0.978 0.968 | 1.07 (0.88-1.30) 4.94E-01 |
| 16  | rs11570151  | 12060579 | T/C                 | 197/35/5              | 1767/306/9      | 0.095     | 0.078         | 0.358        | 93.3% 73.4%    | 0.916 0.721 | 1.24 (0.90-1.73) 1.92E-01 |
| 16  | rs11570152  | 12060681 | A/T                 | 197/35/5              | 1752/304/10     | 0.095     | 0.078         | 0.541        | 93.3% 72.9%    | 0.914 0.717 | 1.23 (0.89-1.71) 2.11E-01 |
| 16  | rs1126889   | 12061910 | C/G                 | 102/117/32             | 1262/1228/322   | 0.361     | 0.333         | 0.373        | 98.8% 99.2%    | 0.989 0.988 | 1.13 (0.93-1.36) 2.11E-01 |
| 16  | rs446289    | 12070486 | T/G                 | 49/88/37              | 394/668/291     | 0.466     | 0.462         | 0.827        | 68.5% 47.7%    | 0.878 0.742 | 1.01 (0.81-1.27) 9.00E-01 |

Chr, chromosome; MAF, minor allele frequency; HWE, Hardy-Weinberg Equilibrium; OR, odds ratio; CI, confidence interval. In European population, the T allele of rs3850997 was the minor allele, which is opposite to the Asian population.

<sup>a</sup> Major allele homozygote/heterozygote/minor allele homozygote.

<sup>b</sup> Derived from the logistic regression analysis using the additive genetic model.
Table S7. Association between rs3850997 and gastric cancer risk in the GWAS stage

| SNP      | Stage | Genetic models | OR (95% CI)<sup>a</sup> | P<sup>a</sup> | OR (95% CI)<sup>b</sup> | P<sup>b</sup> |
|----------|-------|----------------|--------------------------|--------------|--------------------------|--------------|
| rs3850997 T>G | GWAS | Additive       | 0.83 (0.75-0.91)         | 9.29E-05     | 0.83 (0.75-0.91)         | 8.32E-05     |
|          |       | Dominant       | 0.73 (0.64-0.84)         | 5.31E-06     | 0.73 (0.64-0.84)         | 5.50E-06     |
|          |       | Recessive      | 0.88 (0.73-1.05)         | 1.57E-01     | 0.87 (0.73-1.05)         | 1.41E-01     |
|          |       | Codominant     | 0.73 (0.63-0.84)         | 1.54E-05     | 0.73 (0.63-0.84)         | 1.75E-05     |
|          |       |                | 0.74 (0.60-0.90)         | 2.27E-03     | 0.73 (0.60-0.89)         | 1.97E-03     |

OR, odds ratio; CI, confidence interval.

<sup>a</sup> Adjusted for age, sex, and study design in the GWAS stage.

<sup>b</sup> Adjusted for age, sex, study design, and rs2274223 genotypes in the GWAS stage.
Table S8. The relationship between miR-27a-3p and each target gene

| Genes   | TargetScan | PicTar | miRanda/miRsvR | CancerNum | T -log2 FC(T-G) | N -log2 FC(T-G) | FC(T-N) | P  | r  |
|---------|------------|--------|----------------|-----------|----------------|----------------|----------|----|----|
| FOXP2   | 1          | 3      | 2              | 6         | -1.065         | 0.432          | -1.497   | 5.07E-04 | -0.460 |
| SFRP1   | 1          | 2      | 1              | 9         | 0.3            | 3.423          | -3.123   | 6.31E-10 | -0.334 |
| TGFBR3  | 1          | 4      | 1              | 6         | 2.022          | 2.777          | -0.755   | 2.96E-03 | -0.32  |
| PDE7B   | 1          | 3      | 1              | 9         | -0.613         | 0.29           | -0.904   | 2.62E-03 | -0.316 |
| CPEB4   | 1          | 5      | 1              | 8         | 2.056          | 2.396          | -0.341   | 3.32E-03 | -0.297 |
| ARRDC4  | 1          | 4      | 1              | 5         | 2.795          | 3.309          | -0.514   | 3.37E-03 | -0.283 |
| RPS6KA5 | 1          | 3      | 2              | 7         | 1.103          | 1.623          | -0.52    | 3.82E-04 | -0.277 |
| CPEB3   | 1          | 8      | 1              | 8         | 0.567          | 0.892          | -0.325   | 5.32E-03 | -0.276 |
| PPAP2B  | 1          | 3      | 2              | 8         | 4.14           | 4.629          | -0.489   | 4.94E-04 | -0.264 |
| PKIA    | 1          | 2      | 1              | 9         | -0.451         | 0.401          | -0.852   | 1.60E-03 | -0.257 |
| ELL2    | 1          | 4      | 1              | 2         | 2.692          | 3.693          | -1.001   | 9.67E-12 | -0.254 |
| LIFR    | 1          | 11     | 1              | 11        | 0.38           | 1.735          | -1.355   | 8.71E-06 | -0.253 |
| NGFRAP1 | 2          | 2      | 2              | 4         | 4.097          | 4.797          | -0.7     | 5.02E-03 | -0.225 |
| BTG2    | 2          | 4      | 1              | 8         | 5.692          | 7.069          | -1.377   | 6.20E-12 | -0.218 |
| SEMA6D  | 1          | 3      | 1              | 7         | -0.263         | 0.816          | -1.079   | 2.18E-04 | -0.213 |
| TMEM25  | 1          | 2      | 1              | 10        | 1.436          | 2.81           | -1.374   | 5.28E-08 | -0.212 |
| SNAP25  | 1          | 3      | 1              | 7         | -1.404         | -0.065         | -1.339   | 4.27E-03 | -0.203 |
| ST6GALNAC3 | 1      | 1      | 1              | 9         | -0.44          | 0.123          | -0.563   | 8.18E-03 | -0.196 |
| DNAJB9  | 1          | 2      | 1              | 6         | 3.507          | 3.819          | -0.311   | 4.24E-03 | -0.188 |
| FAM13A  | 1          | 2      | 1              | 6         | 1.733          | 2.33           | -0.597   | 1.65E-03 | -0.174 |
| C16orf5 | 1          | 2      | 1              | 7         | 2.679          | 3.322          | -0.642   | 7.99E-04 | -0.171 |
| CSRNP1  | 1          | 1      | 1              | 5         | 3.648          | 4.741          | -1.094   | 8.97E-12 | -0.121 |
| ZFP36   | 1          | 1      | 1              | 3         | 7.304          | 8.398          | -1.094   | 1.10E-08 | -0.098 |
| RELN    | 1          | 1      | 1              | 8         | -3.076         | -1.197         | -1.879   | 5.46E-07 | -0.079 |
| GLTP    | 1          | 1      | 1              | 3         | 4.074          | 4.469          | -0.394   | 8.35E-04 | -0.055 |
| NDUFS4  | 1          | 2      | 1              | 3         | 5.294          | 5.676          | -0.382   | 2.39E-04 | -0.043 |

FC, fold change.

a The gene expression RPKM value for each sample from TCGA was log2 transformed and then averaged for both tumor and normal tissues.

b P values obtained from unpaired t tests comparing expression between tumor and normal tissues.

c r value for the correlation between the expression of miR-27a-3p and each target gene.
Table S9. The demographic characteristics of the two-stage case-control studies

| Variables      | Discovery stage | Validation stage |                |                |                |                |                |                |
|----------------|----------------|------------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                | GWAS           | Nanjing-1        | Nanjing-2      | Nanjing-3      | Yixing         | Nantong        | Jilin           |                |
|                | Cases          | Controls         | Cases          | Controls       | Cases          | Controls       | Cases           | Controls       |
| Age (years)    |                |                  |                |                |                |                |                 |                |
| < 60           | 1,625          | 2,100            | 1,275          | 1,436          | 550            | 1,155          | 940             | 1,178          |
|                | 731            | 1,000            | 482            | 543            | NA             | NA             | 441             | 436            |
| > 60           | 894            | 1,100            | 793            | 893            | NA             | NA             | 499             | 625            |
| Sex            |                |                  |                |                |                |                |                 |                |
| Male           | 1,260          | 1,430            | 742            | 698            | 724            | 805            | 328             | 381            |
| Female         | 365            | 670              | 392            | 467            | 392            | 823            | 372             | 804            |
| Study design   |                |                  |                |                |                |                |                 |                |
| Case-control   | 1,368          | 1,650            | NA             | 573            | 622            | 280            | NA              |                |
| Cohort         | 257            | 450              | NA             | 550            | 622            | 280            | NA              |                |
| Tumor site     |                |                  |                |                |                |                |                 |                |
| Non-cardia     | NA             | 734              | 573            | 550            | 622            | 280            | NA              |                |
| Cardia         | NA             | 403              | 415            | 550            | 622            | 280            | NA              |                |
| Both           | NA             | 61               | 415            | 550            | 622            | 280            | NA              |                |
| Experiments        | Description     | Sequences (5’-3’)                                      |
|--------------------|-----------------|-------------------------------------------------------|
| TaqMan             | SNP ID           | Probe                                                |
|                   | rs850997        | FAM-ACTGGGCCAGGGCT                                   |
|                   |                 | HEX-CTGGCAAGGGCTT                                   |
|                   |                 | Primer                                               |
|                   |                 | F: CTTTACTTCCAATGCTGTCAG                              |
|                   |                 | R: CTTTGGCCTTACTTTGAGATGAG                         |
|                   |                 |                                                       |
| RT-PCR             | Gene name       | Primer-F                                             |
|                   | rs850997        | TTTCCCTGCTGTAGTGT                                   |
|                   |                 | CCAGAGGGAAGGACACT                                    |
|                   |                 |                                                       |
| RT-PCR             | Gene name       | Primer-R                                             |
|                   | rs850997        | CAGGAATCCGAGAAGAAC                                   |
|                   |                 |                                                       |
| Sanger sequencing  | Region           | Primer-F                                             |
|                   | rs3850997       | ACAAGTGTGGCAATGAA                                    |
|                   |                 | Primer-R                                             |
|                   |                 | CAGGAATCCGAGAAGAAC                                   |
| siRNA              | Gene name       | Sequence                                             |
|                   | CTCF-siRNA1     | 5’ GUAGAAGUCAGCAAAUUA dTdT 3’                        |
|                   | CTCF-siRNA2     | 5’ GGUGCAAUUGAGAACAUUA dTdT 3’                       |
|                   | CTCF-siRNA3     | 5’ GGCAAGAAGUAUCUGAUAUA dTdT 3’                      |
| EMSA               | SNP ID           | Primer                                               |
|                   | rs3850997 G     | AGCCAAGCCCTGCCAGATCTCCT                              |
|                   |                 | AGGAGACTGCGACAGGGCTGCT                              |
|                   | rs3850997 T     | AGCCAAGCCCTTGGCCAGTCTCCT                             |
|                   |                 | AGGAGACTGCGACAGGGCTGCT                              |
| ChIP               | Gene name       | Primer-F                                             |
|                   | H19ICR          | CCCATCTTGCTGACACCTC                                  |
|                   |                 | AGACCTGGGACGTTTCTGT                                 |
|                   | ChIP-AS G allele| CTTTACTCCTCAATGCTGTCAG                               |
|                   |                 | GCTCTTTTAGGAGACGCCAGG                               |
|                   | ChIP-AS G allele| CTTTACTCCTCAATGCTGTCAG                               |
|                   |                 | GCTCTTTTAGGAGACGCCAGG                               |
|                   | PSA enhancer    | CAGTAAGCAAGGCTGAGATCTGA                              |
|                   |                 | CTGAGCAAAGAGCGAGCACACT                              |
|                   | HOXC-AS3        | CCAGAATCCGCTGATCTCAG                                  |
|                   |                 | TGGCGAAGCAGAGTCCG                                   |
| 3C                 | Target          |                                                       |
|                   | intron-promoter complex | AACTTTCCCCCGTTTTGGC | Anchor |
|                   |                 | TCACCAGTTCCCTGAATTTACC                               |
Table S11. The results from the reanalysis of the gastric cancer GWAS

| Chr | Position   | SNPs        | Allele Major/Minor | Previously reported\(^a\) | MAF Case/Control | OR (95% CI)\(_{per\ alele}\) | \(P_{1df\ score}\) | dbGaP\(^b\) | MAF Case/Control | OR (95% CI)\(^b\) | \(P\(^b\)\) |
|-----|------------|-------------|--------------------|-----------------------------|-----------------|-------------------------------|----------------|-----------|-----------------|-----------------|-----------|
| 1   | 153401959  | rs4460629   | C/T                |                             | 0.112/0.142     | 0.68 (0.59-0.79)              | 3.37E-07       | 0.102/0.139 | 0.69 (0.60-0.80) | 8.21E-07       |
| 1   | 153428691  | rs4072037   | A/G                |                             | 0.125/0.159     | 0.71 (0.62-0.82)              | 1.10E-06       | 0.116/0.154 | 0.72 (0.62-0.82) | 2.23E-06       |
| 10  | 96041407   | rs753724    | G/T                |                             | 0.190/0.147     | 1.49 (1.31-1.68)              | 2.65E-10       | 0.199/0.143 | 1.49 (1.32-1.69) | 2.42E-10       |
| 10  | 96042501   | rs11187842  | C/T                |                             | 0.190/0.147     | 1.48 (1.31-1.68)              | 3.65E-10       | 0.199/0.143 | 1.49 (1.32-1.69) | 3.07E-10       |
| 10  | 96048288   | rs3765524   | C/T                |                             | 0.259/0.207     | 1.39 (1.25-1.56)              | 2.78E-09       | 0.267/0.207 | 1.40 (1.25-1.56) | 1.95E-09       |
| 10  | 96056331   | rs2274223   | A/G                |                             | 0.259/0.209     | 1.40 (1.25-1.56)              | 2.33E-09       | 0.269/0.208 | 1.40 (1.26-1.56) | 1.73E-09       |
| 10  | 96060365   | rs3781264   | T/C                |                             | 0.199/0.152     | 1.51 (1.33-1.70)              | 3.94E-11       | 0.208/0.148 | 1.51 (1.34-1.71) | 3.50E-11       |

Chr, chromosome; MAF, minor allele frequency; OR, odds ratio; CI, confidence interval.

\(^a\) Reported results were collected from original studies.

\(^b\) We reanalyzed the gastric cancer GWAS dataset from the dbGaP using a logistic regression model with an additive genetic model after adjustment with age (10-year categories), sex, and study design.
Supplementary Figures

**Fig. S1.** Diagram showing the distributions of gene types and genetic variants. (A) Pie chart (top) showing the global overview of gene types based on gene annotations from GENCODE v19, including protein-coding genes and ncRNA genes; sketch (bottom) showing the classification of 4 subgroup intervals on the basis of genomic location, including protein-coding genes, ncRNAs genes, combined intervals of protein-coding and ncRNAs (abbreviated as "the combination"), and intergenic regions. ncRNA, noncoding RNA; lncRNA, long noncoding RNA. (B) Classification of genetic variants in Asian populations [including Han Chinese in Beijing, China (CHB) and Japanese in Tokyo, Japan (JPT)] from the 1000 Genomes Project. (C) Classification of cancer-related risk SNPs from the GWAS catalog (Oct. 2015). (D) Pie chart showing gastric cancer risk SNPs with higher evidence from the study by Mocellin et al. (ref. 12).
Fig. S2. Functional annotations of three tagSNPs. (A) Evolutionary conservation of the tagSNPs rs3850997, rs11570151, and rs446289 in several species. (B) Recent positive selection for 15 candidate SNPs located in the RP11-166B2.1|TNFRSF17 gene set was obtained by calculating the integrated Haplotype Score (iHS) for Asian populations (CHB and JPT). Red square represents the absolute iHS for tagSNP rs3850997 and blue square represents the iHS for rs11570151, but no iHS for rs446289.
**Fig. S3.** eQTL annotations for three tagSNPs from the GTEx database. Each tagSNP showed significant correlations with the expression of multiple genes in specific tissues. The red star (★) represents the eQTL of both rs3850997 and rs446289 on **RP11-16682.1** expression in stomach tissues.
Fig. S4. Forest plot of the stratified analysis of the genetic effect of rs3850997 on gastric cancer risk. Each risk effect was evaluated in subgroups stratified by age (< 60 or ≥ 60), sex (male or female), and tumor site (non-cardia or cardia). OR, odds ratio; CI, confidence interval; $P_{\text{het}}$, $P$ value for the heterogeneity test.
Fig. S5. Identification of the subcellular location of the IncRNA GCLET using FISH. Nuclei were stained blue (DAPI), and the three RNAs (18S, U6, and GCLET) were stained red (Cy3) in both MGC-803 and BGC-823 cells. The 18S and U6 RNAs served as internal controls and were mainly located in the cytoplasm and cytoblast, respectively.
**Fig. S6.** Specific functional annotations for rs3850997. (A) Functional annotation for rs3850997. The top panel shows the representation of the 1-kb region of the **GCLET** gene harboring rs3850997, along with the gastric tissue-specific ChIP-seq info obtained from ENCODE and Roadmap Epigenomics projects, showing that both DNase hypersensitivity and active, but not inactive, histones (H3K4me1 and H3K4me3) are enriched at the region surrounding rs3850997. The bottom panel shows the TF-specific ChIP-seq data, indicating that multiple TFs may aggregate at this region. In particular, CTCF displays the highest enrichment. (B) Prediction and annotation of CTCF motif and binding site. The UCSC Genome Browser shows the genomic region spanning from rs3850997 and **GCLET** promoter. The top plot mainly shows the in situ Hi-C chromatin structure. The bottom plots show the log-likelihood ratio of the $P$ value for predicted binding sites of CTCF by FIMO (52 for rs3850997, left; 244 for promoter, right), and the position of 6 CTCF binding sites (colorful blocks) predicted by CTCFBSDB using a 6 core position weight matrix (PWM). (C) The change in DNA folding energy for the CTCF binding site harboring rs3850997: $\Delta G$ of -38.67 kcal/mol for the region containing rs3850997 T allele, and $\Delta G$ of -41.08 kcal/mol for the G allele.
**Figure A**

1kb of rs3850997 surrounding region

**Figure B**

Transcription Factor CHIP-seq Clusters (161 factors) from ENCODE with FaktorBook Motifs

**Figure C**

- rs3850997 T allele
  - $dG = -38.67$

- rs3850997 G allele
  - $dG = -41.08$

**Additional Details**

- rs3850997
  - FIMO
  - CTCFBSDB

**G functional annotation**

- chr16:12043474-12043862
  - rs3850997
  - FIMO
  - CTCFBSDB

**Additional Details**

- dG of rs3850997 surrounding region
  - T allele: $dG = -38.67$
  - G allele: $dG = -41.08$
**Fig. S7.** Allele-specific effect of rs3850997 on transcription factor binding. (A) An EMSA using total nucleoproteins showed no preference of binding affinity for the T and G alleles of rs3850997. (B) DNA sequencing detected the genotypes of SNP rs3850997 in four stomach cell lines (BGC-823, SGC-7901, MGC-803, and GES-1); only MGC-803 harbored the heterozygous rs3850997 genotype. (C) DNA sequencing of ChIP products showed that CTCF preferentially bound to the T allele of rs3850997. (D) ChIP and AS-qPCR detected the modification region of active histones near rs3850997. Notably, the PCR products shown in lanes 1-5 were amplified using primers specific for the PSA enhancer (ref. 40) and HOXC-AS3 (ref. 41), which served as positive controls (lanes 1 and 5: 100 to 1,500 bp ladder; lane 2: active histones H3K4me1/H3K27ac modified product; lane 3: IgG binding product as a negative control; and lane 4: input product); and products shown in lanes 6-11 were amplified with primers specific for rs3850997 alleles (lanes 6 and 11: 100 to 1,500 bp ladder; lanes 7 and 9: active histones H3K4me1/H3K27ac modified product detected by T and G allelic primers, respectively; and lanes 8 and 10: IgG binding product detected by T and G allelic primers, respectively). (E) The specific PCR products generated by 3C designed to detect the rs3850997 intronic region and GCLET promoter interaction were validated using DNA sequencing. The red sequences and horizontal line represent the *Pst*I restriction sites.
A BGC-823
SGC-7901
MGC-803
GES-1
rs3850997
CTCF Input
A B C

B
BGC-823
SGC-7901
MGC-803
GES-1
rs3850997

C
CTCF
Input

D

E
Target
AACTTCCCCTTCTTTGGCAGCTTCAGTCC
CCATGGCGACGAAAAACCTGTCTCC
AGGACAGCTTGCTACCTGCAAGGACAAA
GGCAGAGAGAGCCTTTATCGAAATGATG
AGGAGAGAAGACATGGAAAAGGAT
GGAATATGCAAGGATCATCGAAATGTAA
AAGCCAGGACCGGAGAGGGAAGCCGA
GTGGGTAACTGGGAAGAACTGGTGA

Anchor
Fig. S8. Associations of rs3850997 with gastric cancer survival and GCLET expression with gastric cancer progression. (A) No significant association of rs3850997 with gastric cancer survival was identified using log-rank test (left) and Cox multivariate regression model (right). HR, hazard ratio; CI, confidence interval. (B to D) No significant associations of GCLET expression with tumor size (B), distant metastasis (C), and histological type (D) were identified using the Mann-Whitney test.
**Fig. S9.** Effect of stable GCLET overexpression on tumors in both cell and mouse models. GCLET/NC lentiviral vectors, namely GCLET-over and NC, were transfected into MGC-803 cells. (A to C) Prominent effects of stable GCLET overexpression on gastric cancer cell proliferation, as detected using the CCK8 (A) and colony-forming assays (B), and invasion and migration (C). (D and E) Tumor burdens inoculated with GCLET/NC lentiviral vectors detected in nude mice (D) and their xenografts (E). (F) The tumor weights in nude mice were determined after three weeks, showing lower weights in GCLET-over group. (G) The tumor volumes were measured every three days after injection, and a smaller size was observed in GCLET-over group. (H) Detection of GCLET expression in tumors of nude mice using qRT-PCR. (I) Images of HE and IHC staining for Ki67 in tumors. (Photo credit: Mulong Du, Nanjing Medical University).
**Fig. S10.** Identification of targets of IncRNA GCLET and miR-27a-3p. (A) Two algorithms were utilized to screen the miRNAs that matched the GCLET sequence. (B) Dual-luciferase reporter assays were used to detect the binding affinity of candidate miRNAs for GCLET. (C to E) Expression correlation analyses for the cascade of correlation analyses of CTCF, GCLET, miR-27a-3p, and FOXP2 expression.
Fig. S11. The efficiency of gene expression in transfected gastric cancer cell lines. (A) GCLET expression was detected using real-time PCR in cells transfected with the CTCF siRNA/overexpression vector. (B) Western blot showing a significant decrease in the protein level of CTCF following RNA interference mediated by siRNAs, and a notable increase in the protein level of CTCF following transfection of the overexpression plasmid. (C) Real-time PCR detected the mRNA level of CTCF in cells transfected with siRNAs or the overexpression plasmid. (D) Analysis of the efficiency of GCLET overexpression in cells subjected to both transient and stable transfection using real-time PCR.