SUPPLEMENTARY MATERIALS

A meta-analysis of genome-wide association studies for adiponectin level in East Asians identifies a novel locus near *WDR11-FGFR2*

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SUPPLEMENTARY TEXT. Study Description

I. Discovery stage

Singapore Prospective Study Programme (SP2)

The Singapore Prospective Study Programme (SP2) was a follow-up of participants from four previous cross-sectional studies carried out from 1982 to 1998 (1,2,3). Each of these studies was based on a random sample of Singapore residents with the minority groups (Malays and Asian Indians) being over-sampled. From 2003 to 2007, all 10,747 participants from these studies were invited to participate in the current study. Clinical data from health examination was available for 5,139 participants, among whom only individuals of Chinese ethnicity (n = 2,483) were genotyped. Written informed consent was obtained from all participants and ethics approval was obtained from the Singapore General Hospital and the

National University Hospital Institutional Review Boards. Adiponectin was measured using an enzyme linked immune-sorbent assay (Sekisui Medical Co Ltd, Tokyo, Japan). The intra- and inter-batch coefficient of variations percent were (18.1, 15.9). A total of 2,865 blood-derived DNA samples were genotyped using IlluminaHumanHap 550, 610 Quad, and 1Mduov3 BeadChips. The data went through quality control (QC) procedures where SNPs with call rate < 0.95, minor allele frequency < 0.01 or Hardy-Weinberg equilibrium P-value < 1×10^{-6} were filtered out. A total of 431 individuals did not pass the QC due to high rates of missingness, excessive heterozygosity, cryptic relatedness, discordant ethnicity and gender discrepancy. Imputation was done with the IMPUTE programme on 22 autosomes using NCBI build 36 HapMapII CHB and JPT data (release 22) as the reference panel. Imputation results of SNPs that were actually genotyped were replaced with experimentally determined genotypes before the association tests were conducted. In total, 2,392 post-QC individuals with genotype, adiponectin and covariates data were included in this analysis.

Korean Cancer Prevention Study II (KCPS-II)

The KCPS-II included 266,258 individuals, 20-77 years of age, who visited 16 health promotion centers nationwide from April 2004 to December 2008 in South Korea. The KCPS-II is an expanded cohort study of the Korean Metabolism Syndrome Research Initiative study (KMSRI), which initiated in December 2005. Subjects were firstly recruited from the KMSRI (4). A total of 9,128 individuals were recruited in 2006, and additional 17,569 individuals were recruited in 2007. Therefore, the total Seoul cohort included 26,697 volunteers. Volunteers from the first round had routine health examinations at the Health Promotion Center in University Hospitals between January 2006 and December 2007. From this total, 6,563 individuals were randomly selected for the measurement of adiponectin levels. Of the 6,563 individuals with adiponectin, 1,004 individuals were genotyped.

The institutional Review Board of Human Research of Yonsei University approved the study protocol, and written informed consent was obtained from all subjects. Subjects were interviewed at baseline to obtain exposure data. Adiponectin levels were measured via an enzyme linked immune-

sorbent assay (ELISA) (Mesdia Co., Ltd., Seoul, South Korea). Intra- and interassay variances for adiponectin ranged from 6.3% to 7.4% and 4.5% to 8.6%, respectively.

A total of 1,004 individuals were genotyped on the Affymetrix Genome-wide Human SNP array 5.0 at DNAlink. For the data obtained from this chip, internal QC measures were used: the QC call rate (dynamic model algorithm) always exceeded 86%, and heterozygosity of X chromosome markers indentified gender for each individual. Genotype calling was performed with the Birdseed (v2) algorithm. PLINK (v1.07) was used to estimate identity by state (IBS) over all SNPs. Of the 1,004 individuals, four individuals were shown to be biological relatives, so one member of each pair was excluded. Eleven individuals were also excluded as a result of gender mismatches. In quality assurance, screening, we flagged SNPs with genotype call rates < 95%, minor allele frequency < 0.01 or Hardy-Weinberg equilibrium *P*-value < 1×10^{-6}. Imputation was done with the IMPUTE programme on 22 autosomes using NCBI build 36 HapMapII CHB and JPT data (release 22) as the reference panel. Imputation results of SNPs that were actually genotyped were replaced with experimentally determined genotypes before the association tests were conducted. Therefore, a total of 993 post-QC individuals with genotype, adiponectin and covariates information were included in this analysis.

Cebu Longitudinal Health and Nutrition Survey (CLHNS)

Data and samples come from the Cebu Longitudinal Health and Nutrition Survey (CLHNS), a community-based birth cohort study that originally enrolled 3,327 pregnant women in 1983–84 (3080 singleton live births), and has since followed them and their offspring to the present (5). In 2005, 1895 healthy Filipino mothers and 1775 of their offspring remained in the study and from whom DNA and measurement of biomarkers were collected. Trained field staff conducted in-home interviews and collected anthropometric measurements and comprehensive environmental data at each visit (data available online at http://www.cpc.unc.edu/projects/cebu/). Blood samples, which were used for biomarker measurement and DNA extraction, were obtained in 2005. Plasma samples were analyzed for adiponectin with a commercially available enzyme-linked immunosorbent assay (R&D Systems

#DY1065). All samples were assayed in duplicate, and control samples were included with each assay to monitor between-assay variation. The percent coefficient of variation (SD/mean) for low, middle and high controls was 9.5, 9.6 and 7.8, respectively. The participants were genotyped with the Affymetrix Genome-Wide Human SNP array 5.0. We used identity-by-descent and identity-by-state estimates calculated in PLINK in combination with our prior knowledge of relationships between CLHNS participants to eliminate 81 estimated first-degree relatives. SNPs with call rate < 97%, MAF < 1%, deviation from Hardy-Weinberg equilibrium ($P < 10^{-6}$) and/or were excluded. Imputation was conducted in MACH using HapMap r22 pooled CEU+CHB+JPT haplotypes, also with markers only polymorphic in CHB+JPT. SNPs with poor imputation quality (MACH Rsq < 0.3) were excluded. Individuals carrying *ADIPOQ* Arg221Ser shown to interfere with adiponectin measurement were excluded (6). Our final sample for the GWA analysis consisted of 1,717 CLHNS mothers with genotypes, adiponectin and covariate data.

Nutrition and Health of Aging Population in China (NHAPC)

The Nutrition and Health of Aging Population in China (NHAPC) is a population-based cohort study among 3,289 individuals (3,210 of them are Chinese Hans), aged 50 to 70 years, recruited from Beijing and Shanghai. The study design, methods and measurements of this cohort study have been described in detail elsewhere (7). Briefly, the participants were recruited using a multistage sampling method from two urban districts and one rural district of each city. Data on demographic variables, health status, health behavior, and physical activity were collected using a standardized questionnaire, and standard anthropometric measurements and overnight fasting blood samples were collected using a standardized protocol when the participants attended a physical examination. Plasma adiponectin concentrations were measured by Luminex xMAP Technology (Linco Research, St Charles, MO) on a Bio-Rad Multiplex Suspension Array System. The DNA samples were genotyped using the Illumina Human660W-Quad BeadChip (Illumina, Inc., San Diego, CA, USA). Quality control filters were applied at the individual and SNP levels. At the individual level, samples with call rates <97%, excessive

heterozygosity or gender mismatches between the reported and genetically inferred were excluded. PLINK (version 1.07) was used to estimate the pair-wise identity-by-descent between individuals in NHAPC, and the sample with lower call rates from each inferred pair of first- and second- degree relatives was excluded. SNPs with call rate < 95%, minor allele frequency < 1% or deviation from Hardy-Weinberg equilibrium at $P < 10^{-4}$ were excluded. Genome-wide imputation was carried out with IMPUTE2 (version 2.2.2) by using 180 phased CHB+JPT haplotypes from HapMap Phase 2 (release 22) as the reference panel. Imputed SNPs with poor quality (score_info < 0.5) were excluded. Finally, 1,364 samples from Beijing and 1,384 samples from Shanghai with genotypes, adiponectin and covariates information were remained for the GWA analysis.

II. *In silico* follow-up

Ansan cohort (Ansan)

Subjects in this cohort were drawn from the Ansan cohort, initiated in 2001 as part of the Korean Genome Epidemiology Study (KoGES). Initial Ansan samples included 5,020 participants aged 40-69 (8). The sampling base for this cohort is Gyeonggi Province, About 30 km west of Seoul. Members of this cohort have been examined every 2 years since their baseline visit, with the third scheduled follow-up study (including family members) completed in 2008. From these 5,020 samples, 3,022 subjects were randomly selected for measurement of adiponectin levels.

Where DNA samples for genotyping were inadequate (mostly owing to degradation; n=129), DNA extracted from Epstein-Barr virus-immortalized lymphoblastoid cell lines was substituted. DNA samples with low concentration (n=55) were amplified prior to genotyping according to the manufacturer's protocol (QIAGEN). A total of 5,020 samples were genotyped with the Affymetrix Genome-wide Human SNP Array 5.0 using 500ng of genomic DNA. Markers with low call rate (<95%), low MAF (<0.01), and/or significant deviation from HWE (P <0.0001). Imputation was done with the IMPUTE programme on 22 autosomes using NCBI build 36 HapMapII CHB and JPT data (release 22) as

the reference panel. Imputation results of SNPs that were actually genotyped were replaced with experimentally determined genotypes before the association tests were conducted.

The institutional Review Board of Human Research of Korea University approved the study protocol, and written informed consent was obtained from all subjects. Subjects were interviewed at baseline to obtain exposure data. Adiponectin levels were measured via an enzyme linked immune-sorbent assay (ELISA) (Mesdia Co., Ltd., Seoul, South Korea). Intra- and interassay variances for adiponectin ranged from 6.3% to 7.4% and 4.5% to 8.6%, respectively.

Kita-Nagoya Genomic Epidemiology Study (KING)

The Kita-Nagoya Genomic Epidemiology (KING) study (ClinicalTrials.gov identifier: NCT00262691) is a population-based cross-sectional study in Kita-Nagoya, Japan, in which a total of 3,975 volunteers were recruited from participants in annual health checkups as described in detail previously (9). Serum adiponectin concentration was measured in 3,298 individuals. One individual with CC genotype of *ADIPOQ* Ile164Thr shown to be strongly associated with the adiponectin concentration was excluded. Therefore, a total of 3,297 individuals were enrolled in this analysis. The study protocol was approved by the ethics committees of Aichi-Gakuin University School of Dentistry and Nagoya University School of Medicine, and all participants provided written informed consent. Blood samples were obtained from subjects in the fasted condition for the measurement of serum adiponectin and extraction of DNA. Serum adiponectin level was determined by use of a latex turbidometric immunoassay (Otsuka Pharmaceutical Corporation, Osaka, Japan) (10). A total of 1,030 blood-derived DNA samples were genotyped using Illumina Human660W-Quad and HumanOmni2.5-8 BeadChips. The data were subjected to quality control (QC) procedures where SNPs with call rate < 0.95, minor allele frequency < 0.01 or Hardy-Weinberg equilibrium P-value < 1×10^{-6} were filtered out. We imputed genotypes by using MACH version 1.0.18 with data from the 1000 genomes project ASN samples (Phase-1 integrated release version 2) as a reference panel. Imputation was performed only for SNP markers located in the ± 500 kb

flanking regions of the 115 target SNPs. Our final sample for the GWA analysis consisted of 1,030 individuals with genotypes, adiponectin and covariate data.

Stanford Asia-Pacific Program of Hypertension and Insulin Resistance (SAPPHIRe)

The Stanford Asia-Pacific Program for Hypertension and Insulin Resistance (SAPPHIRe) was part of the Family Blood Pressure Program of the National Heart, Lung, and Blood Institute of the National Institutes of Health, which aimed to investigate the genetic determinants of hypertension and insulin resistance in Chinese and Japanese populations. The study collected concordant siblings (all siblings with hypertension) and discordant siblings (at least one hypertensive sibling). Index hypertensive cases were ascertained as those with age at onset of 35–60 years or those >60 years of age with documentation of their hypertension status before age 60 years (11). Individuals with pre-existing chronic illness including diabetes, cancer, or diseases of the heart, liver, or kidney were excluded. Participants with screen-detected diabetes were not excluded (12). A total of 2,525 participants of Japanese or Chinese descent were originally recruited from centers at San Francisco, Hawaii, and Taiwan in 1996-2000 (13). These subjects underwent a clinical and fasting laboratory examination, with written informed consent obtained before examination. Whole blood was obtained from all consenting family members for DNA extraction. Among them, 1,601 subjects had adiponectin measured (14). Only 455 subjects involving in the GENESIS consortium (15) had genome-wide association study (GWAS) data typed. The following subjects were removed for possible measurement errors: 45 diabetic subjects or medication users, 7 subjects with gender and pedigree errors identified via PLINK, 13 Japanese, 88 subjects with missing adiponectin and 39 subjects with missing BMI. As a result, a total of 263 subjects were analyzed in the present study. A total of 909,508 SNPs were typed through Affymetrix 6.0 array in the GWA study. SNPs with call rate < 95%, MAF<1%, deviation from Hardy-Weinberg equilibrium ($P < 10\text{-}6$) were excluded. Imputation of the entire 2.5M HapMap SNP set was conducted in MACH. The association analysis between GWAS SNPs and adiponectin was conducted by the regression models

using the generalized estimating equation (GEE) approach where within-family corrections were accounted for.

III. Further follow-up

Kita-Nagoya Genomic Epidemiology Study (KING)

Details of the KING study sample and phenotype measurements are described above. Of the 3,297 samples available for this study, 1,030 were included *in-silico* follow-up analysis. The remaining 2,267 samples were used for *de-novo* follow-up analysis. Genotyping was performed using TaqMan SNP Genotyping assays (Applied Biosystems) according to the manufacturer's protocol. Genotyping success rates of 10 SNPs ranged from 0.995 to 0.999.

Ehime University Hospital Anti-aging Center Study (AAC)

The Ehime University Hospital Anti-aging Center Study (AAC) was composed of consecutive participants in the medical check-up program at Ehime University Hospital Anti-aging Center (AAC) (16). Participants were apparently healthy community residents living in Ehime Prefecture. This check-up program is specifically designed to evaluate aging-related disorders, including atherosclerosis, cardiovascular disease, physical function, and mild cognitive impairment. All clinical data used in this study were obtained through the check-up process. This cross-sectional investigation was carried out as part of the Shimanami Health Promoting Program (J-SHIPP study), a longitudinal study evaluating factors related to cardiovascular disease, dementia, and death. This study was approved by the ethics committee of Ehime University Graduate School of Medicine. All 1,357 study subjects provided informed consent. Plasma samples were obtained from each subject after an overnight fast of more than 11 hours. The samples were immediately frozen and stored at -80 degrees Celsius until measurements were taken. Plasma concentration of total adiponectin was determined using a latex enhanced imunoturbidimetric assay (Mitsubishi Chemical Medience, Tokyo, Japan). The plasma concentration of HMW adiponectin was determined by an ELISA assay (FUJIREBIO INC., Tokyo, Japan) (17). The inter-

and intra-assay coefficient variations of the HMW adiponectin assay were 4.4% and 9.7%, respectively. Genomic DNA was extracted from peripheral blood samples (QIAamp DNA blood kit, QIAGEN GmbH, Hilden, Germany). All SNPs were analyzed by TaqMan probe assay (Applied Biosystems Co., Ltd., Foster City, CA) using commercially available primers and probes purchased from the Assay-on-Demand system.

Nomura Study (Nomura)

The Nomura Study (Nomura) was based on a community (Nomura town) of 11,000 inhabitants in Ehime Prefecture, a largely rural area located in western Japan (18). Subjects were recruited through a community-based annual medical check-up process in 2002 for self-employed individuals, and included farmers and foresters, employees of small companies, and elderly without fixed employment. The sample population consisted of 2,895 middle-aged to elderly residents. Of these, 2,081 subjects with available HMW adiponectin were enrolled in the analysis. Baseline clinical characteristics were obtained from personal health records evaluated during the medical check-up. This study was approved by the ethics committee of Ehime University Graduate School of Medicine. All study subjects provided informed consent. Plasma samples were obtained from each subject after an overnight fast of more than 11 hours. The samples were immediately frozen and stored at -80 degrees Celsius until measurements were taken. The plasma concentration of HMWA was determined by an ELISA assay (FUJIREBIO INC., Tokyo, Japan) (17). The inter- and intra-assay coefficient variations of the HMWA adiponectin assay were 4.4% and 9.7%, respectively. Genomic DNA was extracted from peripheral blood samples (QIAamp DNA blood kit, QIAGEN GmbH, Hilden, Germany). All SNPs were analyzed by TaqMan probe assay (Applied Biosystems Co., Ltd., Foster City, CA) using commercially available primers and probes purchased from the Assay-on-Demand system.

Shanghai Men's Health Study (SMHS)

The 230 male subjects from SMHS with complete adiponectin and genotyping data were selected from the Shanghai Men’s Health Study (SMHS). The SMHS, described in detail elsewhere (19), is a

population-based cohort study of 61,492 Chinese men who were aged between 40 and 74 years, were free of cancer at enrollment, and lived in urban Shanghai, China. Recruitment for the SMHS was initiated in April 2002 and completed in June 2006. A total of 83,058 eligible male residents of eight communities in urban Shanghai were invited to participate by trained interviewers through in-person contact; 61,492 enrolled in the study with a response rate of 74.0%. Reasons for non-participation were refusal (21.1%), out of area during enrollment (3.1%), and other miscellaneous reasons including poor health or hearing problems (1.8%). A blood sample was collected from 46,244 (75.1%) study participants and an exfoliated buccal cell samples from 56% of those who did not donate a blood sample.

IV. The Asian Genetic Epidemiology Network (AGEN) lipids study

The AGEN-lipids study is an ongoing meta-analysis to investigate the SNP associations with triglycerides (TG), high-density lipoproteins (HDL-C), low-density lipoproteins (LDL-C) and total cholesterol (TC) in up to 25,413 individuals of Asian ancestry. In addition to SP2, KCPS II and CLHNS that had participated in the discovery stage of the AGEN adiponectin study, the discovery stage of the AGEN lipids meta-analysis consisted of eight additional studies: the Singapore Malay Eye Study (SiMES), Shanghai Endometrial Cancer Study (SCES), Cardio-metabolic Genome Epidemiology (CAGE), the Korea Association Resource (KARE) project, the Genetic Epidemiology Network of Salt Sensitivity (GenSalt), Taiwan Super Control Study (TWSC), Shanghai Breast Cancer Survival Study (SBCS), and Shanghai Women and Men's Health Study (SWMHS).

Within each participating cohort, individuals known to be on cholesterol-lowering medication were excluded. LDL-C levels were either calculated with Friedewald's formula from fasting blood measurements of the other three lipid traits or directly measured. When calculating the LDL-C levels, individuals with TG greater than 400 mg/dL were excluded. The TG levels were logarithm transformed to approximate normality. Residuals for each lipid trait obtained from linear regression models with adjustment for age, age^2, sex and BMI were inverse-normal transformed. The associations between the normalized residuals and the ~2.5 million genotyped or HapMap imputed SNPs were tested using an

additive mode of inheritance. The inverse-variance weighted model implemented in METAL was applied for meta-analysis.

V. The Asian Genetic Epidemiology Network (AGEN) BMI study

The AGEN-BMI study is an ongoing meta-analysis to investigate SNP associations with obesity and five obesity-related anthropometric measures, including BMI, waist circumference (WC), waist-hip ratio (WHR), BMI-adjusted WC (WCadjBMI) and BMI-adjusted WHR (WHRadjBMI) in up to 86,757 individuals of Asian ancestry. The discovery stage of the AGEN BMI meta-analysis included 17 additional studies that were not in AGEN-adiponectin discovery stage, including the Shanghai Genome-Wide Association Studies (SGWAS), Taiwan Genome Wide Association Study (TGWAS), Cardiometabolic Risk in Chinese study (CRC), Fangchenggang Area Male Health and Examination Survey (FAMHES), the Genetic Epidemiology Network of Salt Sensitivity (GenSalt), Dongfeng-Tongji cohort study (DFTJ), Shanghai Institute of Hypertension GWAS (SIH), Singapore Diabetes Cohort Study (SDCS), the Multi-Ethnic Study of Atherosclerosis (MESA), Taiwan USA Diabetes Retinopathy (TUDR), the Korea Association Resource (KARE) project, Health Examinee (HEXA) shared control study, Health2 cohort, Rural cohort, Singapore Malay Eye Study (SiMES), Cardio-metabolic Genome Epidemiology (CAGE) and REKIN GWAS study.

Rank-based inverse normal transformation was applied to the five quantitative traits for each gender by each study. Within each individual study, linear regression and logistic regression models, assuming an additive genetic model and adjusting for age and age^2, were applied to test for the association for the ~2.5 million genotyped or HapMap imputed SNPs with the five quantitative traits or with obesity as a dichotomous outcome defined as BMI≥27.5 kg/m^2, respectively. Meta-analyses were carried out using a weighted average method with inverse-variance weights implemented in METAL.

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SUPPLEMENTARY FIGURES LEGEND

Supplementary Figure 1. Flow diagram of the study.

Supplementary Figure 2. Genome-wide association with adiponectin level in discovery stage of this study. (A) Manhattan plot, (B) Quantile–quantile plot of observed and expected *P* values for association. Red: all SNPs; blue: after exclusion of the SNPs located within ± 500 kb flanking regions of the index SNP at *CDH13* (rs4783244) and *ADIPOQ* (rs10937273), the two GWA loci previously reported in Asians.

Supplementary Figure 3. A second signal rs266719 near *ADIPOQ* at *EIF4A2* showed association only after conditioning on rs10937273. (A) initial association and (B) conditional on rs10937273.

Supplementary Figure 4. Two independent signals existed at the previously described locus near*GPR109A-ZNF664.* (A) initial association; (B) conditional on *ZNF664*-rs1187415 and (C) conditional on *GPR109A*-rs10847980.

Supplementary Figure 5. Two independent signals existed at the previously described locus near *CMIP-CDH13.* (A) initial association; (B) conditional on *CDH13*-rs4783244 and (C) conditional on *CMIP*-rs2925979.

Supplementary Figure 6. Association with adiponectin for the 1000 Genomes imputed SNPs that are located within ± 500 kb of rs3943077 (chr10: 122,445,086 – 123,445,086; Build 37, hg19). The index SNP rs3943077 is the best SNP near *FGFR2* identified based on HapMap imputed data. LD r^2 were estimated from all Asian samples (ASN) in the 1000 Genomes Projects Phase 1 (2010 November).

Supplementary Figure 7. The previously described *CDH13* only contains one signal (rs4783244). The black arrows indicate the index SNP reported in AdipoGEN (rs12051272) and variants (rs3865188 and rs3865186) representing the two signals suggested in a Korean population (4).

SUPPLEMENTARY TABLES

Supplementary Table 1. Cohort characteristics.

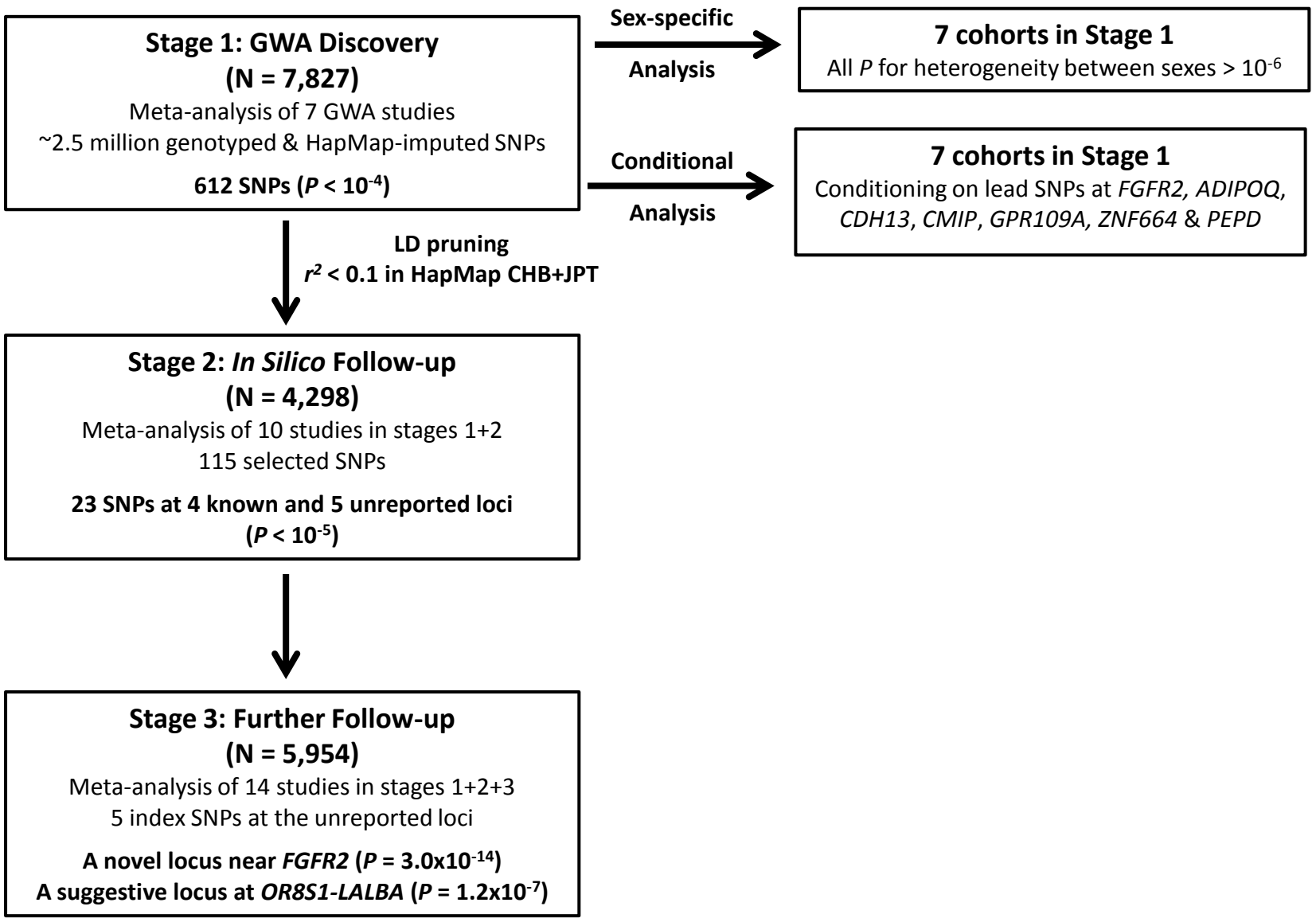
Supplementary Table 2. AGEN evidence of association for adiponectin at other loci previously described.

Supplementary Table 3. Sex-stratified association for loci associated with adiponectin in sex-combined analysis or previously reported.

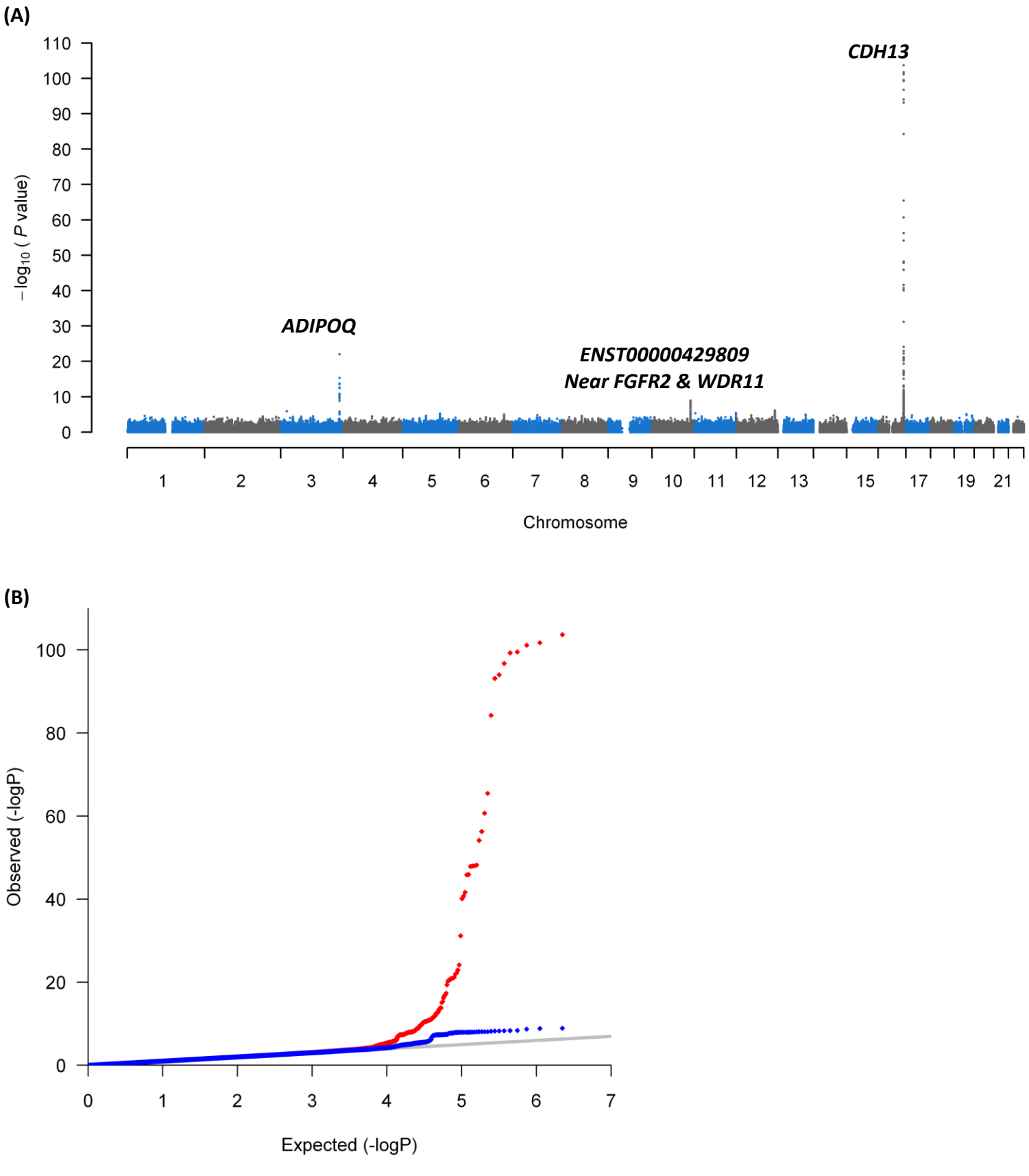
Supplementary Table 4. Partial spearman correlation between adiponectin and other metabolic and cardiovascular-related traits.

Supplementary Table 5. Measures of adiponectin and other metabolic and cardiovascular-related traits.

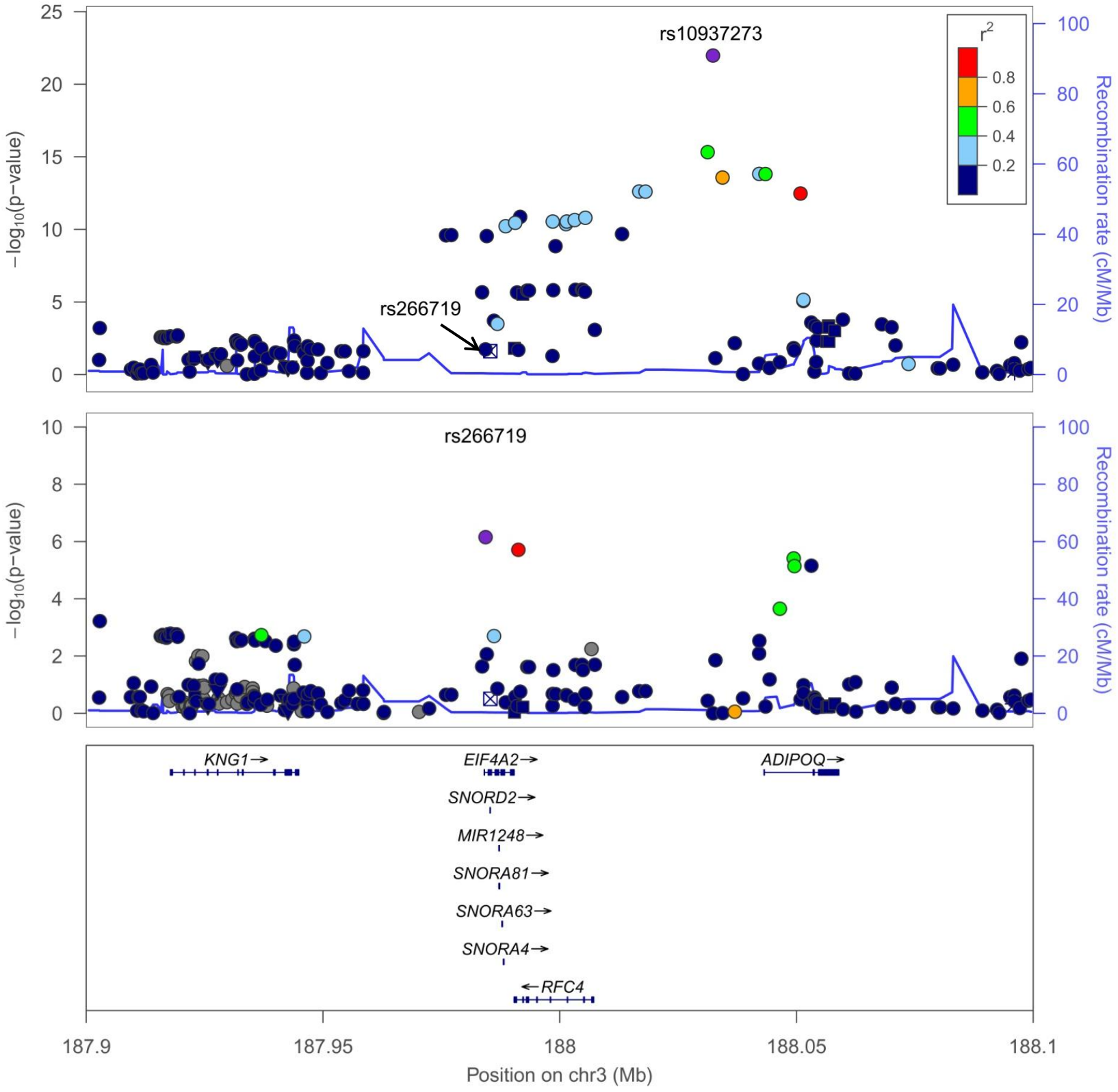
Supplementary Table 6. Regions for conditional analysis and the SNPs used as conditioning variables.



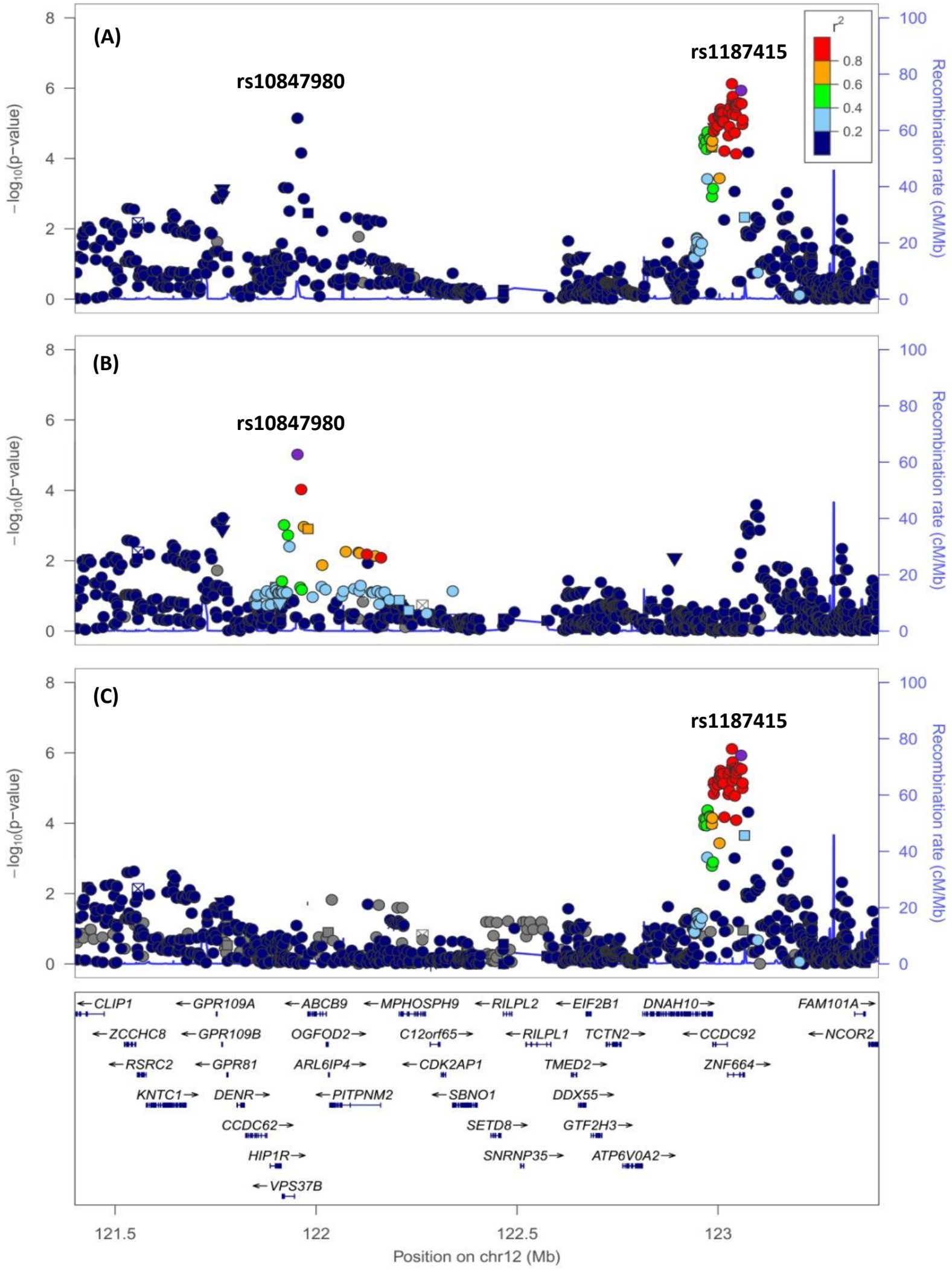
Supplementary Figure 1. Flow diagram of the study.



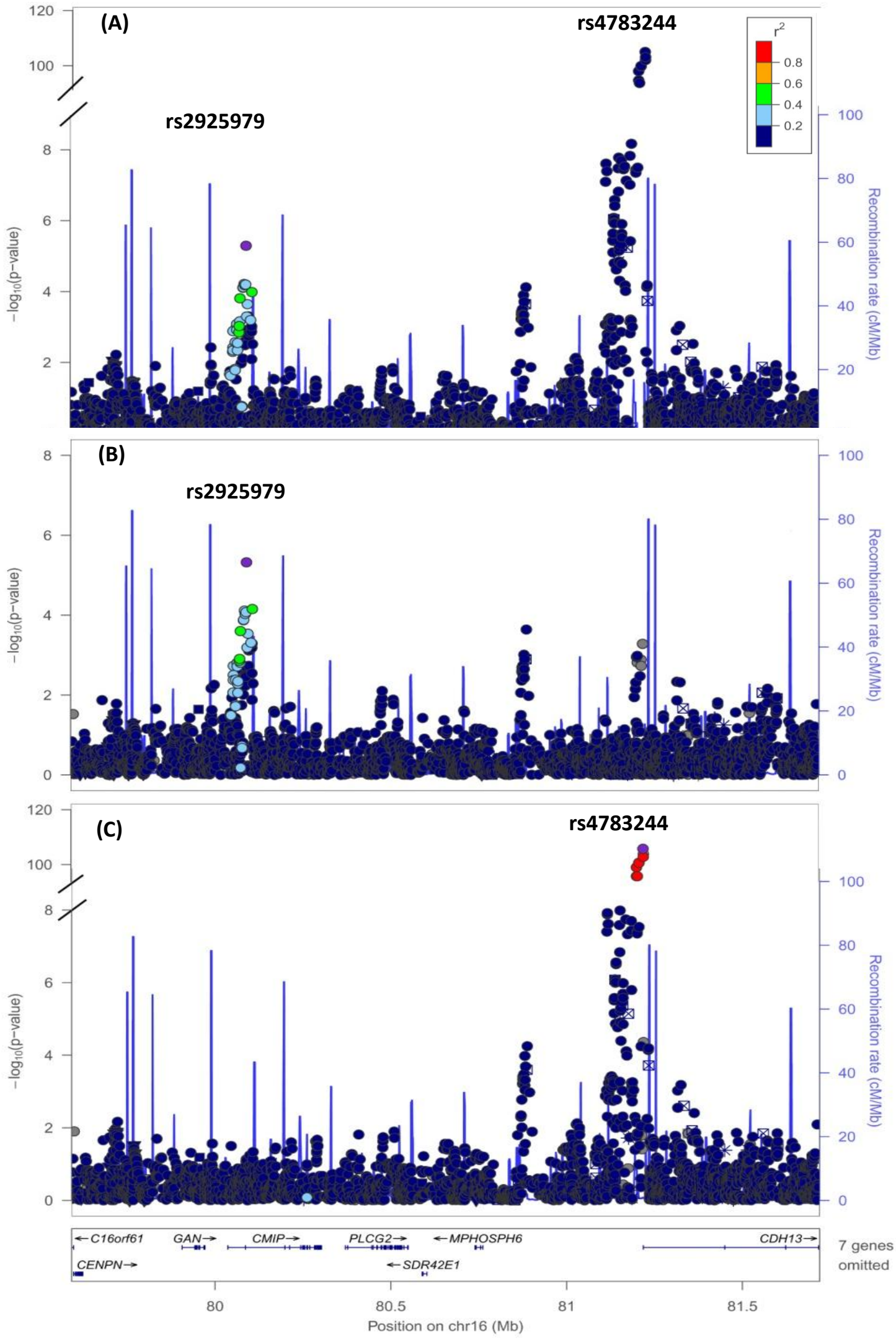
Supplementary Figure 2. Genome-wide association with adiponectin level in discovery stage of this study. (A) Manhattan plot, (B) Quantile–quantile plot of observed and expected *P* values for association. Red: all SNPs; blue: after exclusion of the SNPs located within ± 500 kb flanking regions of the index SNPs at *CDH13* (rs4783244) and *ADIPOQ* (rs10937273), the two GWA loci previously reported in Asians.



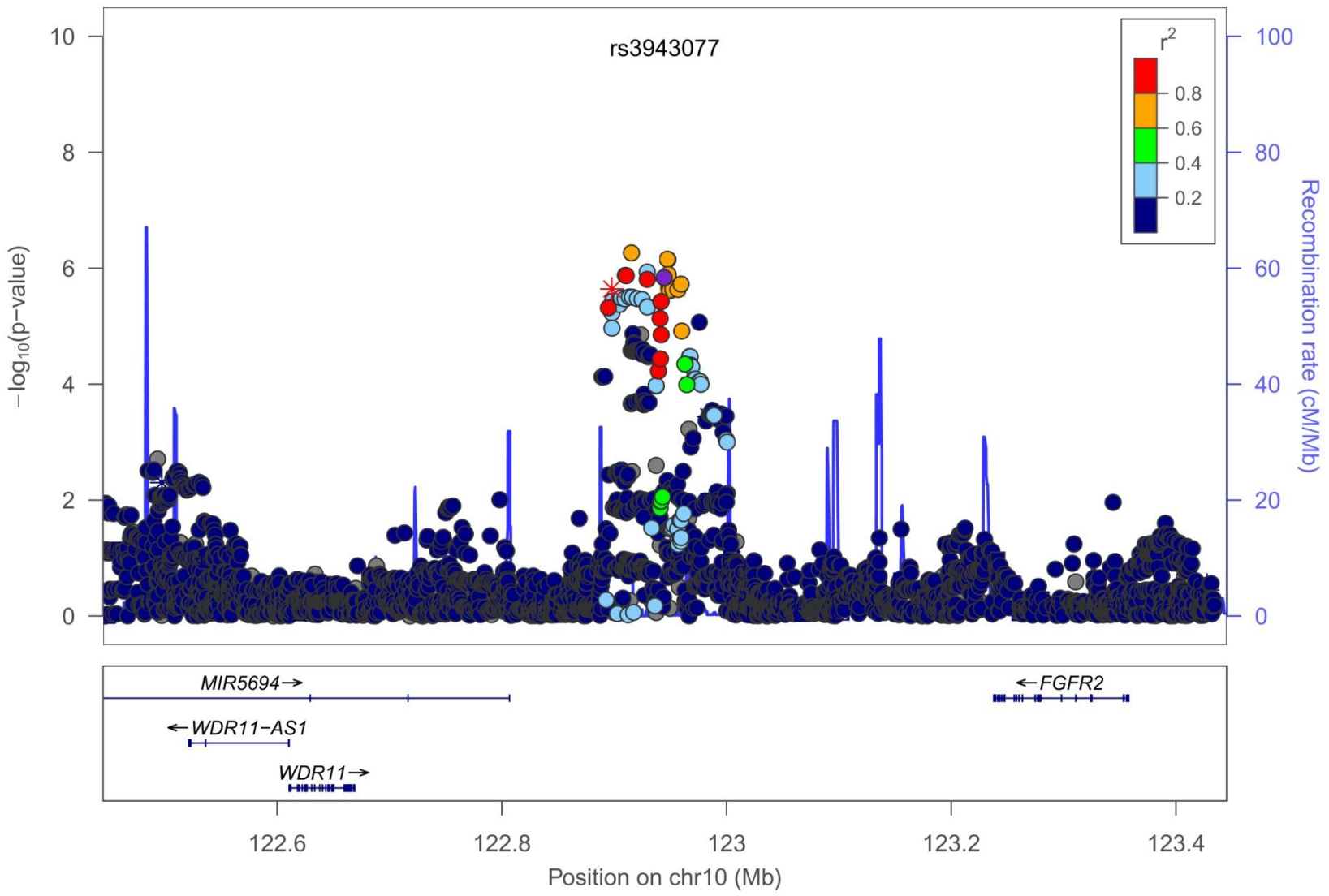
Supplementary Figure 3. A second signal rs266719 near *ADIPOQ* at *EIF4A2* showed association only after conditioning on rs10937273. (A) initial association and (B) conditional on rs10937273.



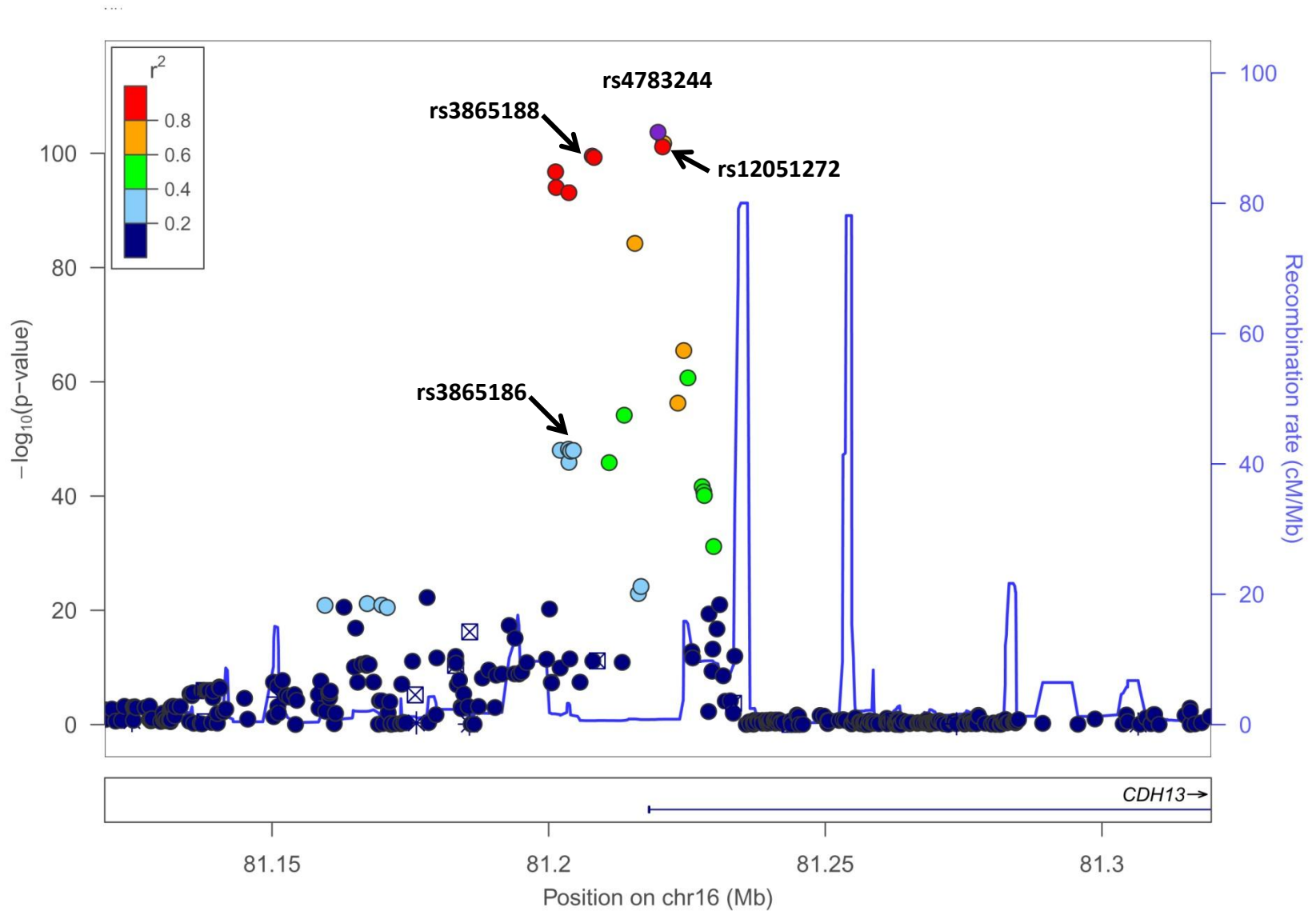
Supplementary Figure 4. Two independent signals existed at the previously described locus near*GPR109A-ZNF664.* (A) initial association; (B) conditional on *ZNF664*-rs1187415 and (C) conditional on *GPR109A*-rs10847980.



Supplementary Figure 5. Two independent signals existed at the previously described locus near *CMIP-CDH13.* (A) initial association; (B) conditional on *CDH13*-rs4783244 and (C) conditional on *CMIP*-rs2925979.



Supplementary Figure 6. Association with adiponectin for the 1000 Genomes imputed SNPs that are located within ± 500 kb of rs3943077 (chr10: 122,445,086 – 123,445,086; Build 37, hg19). The index SNP rs3943077 is the best SNP near *FGFR2* identified based on HapMap imputed data. LD r^2 were estimated from all Asian samples (ASN) in the 1000 Genomes Projects Phase 1 (2010 November).



Supplementary Figure 7. The previously described *CDH13* only contains one signal (rs4783244). The black arrows indicate the index SNP reported in AdipoGEN (rs12051272) and variants (rs3865188 and rs3865186) representing the two signals suggested in a Korean population (Jee et al., Am J Hum Genet 2010).

Supplementary Table 1. Cohort characteristics

	SAMPLES AND PHENOTYPING										GENOTYPING, IMPUTATION AND QUALITY CONTROL									ASSOCIATION ANALYSIS		
	Cohort	Country	Ethnicity	Study Design	Sample Size (% females)	Age [Mean (SD)], yrs	BMI [Mean (SD)], kg/m2	Adiponectin [Median (IQR)], ug/ml	Ln_Adiponectin [Mean (SD)], ug/ml	Adiponectin Measurement	Genoyping Array	Individual Call Rate	SNP Call Rate	HWE P	Software for Imputation	Imputation Reference	Number of SNPs for Imputation	Imputation Quality	MAF	Software for Analysis	Number of SNPs for Analysis	Lambda (GC)
Stage 1: GWA Discovery (n = 7,827)	SP1_1M*	Singapore	Chinese	Population-based	936 (36.6)	46.9 (10.3)	22.9 (3.5)	3.0 (2.2-4.4)	1.13 (0.52)	Enzyme linked immune-sorbent 140 assay (Sekisui Medical Co Ltd, Japan)	Illumina 1M-duov3	≥ 0.95	≥ 0.95	≥ 1E-06	IMPUTE	HapMap R22 CHB+JPT	944,241	Score_info ≥ 0.5	≥ 0.01	SNPTEST	2,301,270	0.997
	SP2_610K*	Singapore	Chinese	Population-based	1125 (76.5)	48.6 (11.3)	22.6 (3.7)	3.8 (2.5-5.1)	1.28 (0.52)	Enzyme linked immune-sorbent 140 assay (Sekisui Medical Co Ltd, Japan)	Illumina Quad 610	≥ 0.95	≥ 0.95	≥ 1E-06	IMPUTE	HapMap R22 CHB+JPT	542,298	Score_info ≥ 0.5	≥ 0.01	SNPTEST	2,232,506	1.004
	SP2_550K	Singapore	Chinese	Population-based	331 (23.6)	49.7 (12.7)	23.6 (3.5)	2.8 (2.0-3.9)	1.06 (0.55)	Enzyme linked immune-sorbent 140 assay (Sekisui Medical Co Ltd, Japan)	Illumina 550	≥ 0.95	≥ 0.95	≥ 1E-06	IMPUTE	HapMap R22 CHB+JPT	504,625	Score_info ≥ 0.5	≥ 0.01	SNPTEST	2,222,495	1.007
	KCPSII	Korea	Korean	Population-based	970 (42.9)	41.6 (8.4)	23.7 (3.1)	7.3 (4.3-10.9)	1.95 (0.66)	ELISA (Mesdia Co., Ltd.)	Affymetrix 500K	≥ 0.95	≥ 0.95	≥ 1E-06	IMPUTE	HapMap R22 CHB+JPT	355,091	Score_info ≥ 0.5	≥ 0.01	SNPTEST	2,047,447	1.033
	CLHNS*	Philippines	Filipino	Population-based	1717 (100)	48.4 (6.1)	24.3 (4.4)	2.5 (1.9-3.3)	0.94 (0.40)	Enzyme-linked immunosorbent assay (R&D Systems #DY1065)†	Affymetrix 5.0	≥ 0.95	≥ 0.90	≥ 1E-06	MACH	HapMap R22 CHB+JPT	424,670	MACH_Rsq ≥ 0.3	≥ 0.01	MACH2qtl	2,077,770	1.022
	NHAPC Beijing	China	Chinese	Population-based	1364 (55.7)	58.4 (6.0)	25.3 (3.7)	13.4 (8.1-21.8)	2.56 (0.76)	Luminex xMAPTM Technology (Linco Research Inc, St Charles, Mo)	Illumina 660W	≥ 0.97	≥ 0.99	≥ 1E-04	IMPUTE	HapMap R22 CHB+JPT	473,679	Score_info ≥ 0.5	≥ 0.01	SNPTEST	2,218,129	1.018
	NHAPC Shanghai	China	Chinese	Population-based	1384 (57.6)	58.9 (6.1)	23.6 (3.4)	14.0 (8.3-22.0)	2.58 (0.74)	Luminex xMAPTM Technology (Linco Research Inc, St Charles, Mo)	Illumina 660W	≥ 0.97	≥ 0.99	≥ 1E-04	IMPUTE	HapMap R22 CHB+JPT	473,679	Score_info ≥ 0.5	≥ 0.01	SNPTEST	2,207,267	1.012
Stage 2: In Silico Follow-up (n = 4,298)	Ansan	Korea	Korean	Population-based	3003 (47.4)	54.5 (7.4)	24.6 (2.9)		1.63 (0.70)	ELISA (Mesdia Co., Ltd.)	Affymetrix 500K	≥ 0.95	≥ 0.95	≥ 1E-06	IMPUTE	HapMap R22 CHB+JPT	~500,000	Score_info ≥ 0.5	≥ 0.01	PLINK	101	----
	KING_GWAS	Japan	Japanese	Population-based	1030 (31.9)	66.2 (5.7)	23.0 (2.8)	10.0 (7.0-14.4)	2.32 (0.54)	Latex turbidometric immunoassay (Otsuka Pharmaceutical Corporation, Osaka, Japan)	Illumina 660W / Omni2.5	≥ 0.98	≥ 0.95	≥ 1E-06	MACH	1000 genomes project ASN samples (Phase 1 integrated release version 2)	~20,000 (660W) and ~50,000 (Omni2.5)	MACH_Rsq ≥ 0.3	≥ 0.01	PLINK	115	----
	SAPPHIRe	Taiwan & USA	Chinese	Family-based	263 (52.8)	48.2 (8.6)	25.2 (3.5)	4.7 (3.2-6.4)	1.54 (0.54)	Radioimmunoassay (RIA; Linco Research Inc., St Charles, MO, USA)	Affymetrix 6.0	≥ 0.98	≥ 0.95	≥ 1E-06	MACH	HapMap R22 CHB	909,508	MACH_Rsq ≥ 0.3	≥ 0.01	R implemented GEE	108	----
Stage 3: Further Follow-up (n = 5,954)	KING_noGWAS	Japan	Japanese	Population-based	2267 (66.7)	62.4 (6.6)	22.8 (3.1)	10.9 (7.8-15.7)	2.41 (0.54)	Latex turbidometric immunoassay (Otsuka Pharmaceutical Corporation, Osaka, Japan)	TaqMan	----	----	----	----	----	----	----	----	PLINK	5	----
	ACC	Japan	Japanese	Population-based	1357 (61.1)	66.2 (8.9)	23.2 (3.1)	3.7 (2.4-5.8)	1.29 (0.66)	Latex enhanced imunoturbidimetric assay (Mitsubishi Chemical Medience, Tokyo, Japan)	TaqMan	----	----	----	----	----	----	----	----	JMP	5	----
	Nomura	Japan	Japanese	Population-based	2100 (55.9)	62.0 (12.6)	23.5 (3.2)	1.3 (0.8-2.0)	1.56 (0.71)	HMW adiponectin: Enzyme-linked immunosorbent assay (FUJIREBIO INC., Tokyo, Japan)	TaqMan	----	----	----	----	----	----	----	----	JMP	5	----
	SMHS	China	Chinese	Population-based	230 (0)	61.3 (9.2)	23.6 (3.0)	7.42(4.73-10.59)	1.97(0.61)	Luminex xMAPTM Technology (Linco Research Inc, St Charles, Mo)	Affymetrix 6.0	≥ 0.95	≥ 0.95	≥ 1E-06	MACH	HapMap R22 CHB+JPT	909,508	MACH_Rsq ≥ 0.3	≥ 0.01	SAS	5	----

* SP2_1M, SP2_610K and CLHNS also have the 1000 Genomes imputed data

† Individuals carrying ADIPOQ Arg221Ser shown to interfere with adiponectin measurement were excluded [Croteau-Chonka et al., Hum Mol Genet (2012) 21: 463-71]

Supplementary Table 2. AGEN evidence of association for adiponectin at other loci previously described

Locus	SNP previously reported	Reference	Chr:position	Effect/ non-effect alleles	AGEN EAF	AGEN Beta	*AGEN P*
LYPLAL1	rs2791553	[1]	chr1:217742665	A/G	0.669	0.02	0.34
TSC22D2	rs1597466 *	[1]	chr3:151538251	n.a.	n.a.	n.a.	n.a.
GNL3	rs2590838	[1]	chr3:52597126	A/G	0.435	0.02	0.14
FER	rs10447248	[2]	chr5:107943635	A/G	0.664	0.01	0.57
ARL15	rs6450176	[1, 3]	chr5:53333782	A/G	0.441	-0.05	8.3E-04
CITED2-RPS3AP24	rs592423	[1]	chr6:139882386	A/C	0.712	-0.02	0.18
VEGFA	rs998584	[1]	chr6:43865874	A/C	0.563	-0.03	0.13
TRIB1	rs2980879	[1]	chr8:126550657	A/T	0.278	-0.02	0.34
PDE3A	rs7955516	[1]	chr12:20389303	A/C	0.880	-0.02	0.32

* The reported SNP was not genotyped or imputed in AGEN samples because it is not polymorphic in HapMap CHB+JPT samples

n.a. Not applicable

Reference

[1] Dastani et al., PLoS Genet (2012) e1002607

[2] Qi et al., Diabetes (2011) 60: 2197-201

[3] Richards et al., PLoS Genet (2009) e:1000768

Supplementary Table 3. Sex-stratified association for loci associated with adiponecin in sex-combined analysis or previously reported

Locus	SNP	Chr:position	Effect/ non-effect alleles	EAF men	Beta men	*P* men	EAF women	Beta women	*P* women	*P* heter
WDR11-FGFR2	rs3943077	chr10:122935076	A/G	0.606	0.10	5.7E-05	0.544	0.09	2.5E-06	0.51
OR8S1-LALBA	rs11168618	chr12:47219500	T/C	0.148	-0.08	3.5E-02	0.113	-0.11	2.3E-04	0.40
HIVEP2	rs12211360	chr6:143161525	A/G	0.973	-0.27	7.9E-04	0.964	-0.20	8.5E-04	0.37
KCNH8	rs12714975	chr3:19060378	C/G	0.032	0.16	1.5E-02	0.020	0.16	2.5E-02	0.73
GAL3ST1	rs6518702	chr22:29278752	T/C	0.253	-0.09	8.1E-04	0.250	-0.07	2.5E-02	0.50
CDH13	rs4783244	chr16:81219769	T/G	0.332	-0.34	5.1E-42	0.379	-0.34	1.2E-63	0.026
ADIPOQ	rs10937273	chr3:188032389	A/G	0.401	0.17	1.2E-11	0.403	0.15	2.8E-13	0.23
ADIPOQ	rs266719	chr3:187984342	T/C	0.091	0.02	7.0E-01	0.099	0.09	3.3E-02	0.15
PEPD	rs889140	chr19:38580840	A/G	0.463	0.06	6.7E-03	0.435	0.08	8.3E-05	0.43
CMIP	rs2925979	chr16:80092291	T/C	0.406	-0.05	4.1E-02	0.411	-0.09	2.1E-02	0.20
ZNF664	rs1187415	chr12:123057482	C/G	0.931	-0.16	1.0E-03	0.922	-0.14	3.7E-02	0.54
GPR109A	rs10847980	chr12:121953875	T/G	0.787	-0.04	1.2E-01	0.762	-0.10	4.4E-06	0.086
IRS1	rs7558386	chr2:227270383	A/G	0.314	-0.03	2.2E-01	0.357	-0.08	1.2E-04	0.13
LYPLAL1	rs12023821	chr1:217606512	C/G	0.577	-0.05	3.1E-02	0.557	-0.03	1.5E-01	0.42
TSC22D2	rs10804747	chr3:151577616	A/C	0.455	-0.06	9.9E-03	0.441	-0.06	1.6E-02	0.71
GNL3	rs3774347	chr3:52930530	T/C	0.939	-0.10	5.8E-02	0.960	-0.09	6.8E-02	0.78
FER	rs9326729	chr5:107875871	T/C	0.242	0.06	3.3E-02	0.208	0.05	6.4E-02	0.65
ARL15	rs697109	chr5:53339573	C/G	0.152	0.08	1.9E-02	0.166	0.08	2.8E-03	0.70
CITED2-RPS3AP24	rs7744360	chr6:139645617	A/C	0.966	0.10	2.3E-01	0.964	0.19	5.5E-02	0.49
VEGFA	rs7767854	chr6:44065304	T/C	0.328	-0.04	1.2E-01	0.314	-0.05	3.5E-02	0.73
TRIB1	rs2980884	chr8:126543538	A/G	0.304	0.02	4.1E-01	0.331	0.06	7.3E-03	0.28
PDE3A	rs10505860	chr12:20233685	C/G	0.683	0.06	3.7E-02	0.689	0.05	5.4E-02	0.75

Supplementary Table 4. Partial spearman correlation between adiponectin and other metabolic and cardiovascular-related traits

Sex	Sex	BMI	WC	WHR	Glucose	Insulin	HOMA-IR	HOMA-B	TG	HDL-C	LDL-C	TC
SP1_1M	men	-0.33 ‡	-0.32 ‡	-0.23 ‡	-0.15 ‡	-0.35 ‡	-0.35 ‡	-0.25 ‡	-0.43 ‡	0.40 ‡	-0.08	-0.11 †
	women	-0.48 ‡	-0.49 ‡	-0.36 ‡	-0.28 ‡	-0.41 ‡	-0.41 ‡	-0.22 ‡	-0.44 ‡	0.54 ‡	-0.12	-0.02
SP2_610K	men	-0.37 ‡	-0.38 ‡	-0.40 ‡	-0.10	-0.38 ‡	-0.36 ‡	-0.21 ‡	-0.36 ‡	0.35 ‡	0.00	-0.05
	women	-0.34 ‡	-0.38 ‡	-0.33 ‡	-0.24	-0.40 ‡	-0.43 ‡	-0.19 ‡	-0.40 ‡	0.42 ‡	-0.02	0.02
SP2_550K	men	-0.37 ‡	-0.38 ‡	-0.40 ‡	-0.33 ‡	-0.29‡	-0.33 ‡	-0.00	-0.32 ‡	0.37 ‡	0.01	0.03
	women	-0.38 ‡	-0.34 ‡	-0.19 ‡	-0.36 †	-0.44 ‡	-0.49 ‡	0.00	-0.31 †	0.50 ‡	0.02	0.08
KCPSII	men	-0.38 ‡	-0.41 ‡	n.a.	-0.21 ‡	n.a.	n.a.	n.a.	-0.34 ‡	0.31 ‡	-0.14 ‡	-0.24 ‡
	women	-0.38 ‡	-0.46 ‡	n.a.	-0.28 ‡	n.a.	n.a.	n.a.	-0.24 ‡	0.37 ‡	-0.17 ‡	-0.08
CLHNS	women	-0.36 ‡	-0.40 ‡	-0.28 ‡	-0.27 ‡	-0.46 ‡	-0.49 ‡	-0.28 ‡	-0.38 ‡	0.19 ‡	-0.04	-0.11 ‡
NHAPC Beijing	men	-0.35 ‡	-0.35 ‡	-0.27 ‡	-0.24 ‡	-0.28 ‡	-0.32 ‡	-0.06	-0.35 ‡	0.29 ‡	-0.16 ‡	-0.16 ‡
	women	-0.24 ‡	-0.21 ‡	-0.17 ‡	-0.13 ‡	-0.29 ‡	-0.30 ‡	-0.13 ‡	-0.39 ‡	0.34 ‡	-0.15 ‡	-0.10 †
NHAPC_Shanghai	men	-0.39 ‡	-0.42 ‡	-0.39 ‡	-0.22 ‡	-0.22 ‡	-0.25 ‡	0.00	-0.35 ‡	0.22 ‡	-0.15 ‡	-0.17 ‡
	women	-0.28 ‡	-0.28 ‡	-0.32 ‡	-0.18 ‡	-0.22 ‡	-0.25 ‡	-0.07	-0.35 ‡	0.36 ‡	-0.08 †	-0.03
Ansan	men	-0.29 ‡	-0.25 ‡	-0.24 ‡	-0.24 ‡	-0.24 ‡	-0.28 ‡	-0.02	-0.32 ‡	0.29 ‡	0.04	-0.04
	women	-0.21 ‡	-0.24 ‡	-0.24 ‡	-0.22 ‡	-0.29 ‡	-0.31 ‡	-0.06 †	-0.29 ‡	0.29 ‡	-0.02	-0.02
KING_GWAS	men	-0.26 ‡	-0.30 ‡	n.a.	-0.14 ‡	-0.32 ‡	-0.32 ‡	-0.26 ‡	-0.33 ‡	0.38 ‡	-0.10 †	-0.04
	women	-0.21 ‡	-0.21 ‡	n.a.	-0.15 †	-0.30 ‡	-0.30 ‡	-0.21 ‡	-0.32 ‡	0.38 ‡	-0.20 ‡	-0.13 †
SAPPHIRe	men	-0.13	-0.20†	-0.16	-0.15	-0.27†	-0.26†	-0.14	-0.16	0.27†	-0.07	-0.04
	women	-0.32‡	-0.32‡	-0.27†	-0.003	-0.30‡	-0.27†	-0.12	-0.21†	0.46‡	0.08	0.14

* The partial spearman correlation coefficient was calculated based on the adjustment for age

† $P < 0.05$

‡ $P < 0.001$

n.a. Not applicable

Supplementary Table 5. Measures of adiponectin and other metabolic and cardiovascular-related traits

Cohort	Sex	Adiponectin (ug/ml)	BMI (kg/m^2)	WC (cm)	WHR	Glucose (mmol/L)	Insulin (pmol/L)	HOMA-IR	HOMA-β (%)	TG (mmol/L)	HDL-C (mmol/L)	LDL-C (mmol/L)	TC (mmol/L)
SP1_1M	men	2.6 (2.0-3.6)	23.3 (3.4)	86.1 (9.8)	0.88 (0.06)	4.8 (4.5-5.1)	39.2 (27.1-59.0)	1.2 (0.8-1.8)	93.8 (62.5-140.0)	1.28 (0.84-1.80)	1.32 (0.31)	3.17 (0.80)	5.17 (0.86)
	women	4.0 (2.9-5.9)	22.1 (3.6)	75.8 (9.7)	0.80 (0.09)	4.6 (4.3-4.9)	38.9 (26.4-52.8)	1.1 (0.7-1.7)	107.0 (73.9-154.8)	0.89 (0.65-1.34)	1.61 (0.38)	3.00 (0.80)	5.11 (0.88)
SP2_610K	men	2.8 (1.9-3.7)	23.5 (4.2)	87.1 (9.8)	0.88 (0.06)	4.9 (4.5-5.4)	41.7 (28.5-62.5)	1.3 (0.8-2.2)	86.3 (57.3-135.4)	1.26 (0.88-1.86)	1.29 (0.28)	3.20 (0.81)	5.16 (0.92)
	women	3.9 (2.8-5.5)	22.4 (3.8)	76.8 (10.2)	0.81 (0.06)	4.6 (4.4-5.0)	38.9 (26.4-59.0)	1.2 (0.8-1.9)	102.0 (69.2-148.6)	1.00 (0.71-1.42)	1.59 (0.36)	3.11 (0.84)	5.23 (0.95)
SP2_550K	men	2.6 (1.9-3.6)	23.8 (3.4)	88.0 (11.7)	0.88 (0.06)	4.8 (4.5-5.1)	39.6 (27.8-62.5)	1.2 (0.8-2.0)	87.3 (59.3-139.4)	1.39 (0.98-1.98)	1.32 (0.29)	3.17 (0.87)	5.21 (0.95)
	women	3.9 (2.4-5.4)	22.9 (4.0)	78.3 (9.8)	0.80 (0.05)	4.7 (4.4-5.1)	43.4 (27.8-61.8)	1.3 (0.8-1.9)	102.9 (64.4-151.4)	0.97 (0.75-1.43)	1.66 (0.35)	3.07 (0.91)	5.25 (1.05)
KCPSII	men	5.4 (3.6-9.0)	24.6 (2.9)	85.6 (8.0)	n.a.	5.2 (4.9-5.7)	n.a.	n.a.	n.a.	1.32 (0.93-1.94)	1.29 (0.27)	2.92 (0.76)	4.91 (0.85)
	women	9.5 (6.4-15.4)	22.5 (3.0)	75.0 (8.3)	n.a.	4.9 (4.6-5.2)	n.a.	n.a.	n.a.	0.81 (0.59-1.13)	1.55 (0.35)	2.64 (0.71)	4.63 (0.84)
CLHNS	women	2.5 (1.9-3.3)	24.3 (4.4)	81.1 (10.9)	0.88 (0.05)	6.1 (5.6-6.6)	46.8 (30.0-75.6)	2.2 (1.3-3.8)	59.7 (39.2-92.2)	1.25 (0.91-1.78)	1.06 (0.27)	3.09 (0.86)	4.83 (1.00)
NHAPC Beijing	men	11.4 (6.8-19.0)	24.8 (3.38)	87.3 (10.4)	0.92 (0.07)	5.7 (5.2-6.3)	70.8 (49.2-97.8)	3.1 (2.1-4.5)	108.5 (74.7-152.3)	1.08 (0.72-1.76)	1.24 (0.33)	3.33 (0.92)	4.73 (0.89)
	women	15.7 (9.4-23.8)	25.7 (3.82)	84.7 (10.4)	0.88 (0.08)	5.6 (5.2-6.1)	87.0 (66.0-118.2)	3.8 (2.7-5.3)	142.9 (95.5-195.0)	1.17 (0.83-1.77)	1.33 (0.32)	3.62 (1.01)	5.06 (1.01)
NHAPC_Shanghai	men	10.9 (6.4-17.7)	23.5 (3.24)	84.1 (10.6)	0.92 (0.07)	5.3 (5.0-5.8)	78.0 (58.2-104.4)	3.1 (2.3-4.4)	143.1 (98.1-205.2)	1.00 (0.70-1.61)	1.19 (0.32)	2.83 (0.84)	4.25 (0.88)
	women	16.7 (10.4-25.1)	23.8 (3.44)	79.9 (9.9)	0.87 (0.07)	5.2 (4.9-5.6)	88.8 (64.8-120.6)	3.5 (2.4-4.9)	169.9 (121.2-254.9)	1.08 (0.77-1.59)	1.31 (0.33)	3.21 (0.93)	4.65 (0.92)
Ansan	men	5.0 (2.7-6.3)	24.5 (3.0)	75.9 (7.9)	0.8 (0.1)	5.8 (4.9-5.8)	73.5 (45.2-80.4)	2.9 (1.5-2.8)	104.2 (65.9-122.5)	1.76 (1.03-2.12)	1.21 (0.28)	3.43 (0.82)	5.29 (0.91)
	women	8.2 (4.7-10.5)	24.7 (2.7)	84.0 (7.2)	0.9 (0.0)	5.2 (4.7-5.3)	68.5 (43.8-77.5)	2.4 (1.3-2.5)	129.0 (82.1-154.1)	1.42 (0.87-1.73)	1.11 (0.26)	3.18 (0.81)	5.09 (0.87)
KING_GWAS	men	8.6 (6.2-12.0)	23.3 (2.6)	84.8 (7.5)	n.a.	5.2 (4.9-5.7)	25.7 (15.3-38.9)	0.9 (0.5-1.4)	40.0 (25.7-62.4)	1.18 (0.85-1.67)	1.51 (0.40)	3.20 (0.80)	5.33 (0.83)
	women	14.2 (10.0-19.6)	22.5 (3.1)	83.0 (8.9)	n.a.	5.1 (4.8-5.5)	27.8 (19.4-43.1)	0.9 (0.6-1.4)	53.3 (33.8-75.8)	1.06 (0.80-1.44)	1.75 (0.39)	3.51 (0.82)	5.80 (0.85)
SAPPHIRe	men	3.7 (2.8-5.6)	25.9 (3.4)	88.2 (9.1)	0.91 (0.05)	5.1 (4.7-5.4)	46.5 (29.2-66.0)	1.5 (0.9-2.2)	85.1 (60.0-126.3)	1.46 (0.97-2.05)	0.98 (0.24)	3.15 (1.03)	4.83 (1.05)
	women	5.3 (3.9-7.2)	24.7 (3.4)	79.9 (10.0)	0.83 (0.08)	4.9 (4.9-5.2)	43.1 (29.9-62.5)	1.3 (0.9-2.1)	101.5 (68.3-141.9)	1.07 (0.75-1.52)	1.15 (0.32)	3.18 (1.07)	4.90 (1.14)

Supplementary Table 6. Regions for conditional analysis and the SNPs used as conditioning variables

Locus	**Conditioned SNP**	**Start position**	**End position**	**Number of SNPs**
FGFR2	rs3943077	122,935,076	122,435,076	1300
HIVEP2	rs12211360	142,661,525	143,661,525	980
CDH13	rs4783244	80,719,769	81,719,769	1900
ADIPOQ	rs10937273	187,532,389	188,532,389	950
PEPD	rs889140	38,080,840	39,080,840	800
CMIP-CDH13	rs4783244	79,592,291	81,719,769	3500
CMIP-CDH13	rs2925979	79,592,291	81,719,769	3500
GPR109A-ZNF664	rs1187415	121,400,000	123,400,000	1300
GPR109A-ZNF664	rs10847980	121,400,000	123,400,000	1300

Positions are based on Build 36, hg18