SUPPLEMENTARY NOTE

Identification of new susceptibility loci for type 2 diabetes and shared etiological pathways with coronary heart disease

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Supplementary Methods

Description of participating cohorts

Pakistan Risk of Myocardial Infarction Study (PROMIS)

PROMIS is an ongoing retrospective case-control study in Pakistan. Since 2005, the study has enrolled close to 42,000 participants; the present investigation has included close to 25,000 participants that had been enrolled until 2011 and on whom DNA samples were available for genotyping. Participants aged 30-80 years were admitted across nine recruitment centers across Pakistan. Participants were not recruited if any of the following features had been evident: i) a previous history of cardiovascular disease (including self-reported MI, angina, coronary revascularization, stroke, transient ischaemic attack, or peripheral vascular disease, presence of cardiogenic shock); ii) a history of a viral or bacterial infection in the previous 2 weeks; iii) current hospitalization for acute cerebrovascular events; iv) MI secondary to any surgery; v) documented chronic conditions, such as malignancy, any chronic infection, leprosy, malaria or other bacterial/parasitic infections, chronic inflammatory disorders, hepatitis or renal failure on past medical history; vi) pregnancy or related conditions; or vii) unable to provide consent. Type-2 diabetes was defined based on HbA1c levels > 6.5 or fasting glucose > 125 or physician's diagnosis or prior use of glucose lowering medications or self-report.

The Bangladesh Risk of Acute Vascular Events Study (BRAVE)

BRAVE is a cross-sectional study of in Bangladesh. Both type-2 diabetes cases and controls (male or female; age between 30-80 years) were enrolled from different collaborating hospitals in Dhaka. Participants were not recruited into BRAVE if any of the following features had been evident: i) a previous history of cardiovascular disease (including self-reported MI, angina, coronary revascularization, stroke, transient ischaemic attack, or peripheral vascular disease, presence of cardiogenic shock); ii) a history of a viral or bacterial infection in the previous 2 weeks; iii) current hospitalization for acute cerebrovascular events; iv) MI secondary to any surgery; v) documented chronic conditions, such as malignancy, any chronic infection, leprosy, malaria or other bacterial/parasitic infections, chronic inflammatory disorders, hepatitis or renal failure on past medical history; vi) pregnancy or related conditions; or vii) unable to provide consent. Type-2 diabetes was defined based on physician's diagnosis, prior use of glucose-lowering medications or self-report.

The Sikh Diabetes Study/Asian Indian Diabetic Heart Study (SDS/AIDHS)

Participants of SDS were recruited from Sikhs living in the Northern states of India, including Punjab, Haryana, Himachal Pradesh, Delhi, and Jammu and Kashmir. Participants comprised individuals with type-2 diabetes mellitus (T2D; defined as physician diagnosis or treatment, a fasting plasma glucose level of ≥7.0mmol/L, or 2-hour post glucose load level of ≥11.1mmol/L, on more than one occasion with symptoms of diabetes) or controls with no prior history of diabetes and normal glucose tolerance (fasting glucose <6mmol/L, post glucose <7.8mmol/L). All participants provided a written informed consent for investigations. All SDS protocols and consent documents were reviewed and approved by the University of Oklahoma and the University of Pittsburgh Institutional Review Boards as well as the Human Subject Protection Committees at the participating hospitals and institutes in India.

Risk Assessment of Cerebrovascular Events study (RACE)

RACE is an ongoing retrospective cross-sectional study that aims to identify and evaluate genetic, lifestyle and biomarker determinants of stroke and its subtypes in Pakistan. Samples were recruited from six hospital centers in Pakistan. Participants were not recruited if any of the following features had been evident: i) a previous history of cardiovascular disease (including self-reported MI, angina, coronary revascularization, stroke, transient ischemic attack, or peripheral vascular disease, presence of cardiogenic shock); ii) a history of a viral or bacterial infection in the previous 2 weeks; iii) current hospitalization for acute cerebrovascular events; iv) MI secondary to any surgery; v) documented chronic conditions, such as malignancy, any chronic infection, leprosy, malaria or other bacterial/parasitic infections, chronic inflammatory disorders, hepatitis or renal failure on past medical history; vi) pregnancy or related conditions; or vii)

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unable to provide consent. Type-2 diabetes was defined based on HbA1c levels > 6.5 or fasting glucose > 125 or physician's diagnosis or prior use of glucose lowering medications or self-report.

EpiDREAM – A prospective cohort to determine environment and genetic determinants of metabolic syndrome related factors (EPIDREAM)

The EpiDREAM study included 25,063 participants from 191 centers who were screened for the DREAM clinical trial. Individuals at risk for dysglycemia because of family history, ethnicity, and abdominal obesity, between the ages of 18 and 85 years, were screened using an oral glucose tolerance test from July 2001 to August 2003 as previously described. 5,269 individuals with impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) (or both) participated in the DREAM trial. 13,721 individuals who were not eligible for the DREAM trial or who declined to enter the trial agreed to long-term follow-up. Thus, in total, 18,990 individuals were prospectively followed up for a median of 3.3 years and 18,486 individuals who provided a blood sample for DNA were available for analysis. The 2003 American Association criteria were used for the definition of T2D: either the fasting plasma glucose was ≥7.0 mmol/L or the 2-h glucose was ≥11.1 mmol/L.

The National FINRISK Study (FINRISK)

FINRISK studies get their roots from the North Karelia project, initiated in the early 1970's. Nowadays they are carried at 5 year intervals and designed to assess the levels of coronary risk factors in random population samples in different geographical areas of Finland. The study design is a cross-sectional population survey stratified to contain at least 250 subjects of each sex and 10 year age group (25-34, 35-44, 45-54, 55-64, and 65-74 years of age) from each area. All participants are clinically screened for assessment of the most established environmental cardiovascular risk factors and fill out a questionnaire. The protocols are the same as those established by the MONICA and EHES projects. The projects are routinely followed by linking them annually to country-wide electronic health registry data as well as to the National Causes-of-Death register.

The study individuals were invited for a clinical examination and series of interviews, performed by nurses. Questionnaires were filled before this visit and overviewed by a study nurse at the visit. The study protocol is submitted for review boards before each 5-year study. All participants give written informed consent, and the studies are approved by the institutional review board of the Helsinki and Uusimaa Hospital District, Helsinki, Finland (previously studies also approved by the institutional review board of the National Public Health Institute).

Main topics of questionnaire data have been: Detailed dietary questions, marital status, education, occupation, household income, history of myocardial infarction, stroke or cerebral hemorrhage, blood pressure, cardiac insufficiency, effort angina (angina pectoris), cancer, asthma, pulmonary emphysema, bronchitis, chronic bronchial catarrh, gallstones, cholecystitis, rheumatoid arthritis, other disease of the joints, degenerative arthritis of the back, other illness of the back, chronic urinary tract infection, kidney problems, high blood cholesterol level, high blood pressure, medication, parental CVD, diabetes, phlegm cough, work and leisure time exercise, smoking, weight gain, alcohol.

Each study participant donated blood for both first-line laboratory measurements and for further analyses. First-line analyses from all included: joint status, height, weight, waist-hip ratio, pulse, blood pressure, cholesterol, HDL, triglycerides, and GGT.

MedStar

The MedStar study is a Washington Hospital Center based study that recruited a cohort of patients undergoing cardiac catheterization at Washington Hospital. All subjects have been enrolled in a Washington Hospital Institutional Review Board approved protocol and all subjects gave written informed consent. Enrolment criteria include any clinical indication for cardiac catheterization and ability to give informed consent. Type-2 diabetes was defined based on physician's diagnosis, prior use of glucose lowering medications or self-report.

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The London Life Sciences Prospective Population study (LOLIPOP)

The LOLIPOP study is a population-based cohort of South Asian and European men and women aged 35-75 years living in West London. Participants were recruited from the lists of 58 GPs between 2002 and 2008. South Asians were of self-reported South Asian ancestry, and were recruited to the study if all 4 grandparents were born in the Indian Subcontinent (countries of India, Pakistan, Sri Lanka or Bangladesh). Data on medical history, family history, current prescribed medication, cardiovascular risk factors, alcohol intake and leisure-time physical activity were obtained by a trained research nurse using an interviewer-administered questionnaire. Country of birth of participants, parents, and grandparents were recorded together with language and religion, for assignment of ethnic subgroups. Physical measurements included blood pressure (mean of 3 readings, taken with an Omron 705CP), height, weight, waist and hip circumference, and 12 lead ECG. Blood was collected after an 8 hour fast for plasma glucose, total and HDL cholesterol, triglycerides, insulin and high sensitivity C-reactive protein. T2D was defined as physician diagnosis on treatment or fasting glucose ≥7.0mmol/L. Controls had no history of T2D, and had fasting glucose <7mmol/L. All participants gave written informed consent, and the study was approved by the Local Research Ethics Committee.

Singapore Indian Eye Study (SINDI)

SINDI is a population-based, cross-sectional study of 3,400 men and women of South Asian ancestry (self reported), living in the South-Western part of Singapore, recruited as part of the Singapore Indian Chinese Cohort Eye Study. Age stratified random sampling was used to select 6,350 eligible participants, of which 3,400 participated in the study (75.6% response rate). T2D cases and controls were selected from the population based cross sectional study where T2D was defined as either a history of diabetes or HbA1c level more than 6.5%. Controls had no history of diabetes and HbA1c level <6.0%.

The TAIwan metaboCHIp consortium (TAICHI)

The TAICHI consortium is formed of seven studies through a collaborative effort between investigators based in the U.S. and Taiwan. The main U.S academic sites participating in the TAICHI consortium include Stanford University School of Medicine in Stanford, California; Hudson-Alpha Biotechnology Institute in Huntsville, Alabama; and Harbor-UCLA in Los Angeles, California. The main academic sites in Taiwan include National Health Research Institute (NHRI); National Taiwan University Hospital (NTUH); Taipei and Taichung Veteran's General Hospitals (VGH) and Tri-Service General Hospital (TSGH). These investigators have assembled a large, well-phenotyped sample set consisting of >13,000 Han Chinese from seven existing studies. The consortium aims to identify genetic determinants of atherosclerosis and diabetes related traits in East Asians and to fine map validated loci identified in other race/ethnic groups.

1. **Taiwan Diabetes and RelAted Genetic COmplicatioN (Taiwan DRAGON) cohort study (PI - Dr. Wayne Huey-Herng Sheu)** of type 2 diabetes (T2D) at the Veteran's General Hospital in Taichung, Taiwan (Taichung VGH). Participants include individuals with either newly diagnoses or established diabetes who visit the diabetes outpatient clinic on a regular basis. Subjects with hyperglycemia who do not meet criteria for T2D defined by IDF are not included. Individuals participate in a health examination program at Taichung VGH are also interviewed. Specialized tests include an oral glucose tolerance tests (OGTT) in subjects without an established diagnosis of diabetes.
2. **Taiwan USA Diabetes Retinopathy (TUDR) cohort study (PI - Dr. Wayne Huey-Herng Sheu)** enrolled subjects with T2D receiving care at Taiching Veteran's General Hospital, a small number of subjects were included from Tri-Service General Hospital (TSGH). All TUDR subjects underwent a complete fundoscopic examination to carefully document the presence and extent of retinopathy. To date, a total of 2,222 unrelated T2D subjects with and without retinopathy were ascertained and have undergone metabochip genotyping. Of the 2,222 subjects, 1,201 were T2D without eye diseases, 479 were T2D with NPDR and 542 T2D with PDR. In addition to DNA and buffy coats, fasting blood for future measurement of serum/plasma biomarkers has also been

Nature Genetics: doi:10.1038/ng.3943

banked. A variety of additional clinical related phenotypes are available. All 2,222 overlaps with the Taiwan Dragon Study.

3. **Healthy Aging Longitudinal Study in Taiwan (HALST) (PI – Dr. Agnes Chao Hsiung)** is a population based multi-site cohort study of ambulatory adults aged > 55 years living in 7 major geographic regions of Taiwan, established by the NHRI. The aim of the study is to investigate the multidimensional determinants, including lifestyle, genetic, metabolic, and inflammatory factors, of an older Asian population. These 7 locations include both urban and rural areas: two are in the north (Taipei's Shilin District and Taoyuan County's Yangmei Township), two in central Taiwan (Miaoli City in Miaoli County and Changhua City in Changhua County), two in the south (Puzi, Chiayi County, and Kaohsiung's Lingya District), and one in the east (Hualien City/County). The only exclusion criteria are presence of highly contagious diseases, advanced illnesses with limited life span or bedridden status, dementia, other advanced neurological deficit, severe hearing loss, and institutionalization in a chronic care facility for any reason. Over 5000 subjects have been recruited over a five-year period (2008-2012) from seven recruitment sites across the country. Follow-up in person visits are currently ongoing and will continue throughout a second 5-year study cycle scheduled that began in 2013 (~1000 subjects / year). Within each wave, participants are to be followed up by telephone contact every year for vital status and for updates on health-related conditions. Medical records are requested to confirm the development of any new health conditions. Vital status, health claims, health care utilization data are being collected for the cohort on a regular basis by linking to the National Death Registry Database and the National Health Insurance Database. HALST served as one the main "control" cohorts for this study after exclusions of subjects with a self-report of CAD or a ECG diagnostic of prior MI.
4. **Stanford-Asian Pacific Program in Hypertension and Insulin Resistance (SAPPHIRe) family based study (PIs – Dr. Thomas Quertermous, Agnes Chao Hsiung, and Wayne Huey-Herng Sheu**) was established in 1995 with an initial goal of identifying major genetic loci underlying hypertension and insulin resistance through linkage in East Asian populations. SAPPHIRe was also one of four networks participating the NHLBI's Family Blood Pressure Program (FBPP). At the outset, SAPPHIRe involved recruitment sites in the San Francisco Bay Area, Hawaii, and Taiwan. However, a majority of the ~1,700 sibpairs in SAPPHIRe were recruited from 3 centers in Taiwan (NTUH, Taipei VGH and Taichung VGH) with NHRI being the DCC. Sibpairs were either highly concordant or discordant for blood pressure and a subset underwent an insulin suppression test. Many metabolic variables associated with blood pressure and insulin resistance were examined in the first 5-year investigative cycle funded by the NIH (1995-2000). Further extensive phenotyping through return visits and regular follow ups occurred between 2001 and 2008 in the Taiwanese SAPPHIRe participants which included echocardiographic and multi-detector row CT imaging procedures. These efforts were facilitated by a programmatic collaboration between the NHLBI's FBPP and the National Health Research Institute in Taiwan. Like HALST, SAPPHIRe served predominantly as a "control" cohort in this study. Only one sib per family was included as a control in this study.

BioBank Japan (BBJ)

We selected T2D cases from individuals registered in BioBank Japan as having T2D (BBJ1 cases, n = 9,817). Control groups consisted of individuals registered in BioBank Japan as not having T2D but with diseases other than T2D (cerebral aneurysm, esophageal cancer, endometrial cancer, chronic pulmonary emphysema or glaucoma) or volunteers from the Osaka-Midosuj Rotary Club and Pharma SNP consortium (BBJ1 controls, n = 6,763). We also analyzed independent case and control individuals registered in the BioBank Japan (BBJ2, cases, n = 5,646 and controls, n = 19,420). Controls were individuals registered in BioBank Japan as not having T2D but with diseases other than T2D (colorectal cancer, breast cancer, prostate cancer, lung cancer, gastric cancer, arteriosclerosis obliterans, cardiac arrhythmias, brain infarction, myocardial infarction, gallbladder cancer and cholangiocarcinoma, pancreatic cancer, drug eruptions, rheumatoid arthritis,

Nature Genetics: doi:10.1038/ng.3943

amyotrophic lateral sclerosis, liver cancer, liver cirrhosis, osteoporosis, or uterine myoma). There was no overlap in individuals in BBJ1 and BBJ2.

The Mount Sinai BioMe Biobank

The Bio*Me* Biobank is an ongoing, prospective, hospital- and outpatient- based population research program operated by The Charles Bronfman Institute for Personalized Medicine (IPM) at Mount Sinai and has enrolled over 33,000 participants since September 2007. Bio*Me* is an Electronic Medical Record (EMR)-linked biobank that integrates research data and clinical care information for consented patients at The Mount Sinai Medical Center, which serves diverse local communities of upper Manhattan with broad health disparities. Bio*Me* populations include 25% of African ancestry (AA), 36% of Hispanic Latino ancestry (HL), 30% of white European ancestry (EA), and 9% of other ancestry. The Bio*Me* disease burden is reflective of health disparities in the local communities. Bio*Me* operations are fully integrated in clinical care processes, including direct recruitment from clinical sites waiting areas and phlebotomy stations by dedicated recruiters independent of clinical care providers, prior to or following a clinician standard of care visit. Recruitment currently occurs at a broad spectrum of over 30 clinical care sites.

The T2D case and control definition algorithms used were developed by a multidisciplinary team of scientists, clinicians and software specialists have been validated with excellent performance statistics; 100% sensitivity and >98% positive predictive value for cases, and ≥98% sensitivity and ≥98% positive predictive value for controls. Comprehensive documentation of the algorithms can be found at https://www.phekb.org/phenotype/type-2-diabetes-mellitus.

Details on studies contributing to the CHD meta-analysis

The Cambridge MI studies comprised of 16,093 CHD cases and 16,616 unaffecteds from the EPIC-CVD study, a case-cohort study recruited across 10 European countries, the Copenhagen City Heart Study (CCHS), the Copenhagen Ischemic Heart Disease Study (CIHDS) and the Copenhagen General Population Study (CGPS) all recruited within Copenhagen, Denmark. The Carmbridge MI SAS studies comprised up to 7,654 CHD cases and 7,014 controls from the Pakistan Risk of Myocardial Infarction Study (PROMIS) a case-control study that recruited samples from 9 sites in Pakistan, and the Bangladesh Risk of Acute Vascular Events (BRAVE) study based in Dhaka, Bangladesh. The EA studies comprised 4,129 CHD cases and 6,369 controls recruited from 7 studies across Taiwan that collectively comprise the TAIwan metaboCHIp (TAICHI) Consortium. Samples from EPIC-CVD, CCHS, CIHDS, CGPS, BRAVE and PROMIS were all genotyped on a customized version of the Illumina CardioMetabochip (manufactured by Illumina, San Diego, USA) referred to as the Metabochip+, in two Illumina-certified laboratories located in Cambridge, UK, and Copenhagen, Denmark. TAICHI samples were genotyped using the standard CardioMetabochip. For each study, samples were removed if they had a call rate < 0.97, average heterozygosity >±3 standard deviations away from the overall mean heterozygosity or their genotypic sex did not match their reported sex. One of each pair of duplicate samples and first-degree relatives (assessed with a kinship co-efficient > 0.2) were removed. Cardio-metabochip data were also obtained from the Women Health Initiative Study and the ARIC study; the two studies underwent same QC as described for the TAICH study. Across all studies, SNP exclusions were based on minor allele frequency (MAF) < 0.01, P < 1x10-6 for Hardy-Weinberg Equilibrium or call rate (CR) less than 0.97. CARDIoGRAMplusC4D Consortium data were obtained from http://www.cardiogramplusc4d.org/. Only non-overlapping samples were used for meta-analyses. Fixed effects inverse variance weighted meta-analysis was used to combine the effects across studies in METAL.

Comparison of bivariate scan based on summary statistics with direct genotypes

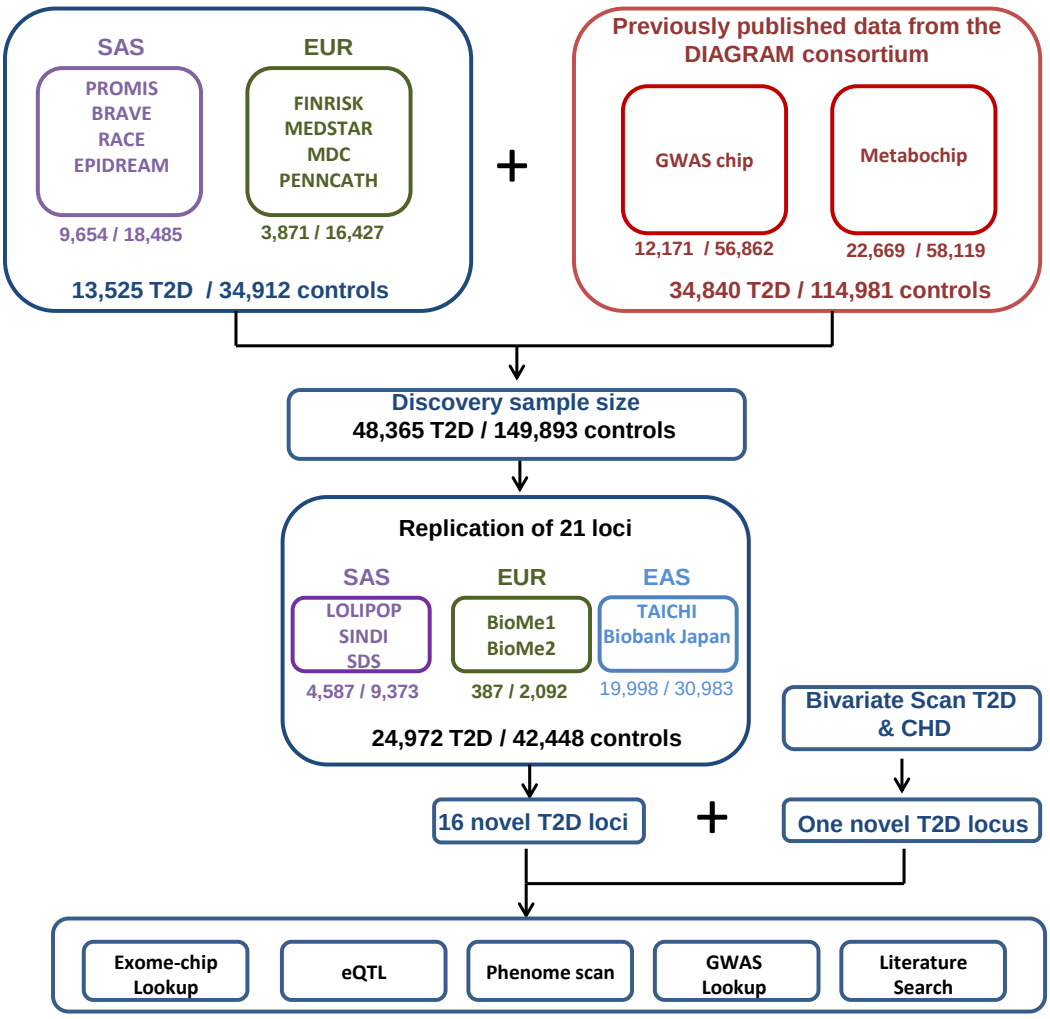
To investigate the behavior of our bivariate analysis under the null hypothesis, we obtained data from the PROMIS cohort. We used two independent groups in PROMIS: PROMIS1 including 4632 individuals with myocardial infarction and 4459 controls totaling 9091 individuals and PROMIS 2 including 4346 individuals with type 2 diabetes and 4028 controls totaling 8374 individuals. The samples selected for both groups are not overlapping. We selected a subset of variants that were pruned for LD (reflecting independent SNPs), with minor allele frequencies greater than 5%, excluded variants that departed HWE ($P < 10^{-5}$), and had high imputation accuracy (INFO scores greater than 0.7). This included 24030 variants in total. For these variants, we calculate association Z-scores for both endpoints (analyzed separately). We also calculated

Nature Genetics: doi:10.1038/ng.3943

individual Z-score in a second analysis where both sets (individual level data) were combined together. Bivariate (2 df test) statistics were then calculated for (i) Z-scores for the sets analyzed separately, and (ii) Z-scores with the two data sets analyzed together. While not completely a perfect comparison, **Supplementary Figure 7b** shows that both sets of scores are correlated (rho = 0.61 – 0.67) indicating that the information obtains by the summary method is similar to what one would obtain (under the null) for individual level data analyzed jointly.

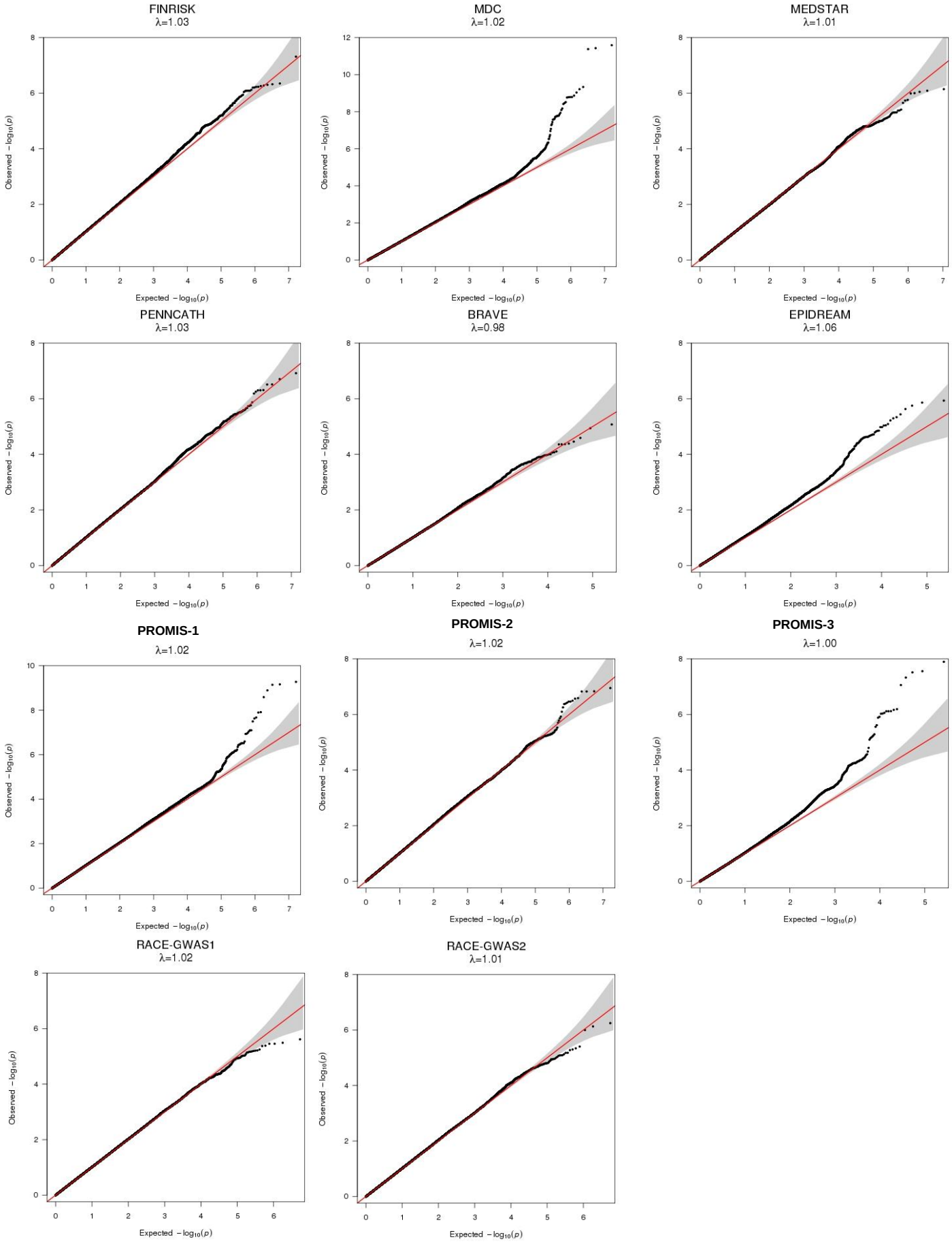
Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 1a. A flowchart depicting the design of our study. The sample-size information is provided as number of cases/number of controls. In Supplementary Figure 2, BioMe1 is listed as MSSE-AFFY, and BioMe2 is listed as MSSE-ILLU.



Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 1b. QQ plots for each discovery cohorts.

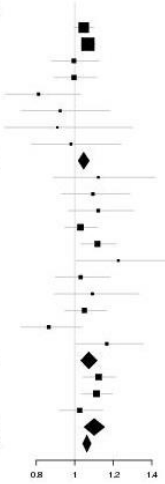


Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 2. Forest plots for previously unreported SNPs in association with T2D.

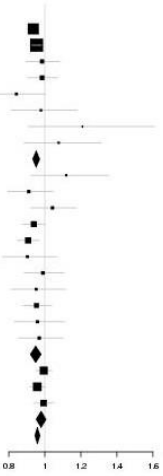
rs2867125, *TMEM18*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	C	T	0.83	1.05	1.00	1.10	6.08e-02	9495	53076	
DIAGRAM metabo	C	T	0.83	1.07	1.03	1.11	3.44e-04	22669	58119	
FINRISK	C	T	0.85	1.00	0.88	1.13	9.44e-01	1563	7553	
MDC	C	T	0.83	1.00	0.89	1.11	9.48e-01	1418	5722	
MEDSTAR	C	T	0.16	0.81	0.64	1.03	8.86e-02	358	964	
PENNCATH	C	T	0.18	0.92	0.72	1.18	5.30e-01	278	1113	
MSSE AFFY	C	T	0.81	0.91	0.64	1.30	6.06e-01	132	445	
MSSE ILLU	C	T	0.79	0.98	0.78	1.24	8.67e-01	255	1647	
META in EUR	**C**	**T**		**1.05**	**1.02**	**1.07**	**8.59e-04**	**36168**	**128639**	**0.21**
BRAVE	C	T	0.81	1.12	0.89	1.42	3.36e-01	250	2189	
EPIDREAM	C	T	0.80	1.09	0.93	1.29	2.76e-01	612	2039	
PROMIS GWAS1	C	T	0.80	1.12	0.96	1.31	1.37e-01	737	1804	
PROMIS GWAS2	C	T	0.80	1.03	0.95	1.12	4.87e-01	3930	3250	
PROMIS metabo	C	T	0.80	1.12	1.03	1.21	8.42e-03	2439	7088	
RACE GWAS1	C	T	0.77	1.23	1.00	1.50	4.56e-02	602	598	
RACE GWAS2	C	T	0.80	1.03	0.90	1.18	6.66e-01	1084	1527	
LOLIPOP IA317	C	T	0.80	1.09	0.89	1.33	3.90e-01	434	1686	
LOLIPOP IA610	C	T	0.81	1.05	0.95	1.16	3.54e-01	1779	4768	
SIKH	C	T	0.82	0.87	0.72	1.04	7.16e-02	826	748	
SINDI	C	T	0.80	1.17	1.00	1.36	2.96e-02	1169	2146	
META in SAS	**C**	**T**		**1.07**	**1.03**	**1.12**	**3.68e-04**	**13862**	**27843**	**0.11**
JAPAN1	C	T	0.91	1.12	1.04	1.21	2.61e-03	9817	6763	
JAPAN2	C	T	0.90	1.11	1.04	1.20	4.24e-03	5646	19420	
TAICHI	C	T	0.93	1.03	0.92	1.15	6.50e-01	4535	4800	
META in EAS	**C**	**T**		**1.10**	**1.05**	**1.15**	**7.75e-05**	**19998**	**30983**	**0.00**
META in ALL	**C**	**T**		**1.06**	**1.04**	**1.08**	**2.18e-09**	**70028**	**187465**	**0.18**



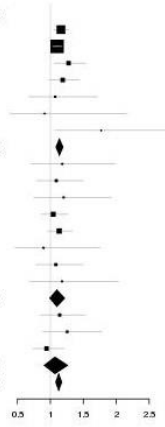
rs11123406, *BCL2L11*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	C	T	0.64	0.94	0.90	0.97	1.35e-04	12171	56862	
DIAGRAM metabo	C	T	0.64	0.95	0.93	0.98	1.03e-03	22669	58119	
FINRISK	C	T	0.65	0.98	0.90	1.08	7.44e-01	1563	7553	
MDC	C	T	0.62	0.98	0.90	1.07	7.18e-01	1418	5722	
MEDSTAR	C	T	0.38	0.84	0.71	1.00	5.35e-02	358	964	
PENNCATH	C	T	0.38	0.98	0.81	1.18	8.20e-01	278	1113	
MSSE AFFY	C	T	0.60	1.21	0.91	1.61	1.94e-01	132	445	
MSSE ILLU	C	T	0.62	1.08	0.88	1.31	4.64e-01	255	1647	
META in EUR	**C**	**T**		**0.95**	**0.93**	**0.97**	**1.34e-06**	**38844**	**132425**	**0.15**
BRAVE	C	T	0.37	1.12	0.92	1.36	2.53e-01	250	2189	
EPIDREAM	C	T	0.33	0.91	0.79	1.05	1.87e-01	612	2039	
PROMIS GWAS1	C	T	0.41	1.04	0.92	1.18	5.02e-01	737	1804	
PROMIS GWAS2	C	T	0.41	0.94	0.88	1.00	6.38e-02	3930	3250	
PROMIS metabo	C	T	0.41	0.91	0.85	0.97	3.87e-03	2439	7088	
RACE GWAS1	C	T	0.41	0.90	0.76	1.07	2.33e-01	602	598	
RACE GWAS2	C	T	0.39	0.99	0.88	1.11	8.51e-01	1084	1527	
LOLIPOP IA317	C	T	0.43	0.95	0.81	1.12	5.43e-01	434	1686	
LOLIPOP IA610	C	T	0.41	0.95	0.88	1.04	2.59e-01	1779	4768	
SIKH	C	T	0.40	0.96	0.83	1.11	7.83e-01	826	748	
SINDI	C	T	0.34	0.97	0.85	1.10	9.20e-01	1169	2146	
META in SAS	**C**	**T**		**0.95**	**0.92**	**0.98**	**1.11e-03**	**13862**	**27843**	**0.00**
JAPAN1	C	T	0.57	0.99	0.95	1.04	8.00e-01	9817	6763	
JAPAN2	C	T	0.56	0.96	0.92	1.00	4.43e-02	5646	19420	
TAICHI	C	T	0.54	0.99	0.94	1.05	8.06e-01	4535	4800	
META in EAS	**C**	**T**		**0.98**	**0.95**	**1.01**	**1.30e-01**	**19998**	**30983**	**0.00**
META in ALL	**C**	**T**		**0.96**	**0.94**	**0.97**	**8.57e-09**	**72704**	**191251**	**0.02**



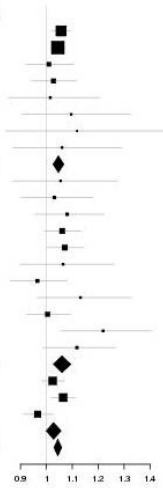
rs2706785, *TMEM155*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	G	A	0.05	1.16	1.06	1.27	1.75e-03	8548	48669	
DIAGRAM metabo	G	A	0.05	1.10	1.04	1.17	2.00e-03	22669	58119	
FINRISK	G	A	0.06	1.28	1.06	1.53	9.33e-03	1563	7553	
MDC	G	A	0.05	1.19	0.98	1.44	7.91e-02	1418	5722	
PENNCATH	G	A	0.04	1.07	0.67	1.72	7.66e-01	278	1113	
MSSE AFFY	G	A	0.04	0.91	0.39	2.16	8.36e-01	132	445	
MSSE ILLU	G	A	0.04	1.77	1.07	2.93	2.64e-02	255	1647	
META in EUR	**G**	**A**		**1.14**	**1.08**	**1.19**	**1.15e-07**	**34863**	**123268**	**0.02**
BRAVE	G	A	0.03	1.18	0.70	1.99	5.29e-01	250	2189	
EPIDREAM	G	A	0.04	1.09	0.79	1.51	6.03e-01	612	2039	
PROMIS GWAS1	G	A	0.02	1.20	0.75	1.93	4.47e-01	737	1804	
PROMIS GWAS2	G	A	0.03	1.04	0.86	1.27	6.74e-01	3930	3250	
PROMIS metabo	G	A	0.04	1.13	0.96	1.34	1.44e-01	2439	7088	
RACE GWAS1	G	A	0.03	0.90	0.46	1.75	7.50e-01	602	598	
RACE GWAS2	G	A	0.03	1.08	0.78	1.50	6.31e-01	1084	1527	
SIKH	G	A	0.02	1.18	0.68	2.03	2.19e-01	826	748	
META in SAS	**G**	**A**		**1.10**	**0.99**	**1.22**	**7.45e-02**	**10480**	**19243**	**0.00**
JAPAN1	G	A	0.01	1.14	0.85	1.53	3.78e-01	9817	6763	
JAPAN2	G	A	0.01	1.25	0.89	1.78	2.02e-01	5646	19420	
TAICHI	G	A	0.01	0.94	0.73	1.21	6.34e-01	4535	4800	
META in EAS	**G**	**A**		**1.07**	**0.91**	**1.26**	**4.31e-01**	**19998**	**30983**	**0.00**
META in ALL	**G**	**A**		**1.13**	**1.08**	**1.17**	**2.40e-08**	**65341**	**173494**	**0.00**



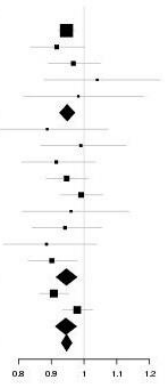
rs329122, *PHF15*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	A	G	0.43	1.06	1.02	1.09	1.51e-03	12171	56862	
DIAGRAM metabo	A	G	0.43	1.04	1.02	1.07	1.81e-03	22669	58119	
FINRISK	A	G	0.41	1.01	0.92	1.11	8.34e-01	1563	7553	
MDC	A	G	0.42	1.03	0.95	1.12	5.24e-01	1418	5722	
MEDSTAR	A	G	0.42	1.01	0.85	1.21	8.66e-01	358	964	
PENNCATH	A	G	0.42	1.10	0.91	1.33	3.44e-01	278	1113	
MSSE AFFY	A	G	0.41	1.12	0.84	1.48	4.38e-01	132	445	
MSSE ILLU	A	G	0.44	1.06	0.87	1.29	5.54e-01	255	1647	
META in EUR	**A**	**G**		**1.05**	**1.03**	**1.07**	**6.15e-06**	**38844**	**132425**	**0.00**
BRAVE	A	G	0.36	1.05	0.87	1.28	5.87e-01	250	2189	
EPIDREAM	A	G	0.39	1.03	0.90	1.18	6.51e-01	612	2039	
PROMIS GWAS1	A	G	0.38	1.08	0.96	1.22	2.19e-01	737	1804	
PROMIS GWAS2	A	G	0.38	1.06	0.99	1.14	8.55e-02	3930	3250	
PROMIS metabo	A	G	0.38	1.07	1.00	1.14	4.18e-02	2439	7088	
RACE GWAS1	A	G	0.37	1.06	0.90	1.26	4.71e-01	602	598	
RACE GWAS2	A	G	0.39	0.97	0.86	1.08	5.46e-01	1084	1527	
LOLIPOP IA317	A	G	0.39	1.13	0.96	1.33	1.30e-01	434	1686	
LOLIPOP IA610	A	G	0.39	1.00	0.93	1.09	9.13e-01	1779	4768	
SIKH	A	G	0.41	1.22	1.06	1.41	2.77e-02	826	748	
SINDI	A	G	0.36	1.12	0.99	1.27	8.72e-02	1169	2146	
META in SAS	**A**	**G**		**1.06**	**1.03**	**1.09**	**2.85e-04**	**13862**	**27843**	**0.00**
JAPAN1	A	G	0.37	1.02	0.98	1.07	2.92e-01	9817	6763	
JAPAN2	A	G	0.36	1.07	1.02	1.11	4.44e-03	5646	19420	
TAICHI	A	G	0.40	0.97	0.91	1.03	2.57e-01	4535	4800	
META in EAS	**A**	**G**		**1.03**	**1.00**	**1.06**	**5.21e-02**	**19998**	**30983**	**0.71**
META in ALL	**A**	**G**		**1.04**	**1.03**	**1.06**	**3.02e-09**	**72704**	**191251**	**0.00**



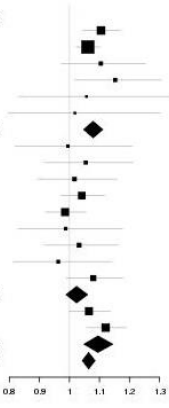
rs622217, *SLC22A1*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAM metabo	C	T	0.48	0.95	0.92	0.97	6.11e-05	22669	58119	
FINRISK	C	T	0.50	0.92	0.84	1.00	5.85e-02	1563	7553	
MDC	C	T	0.47	0.97	0.89	1.05	4.28e-01	1418	5722	
MEDSTAR	C	T	0.47	1.04	0.88	1.23	6.51e-01	358	964	
PENNCATH	C	T	0.49	0.98	0.82	1.18	8.53e-01	278	1113	
META in EUR	**C**	**T**		**0.95**	**0.93**	**0.97**	**1.75e-05**	**26286**	**73471**	**0.00**
BRAVE	C	T	0.39	0.89	0.73	1.07	2.19e-01	250	2189	
EPIDREAM	C	T	0.41	0.99	0.87	1.13	8.82e-01	612	2039	
PROMIS GWAS1	C	T	0.41	0.92	0.81	1.04	1.59e-01	737	1804	
PROMIS GWAS2	C	T	0.40	0.95	0.89	1.01	1.10e-01	3930	3250	
PROMIS metabo	C	T	0.40	0.99	0.93	1.06	7.87e-01	2439	7088	
RACE GWAS1	C	T	0.40	0.96	0.81	1.14	6.38e-01	602	598	
RACE GWAS2	C	T	0.42	0.94	0.84	1.05	3.00e-01	1084	1527	
LOLIPOP IA317	C	T	0.40	0.89	0.75	1.04	1.36e-01	434	1686	
LOLIPOP IA610	C	T	0.41	0.90	0.83	0.98	1.35e-02	1779	4768	
META in SAS	**C**	**T**		**0.95**	**0.92**	**0.98**	**1.10e-03**	**11867**	**24949**	**0.00**
JAPAN1	C	T	0.29	0.91	0.86	0.95	9.65e-05	9817	6763	
JAPAN2	C	T	0.28	0.98	0.93	1.03	3.90e-01	5646	19420	
META in EAS	**C**	**T**		**0.94**	**0.91**	**0.98**	**9.06e-04**	**15463**	**26183**	**0.79**
META in ALL	**C**	**T**		**0.95**	**0.93**	**0.96**	**2.47e-10**	**53616**	**124603**	**0.00**



rs9648716, *BRAF*

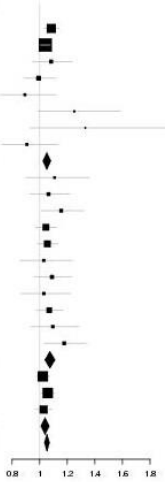
Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	T	A	0.15	1.11	1.04	1.17	7.30e-04	9495	53076	
DIAGRAM metabo	T	A	0.15	1.06	1.02	1.10	1.93e-03	22669	58119	
FINRISK	T	A	0.15	1.10	0.97	1.25	1.24e-01	1563	7553	
MDC	T	A	0.12	1.15	1.02	1.31	2.70e-02	1418	5722	
MEDSTAR	T	A	0.15	1.06	0.83	1.34	6.54e-01	358	964	
PENNCATH	T	A	0.17	1.02	0.80	1.30	8.87e-01	278	1113	
META in EUR	**T**	**A**		**1.08**	**1.05**	**1.11**	**4.01e-07**	**35781**	**126547**	**0.00**
BRAVE	T	A	0.33	0.99	0.82	1.21	9.59e-01	250	2189	
EPIDREAM	T	A	0.30	1.05	0.92	1.21	4.60e-01	612	2039	
PROMIS GWAS1	T	A	0.31	1.02	0.89	1.16	8.01e-01	737	1804	
PROMIS GWAS2	T	A	0.31	1.04	0.97	1.12	2.59e-01	3930	3250	
PROMIS metabo	T	A	0.32	0.99	0.92	1.06	6.80e-01	2439	7088	
RACE GWAS1	T	A	0.32	0.99	0.83	1.18	8.88e-01	602	598	
RACE GWAS2	T	A	0.32	1.03	0.92	1.16	6.01e-01	1084	1527	
LOLIPOP IA317	T	A	0.30	0.96	0.81	1.14	6.62e-01	434	1686	
LOLIPOP IA610	T	A	0.30	1.08	0.99	1.18	8.55e-02	1779	4768	
META in SAS	**T**	**A**		**1.02**	**0.99**	**1.06**	**1.85e-01**	**11867**	**24949**	**0.00**
JAPAN1	T	A	0.13	1.07	1.00	1.14	5.62e-02	9817	6763	
JAPAN2	T	A	0.13	1.12	1.06	1.19	1.86e-04	5646	19420	
META in EAS	**T**	**A**		**1.10**	**1.05**	**1.14**	**4.20e-05**	**15463**	**26183**	**0.24**
META in ALL	**T**	**A**		**1.06**	**1.04**	**1.09**	**1.16e-09**	**63111**	**177679**	**0.00**



Nature Genetics: doi:10.1038/ng.3943

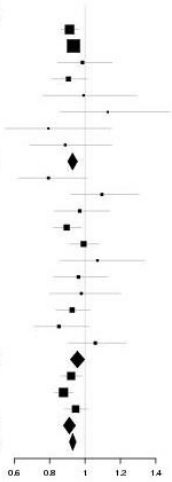
rs12681990, *KCNU1*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	C	T	0.15	1.08	1.03	1.14	1.65e-03	9495	53076	
DIAGRAM metabo	C	T	0.15	1.04	1.00	1.08	2.61e-02	22669	58119	
FINRISK	C	T	0.13	1.08	0.95	1.24	2.38e-01	1563	7553	
MDC	C	T	0.15	0.99	0.88	1.11	8.97e-01	1418	5722	
MEDSTAR	C	T	0.18	0.89	0.71	1.12	3.24e-01	358	964	
PENNCATH	C	T	0.20	1.25	0.99	1.59	6.51e-02	278	1113	
MSSE AFFY	C	T	0.20	1.33	0.93	1.91	1.21e-01	132	445	
MSSE ILLU	C	T	0.24	0.91	0.73	1.13	3.94e-01	255	1647	
META in EUR	**C**	**T**		**1.05**	**1.02**	**1.08**	**2.37e-04**	**36168**	**128639**	**0.32**
BRAVE	C	T	0.29	1.11	0.90	1.36	3.26e-01	250	2189	
EPIDREAM	C	T	0.32	1.06	0.93	1.22	3.73e-01	612	2039	
PROMIS GWAS1	C	T	0.29	1.16	1.01	1.32	3.39e-02	737	1804	
PROMIS GWAS2	C	T	0.29	1.05	0.97	1.13	2.36e-01	3930	3250	
PROMIS metabo	C	T	0.29	1.06	0.98	1.13	1.35e-01	2439	7088	
RACE GWAS1	C	T	0.27	1.03	0.86	1.24	7.56e-01	602	598	
RACE GWAS2	C	T	0.29	1.09	0.96	1.23	1.78e-01	1084	1527	
LOLIPOP IA317	C	T	0.29	1.03	0.87	1.23	7.38e-01	434	1686	
LOLIPOP IA610	C	T	0.29	1.07	0.98	1.17	1.39e-01	1779	4768	
SIKH	C	T	0.27	1.10	0.93	1.28	3.62e-02	826	748	
SINDI	C	T	0.32	1.18	1.04	1.34	1.87e-02	1169	2146	
META in SAS	**C**	**T**		**1.07**	**1.04**	**1.11**	**3.63e-05**	**13862**	**27843**	**0.00**
JAPAN1	C	T	0.39	1.02	0.98	1.07	3.19e-01	9817	6763	
JAPAN2	C	T	0.39	1.06	1.01	1.11	1.21e-02	5646	19420	
TAICHI	C	T	0.34	1.03	0.97	1.09	3.63e-01	4535	4800	
META in EAS	**C**	**T**		**1.04**	**1.01**	**1.07**	**9.37e-03**	**19998**	**30983**	**0.00**
META in ALL	**C**	**T**		**1.05**	**1.03**	**1.07**	**3.07e-09**	**70028**	**187465**	**0.00**



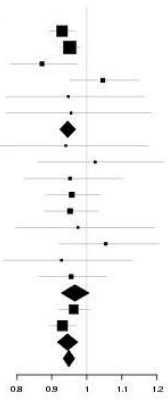
rs576674, *KL*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	A	G	0.84	0.91	0.86	0.96	1.08e-03	8473	52001	
DIAGRAM metabo	A	G	0.84	0.93	0.90	0.97	4.10e-04	22669	58119	
FINRISK	A	G	0.91	0.99	0.84	1.15	8.58e-01	1563	7553	
MDC	A	G	0.85	0.91	0.81	1.01	8.72e-02	1418	5722	
MEDSTAR	A	G	0.14	0.99	0.76	1.30	9.51e-01	358	964	
PENNCATH	A	G	0.16	1.13	0.86	1.48	3.84e-01	278	1113	
MSSE AFFY	A	G	0.81	0.79	0.55	1.15	2.20e-01	132	445	
MSSE ILLU	A	G	0.83	0.89	0.69	1.15	3.69e-01	255	1647	
META in EUR	**A**	**G**		**0.93**	**0.90**	**0.96**	**5.79e-07**	**35146**	**127564**	**0.00**
BRAVE	A	G	0.83	0.79	0.62	1.01	6.35e-02	250	2189	
EPIDREAM	A	G	0.82	1.10	0.92	1.30	3.05e-01	612	2039	
PROMIS GWAS1	A	G	0.84	0.97	0.83	1.14	7.11e-01	737	1804	
PROMIS GWAS2	A	G	0.85	0.90	0.82	0.98	1.91e-02	3930	3250	
PROMIS metabo	A	G	0.83	0.99	0.91	1.08	8.55e-01	2439	7088	
RACE GWAS1	A	G	0.83	1.07	0.86	1.34	5.49e-01	602	598	
RACE GWAS2	A	G	0.84	0.96	0.82	1.13	6.35e-01	1084	1527	
LOLIPOP IA317	A	G	0.84	0.98	0.80	1.20	8.41e-01	434	1686	
LOLIPOP IA610	A	G	0.83	0.93	0.83	1.03	1.58e-01	1779	4768	
SIKH	A	G	0.81	0.85	0.71	1.02	1.53e-01	826	748	
SINDI	A	G	0.82	1.06	0.91	1.24	5.64e-01	1169	2146	
META in SAS	**A**	**G**		**0.96**	**0.92**	**1.00**	**3.41e-02**	**13862**	**27843**	**0.15**
JAPAN1	A	G	0.86	0.92	0.86	0.98	1.38e-02	9817	6763	
JAPAN2	A	G	0.86	0.88	0.83	0.93	1.54e-05	5646	19420	
TAICHI	A	G	0.77	0.95	0.88	1.01	1.20e-01	4535	4800	
META in EAS	**A**	**G**		**0.91**	**0.88**	**0.95**	**7.38e-07**	**19998**	**30983**	**0.29**
META in ALL	**A**	**G**		**0.93**	**0.91**	**0.95**	**9.27e-13**	**69006**	**186390**	**0.04**



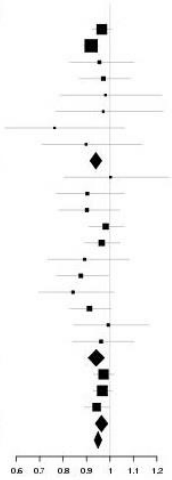
rs10507349, *RNF6*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	A	G	0.22	0.93	0.89	0.97	2.33e-04	12171	56862	
DIAGRAM metabo	A	G	0.22	0.95	0.92	0.98	2.85e-03	22669	58119	
FINRISK	A	G	0.21	0.87	0.78	0.97	1.55e-02	1563	7553	
MDC	A	G	0.26	1.05	0.95	1.15	3.49e-01	1418	5722	
MEDSTAR	A	G	0.22	0.95	0.77	1.16	6.07e-01	358	964	
PENNCATH	A	G	0.24	0.96	0.77	1.19	6.78e-01	278	1113	
META in EUR	**A**	**G**		**0.95**	**0.92**	**0.97**	**2.40e-06**	**38457**	**130333**	**0.32**
BRAVE	A	G	0.22	0.94	0.75	1.18	5.90e-01	250	2189	
EPIDREAM	A	G	0.16	1.02	0.86	1.22	7.90e-01	612	2039	
PROMIS GWAS1	A	G	0.21	0.95	0.82	1.10	5.11e-01	737	1804	
PROMIS GWAS2	A	G	0.21	0.96	0.88	1.04	2.90e-01	3930	3250	
PROMIS metabo	A	G	0.21	0.95	0.88	1.03	2.39e-01	2439	7088	
RACE GWAS1	A	G	0.22	0.97	0.80	1.19	8.05e-01	602	598	
RACE GWAS2	A	G	0.22	1.05	0.92	1.21	4.40e-01	1084	1527	
LOLIPOP IA317	A	G	0.20	0.93	0.76	1.13	4.52e-01	434	1686	
LOLIPOP IA610	A	G	0.21	0.96	0.86	1.06	3.75e-01	1779	4768	
META in SAS	**A**	**G**		**0.97**	**0.93**	**1.01**	**9.61e-02**	**11867**	**24949**	**0.00**
JAPAN1	A	G	0.45	0.96	0.92	1.01	9.23e-02	9817	6763	
JAPAN2	A	G	0.45	0.93	0.89	0.97	7.77e-04	5646	19420	
META in EAS	**A**	**G**		**0.95**	**0.92**	**0.97**	**2.66e-04**	**15463**	**26183**	**0.16**
META in ALL	**A**	**G**		**0.95**	**0.93**	**0.96**	**9.69e-10**	**65787**	**181465**	**0.00**



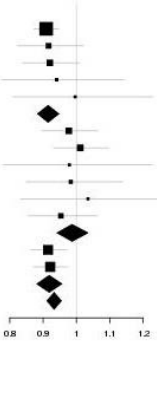
rs9940149, *ITFG3*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	A	G	0.17	0.97	0.92	1.01	1.15e-01	12171	56862	
DIAGRAM metabo	A	G	0.17	0.92	0.89	0.95	8.27e-06	22669	58119	
FINRISK	A	G	0.11	0.95	0.83	1.10	5.25e-01	1563	7553	
MDC	A	G	0.17	0.97	0.87	1.09	6.17e-01	1418	5722	
MEDSTAR	A	G	0.18	0.98	0.79	1.22	8.64e-01	358	964	
PENNCATH	A	G	0.19	0.97	0.77	1.23	8.06e-01	278	1113	
MSSE AFFY	A	G	0.24	0.76	0.55	1.06	1.08e-01	132	445	
MSSE ILLU	A	G	0.22	0.90	0.71	1.14	3.71e-01	255	1647	
META in EUR	**A**	**G**		**0.94**	**0.92**	**0.96**	**3.59e-06**	**38844**	**132425**	**0.00**
BRAVE	A	G	0.23	1.00	0.80	1.25	9.82e-01	250	2189	
EPIDREAM	A	G	0.20	0.90	0.77	1.06	2.14e-01	612	2039	
PROMIS GWAS1	A	G	0.24	0.90	0.78	1.04	1.61e-01	737	1804	
PROMIS GWAS2	A	G	0.25	0.98	0.91	1.06	6.43e-01	3930	3250	
PROMIS metabo	A	G	0.22	0.96	0.89	1.04	3.66e-01	2439	7088	
RACE GWAS1	A	G	0.27	0.89	0.73	1.08	2.47e-01	602	598	
RACE GWAS2	A	G	0.26	0.88	0.77	0.99	4.04e-02	1084	1527	
LOLIPOP IA317	A	G	0.23	0.84	0.70	1.02	7.58e-02	434	1686	
LOLIPOP IA610	A	G	0.23	0.91	0.83	1.01	6.65e-02	1779	4768	
SIKH	A	G	0.25	0.99	0.84	1.17	9.77e-01	826	748	
SINDI	A	G	0.26	0.96	0.84	1.10	9.97e-01	1169	2146	
META in SAS	**A**	**G**		**0.94**	**0.91**	**0.98**	**1.11e-03**	**13862**	**27843**	**0.00**
JAPAN1	A	G	0.40	0.97	0.93	1.02	2.21e-01	9817	6763	
JAPAN2	A	G	0.40	0.97	0.93	1.01	1.39e-01	5646	19420	
TAICHI	A	G	0.44	0.94	0.89	1.00	4.57e-02	4535	4800	
META in EAS	**A**	**G**		**0.96**	**0.94**	**0.99**	**8.15e-03**	**19998**	**30983**	**0.00**
META in ALL	**A**	**G**		**0.95**	**0.93**	**0.97**	**1.09e-09**	**72704**	**191251**	**0.00**



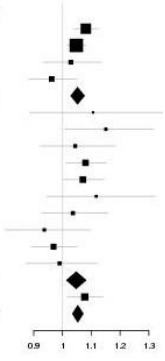
rs7985179, *MIR17HG*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	A	T	0.28	0.91	0.87	0.95	9.11e-06	9495	53076	
FINRISK	A	T	0.21	0.92	0.82	1.02	1.17e-01	1563	7553	
MDC	A	T	0.26	0.92	0.84	1.01	8.06e-02	1418	5722	
MEDSTAR	A	T	0.26	0.94	0.77	1.14	5.36e-01	358	964	
PENNCATH	A	T	0.27	1.00	0.81	1.23	9.71e-01	278	1113	
META in EUR	**A**	**T**		**0.91**	**0.88**	**0.95**	**6.43e-07**	**13112**	**68428**	**0.00**
PROMIS GWAS1	A	T	0.17	0.98	0.90	1.07	5.98e-01	2718	6326	
PROMIS GWAS2	A	T	0.16	1.01	0.93	1.10	7.86e-01	4365	3984	
RACE GWAS1	A	T	0.16	0.98	0.78	1.23	8.54e-01	602	598	
RACE GWAS2	A	T	0.17	0.98	0.85	1.14	8.20e-01	1084	1527	
LOLIPOP IA317	A	T	0.15	1.03	0.83	1.29	7.61e-01	434	1686	
LOLIPOP IA610	A	T	0.17	0.95	0.85	1.06	3.89e-01	1779	4768	
META in SAS	**A**	**T**		**0.99**	**0.94**	**1.03**	**5.84e-01**	**10982**	**18889**	**0.00**
JAPAN1	A	T	0.18	0.91	0.86	0.97	2.72e-03	9817	6763	
JAPAN2	A	T	0.18	0.92	0.87	0.98	4.43e-03	5646	19420	
META in EAS	**A**	**T**		**0.92**	**0.88**	**0.96**	**4.22e-05**	**15463**	**26183**	**0.00**
META in ALL	**A**	**T**		**0.93**	**0.91**	**0.95**	**4.16e-09**	**39557**	**113500**	**0.00**



rs2050188, *HLA-DRB5*

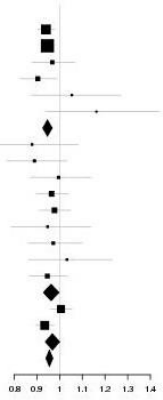
Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	T	C	0.67	1.08	1.04	1.12	8.06e-05	9495	53076	
DIAGRAM metabo	T	C	0.67	1.05	1.02	1.08	2.51e-03	22669	58119	
FINRISK	T	C	0.71	1.03	0.93	1.14	5.71e-01	1563	7553	
MDC	T	C	0.69	0.96	0.88	1.05	3.99e-01	1418	5722	
META in EUR	**T**	**C**		**1.05**	**1.03**	**1.08**	**9.15e-06**	**35145**	**124470**	**0.50**
BRAVE	T	C	0.74	1.11	0.89	1.38	3.75e-01	250	2189	
EPIDREAM	T	C	0.62	1.15	1.01	1.32	4.08e-02	612	2039	
PROMIS GWAS1	T	C	0.52	1.04	0.92	1.18	5.01e-01	737	1804	
PROMIS GWAS2	T	C	0.49	1.08	1.01	1.15	2.18e-02	3930	3250	
PROMIS metabo	T	C	0.51	1.07	1.00	1.14	3.98e-02	2439	7088	
RACE GWAS1	T	C	0.51	1.12	0.94	1.32	1.95e-01	602	598	
RACE GWAS2	T	C	0.51	1.04	0.93	1.16	5.31e-01	1084	1527	
LOLIPOP IA317	T	C	0.53	0.94	0.80	1.10	4.18e-01	434	1686	
LOLIPOP IA610	T	C	0.55	0.97	0.89	1.05	4.50e-01	1779	4768	
SINDI	T	C	0.64	0.99	0.87	1.12	7.15e-01	1169	2146	
META in SAS	**T**	**C**		**1.05**	**1.01**	**1.08**	**4.48e-03**	**13036**	**27095**	**0.11**
TAICHI	T	C	0.55	1.08	1.02	1.14	1.19e-02	4535	4800	
META in ALL	**T**	**C**		**1.05**	**1.03**	**1.07**	**7.56e-09**	**52716**	**156365**	**0.17**



Nature Genetics: doi:10.1038/ng.3943

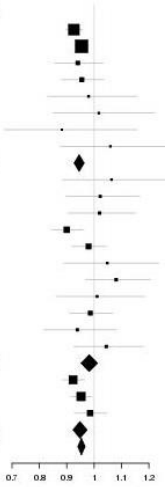
rs2925979, *CMIP*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	C	T	0.71	0.94	0.90	0.98	2.43e-03	9062	51638	
DIAGRAM metabo	C	T	0.71	0.95	0.92	0.97	1.96e-04	22669	58119	
FINRISK	C	T	0.69	0.97	0.88	1.07	5.10e-01	1563	7553	
MDC	C	T	0.70	0.90	0.83	0.99	2.63e-02	1418	5722	
MEDSTAR	C	T	0.31	1.05	0.87	1.27	5.81e-01	358	964	
PENNCATH	C	T	0.30	1.16	0.94	1.44	1.65e-01	278	1113	
META in EUR	**C**	**T**		**0.95**	**0.93**	**0.97**	**7.71e-07**	**35348**	**125109**	**0.20**
BRAVE	C	T	0.74	0.88	0.71	1.08	2.22e-01	250	2189	
EPIDREAM	C	T	0.77	0.89	0.77	1.03	1.23e-01	612	2039	
PROMIS GWAS1	C	T	0.73	1.00	0.87	1.14	9.43e-01	737	1804	
PROMIS GWAS2	C	T	0.72	0.96	0.90	1.04	3.29e-01	3930	3250	
PROMIS metabo	C	T	0.71	0.98	0.91	1.05	5.28e-01	2439	7088	
RACE GWAS1	C	T	0.72	0.95	0.79	1.14	5.60e-01	602	598	
RACE GWAS2	C	T	0.72	0.97	0.86	1.10	6.48e-01	1084	1527	
LOLIPOP IA317	C	T	0.71	1.03	0.86	1.23	7.28e-01	434	1686	
LOLIPOP IA610	C	T	0.70	0.95	0.87	1.03	2.18e-01	1779	4768	
META in SAS	**C**	**T**		**0.96**	**0.93**	**1.00**	**3.65e-02**	**11867**	**24949**	**0.00**
JAPAN1	C	T	0.66	1.01	0.96	1.05	7.86e-01	9817	6763	
JAPAN2	C	T	0.67	0.93	0.89	0.98	2.53e-03	5646	19420	
META in EAS	**C**	**T**		**0.97**	**0.94**	**1.00**	**4.98e-02**	**15463**	**26183**	**0.80**
META in ALL	**C**	**T**		**0.95**	**0.94**	**0.97**	**2.41e-08**	**62678**	**176241**	**0.00**



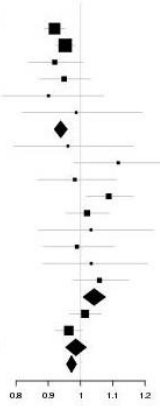
rs2421016, *PLEKHA1*

Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	T	C	0.47	0.93	0.90	0.96	4.86e-06	12171	56862	
DIAGRAM metabo	T	C	0.47	0.95	0.93	0.98	7.33e-04	22669	58119	
FINRISK	T	C	0.63	0.94	0.86	1.03	1.96e-01	1563	7553	
MDC	T	C	0.49	0.95	0.88	1.04	2.69e-01	1418	5722	
MEDSTAR	T	C	0.49	0.98	0.83	1.16	8.11e-01	358	964	
PENNCATH	T	C	0.47	1.02	0.85	1.22	8.54e-01	278	1113	
MSSE AFFY	T	C	0.48	0.88	0.67	1.16	3.67e-01	132	445	
MSSE ILLU	T	C	0.47	1.06	0.88	1.28	5.53e-01	255	1647	
META in EUR	**T**	**C**		**0.95**	**0.93**	**0.96**	**1.52e-08**	**38844**	**132425**	**0.00**
BRAVE	T	C	0.54	1.06	0.88	1.28	5.18e-01	250	2189	
EPIDREAM	T	C	0.55	1.02	0.90	1.17	7.41e-01	612	2039	
PROMIS GWAS1	T	C	0.54	1.02	0.90	1.15	7.49e-01	737	1804	
PROMIS GWAS2	T	C	0.56	0.90	0.84	0.96	1.38e-03	3930	3250	
PROMIS metabo	T	C	0.54	0.98	0.92	1.05	5.36e-01	2439	7088	
RACE GWAS1	T	C	0.54	1.05	0.89	1.24	5.74e-01	602	598	
RACE GWAS2	T	C	0.54	1.08	0.97	1.21	1.69e-01	1084	1527	
LOLIPOP IA317	T	C	0.56	1.01	0.86	1.19	8.95e-01	434	1686	
LOLIPOP IA610	T	C	0.55	0.99	0.91	1.07	7.35e-01	1779	4768	
SIKH	T	C	0.58	0.94	0.81	1.08	2.48e-01	826	748	
SINDI	T	C	0.55	1.04	0.93	1.18	5.51e-01	1169	2146	
META in SAS	**T**	**C**		**0.98**	**0.95**	**1.01**	**2.42e-01**	**13862**	**27843**	**0.26**
JAPAN1	T	C	0.59	0.92	0.88	0.97	4.28e-04	9817	6763	
JAPAN2	T	C	0.58	0.95	0.91	0.99	2.36e-02	5646	19420	
TAICHI	T	C	0.63	0.99	0.93	1.05	6.25e-01	4535	4800	
META in EAS	**T**	**C**		**0.95**	**0.92**	**0.97**	**1.19e-04**	**19998**	**30983**	**0.33**
META in ALL	**T**	**C**		**0.95**	**0.94**	**0.97**	**3.68e-11**	**72704**	**191251**	**0.17**



rs7674212, *CISD2*

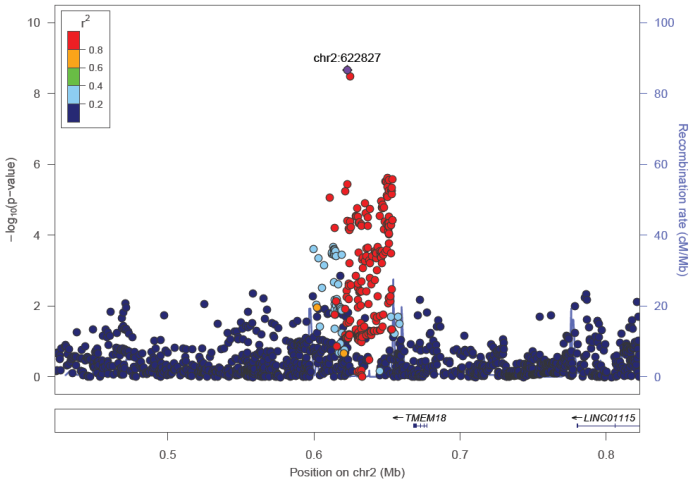
Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls	I2
DIAGRAMv3	T	G	0.42	0.92	0.89	0.95	6.17e-06	9495	53076	
DIAGRAM metabo	T	G	0.42	0.95	0.92	0.98	1.58e-03	22669	58119	
FINRISK	T	G	0.43	0.92	0.84	1.01	7.67e-02	1563	7553	
MDC	T	G	0.44	0.95	0.87	1.03	2.19e-01	1418	5722	
MEDSTAR	T	G	0.42	0.90	0.76	1.07	2.39e-01	358	964	
PENNCATH	T	G	0.43	0.99	0.82	1.19	8.89e-01	278	1113	
META in EUR	**T**	**G**		**0.94**	**0.92**	**0.96**	**6.85e-09**	**35781**	**126547**	**0.00**
BRAVE	T	G	0.41	0.96	0.79	1.17	6.87e-01	250	2189	
EPIDREAM	T	G	0.39	1.12	0.98	1.28	1.02e-01	612	2039	
PROMIS GWAS1	T	G	0.41	0.98	0.87	1.11	7.80e-01	737	1804	
PROMIS GWAS2	T	G	0.41	1.09	1.02	1.16	1.40e-02	3930	3250	
PROMIS metabo	T	G	0.42	1.02	0.95	1.09	5.51e-01	2439	7088	
RACE GWAS1	T	G	0.43	1.03	0.87	1.23	7.15e-01	602	598	
RACE GWAS2	T	G	0.42	0.99	0.89	1.10	8.44e-01	1084	1527	
LOLIPOP IA317	T	G	0.42	1.03	0.88	1.21	6.80e-01	434	1686	
LOLIPOP IA610	T	G	0.41	1.06	0.98	1.15	1.69e-01	1779	4768	
META in SAS	**T**	**G**		**1.04**	**1.01**	**1.08**	**1.48e-02**	**11867**	**24949**	**0.00**
JAPAN1	T	G	0.36	1.01	0.97	1.07	5.69e-01	9817	6763	
JAPAN2	T	G	0.36	0.96	0.92	1.01	9.80e-02	5646	19420	
META in EAS	**T**	**G**		**0.99**	**0.95**	**1.02**	**3.72e-01**	**15463**	**26183**	**0.57**
META in ALL	**T**	**G**		**0.97**	**0.96**	**0.99**	**4.06e-04**	**63111**	**177679**	**0.59**



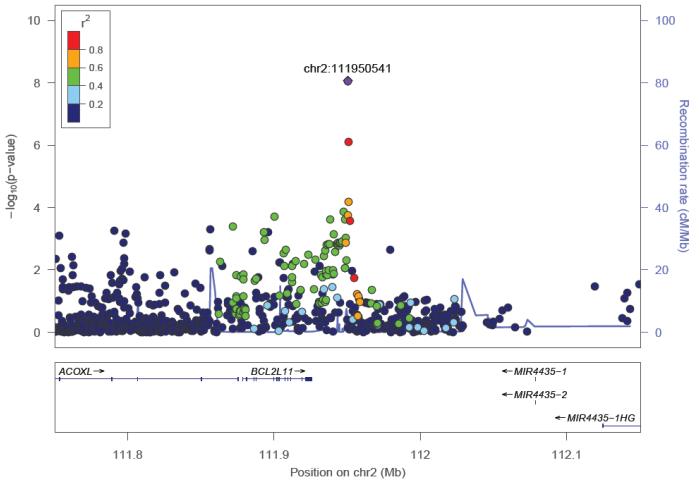
Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 3. Regional association plots of the previously unreported T2D loci.

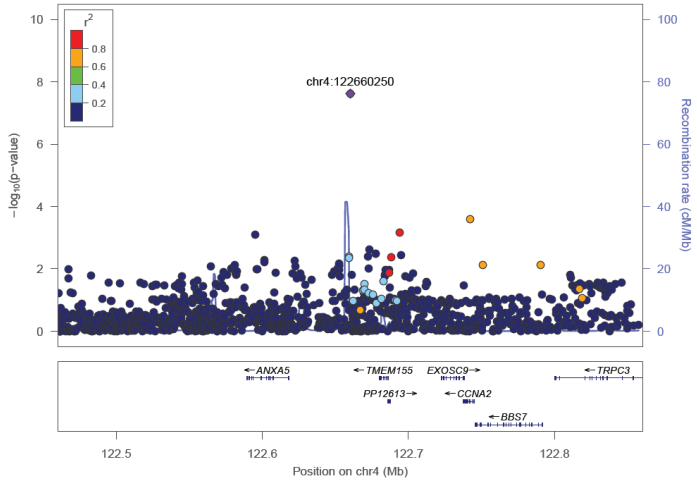
rs2867125, *TMEM18*



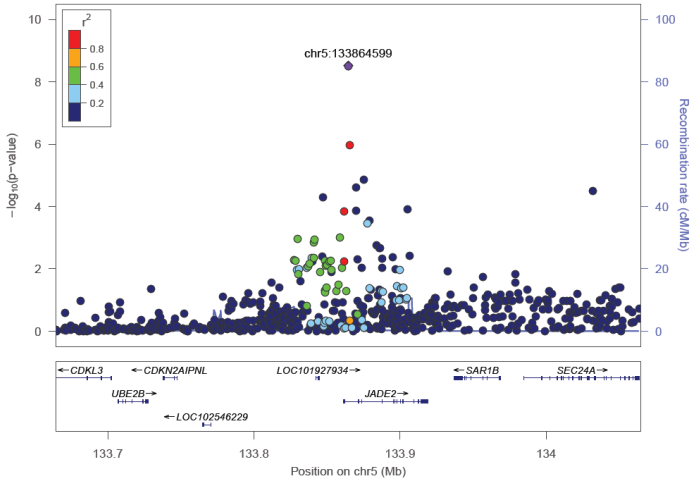
rs11123406, *BCL2L11*



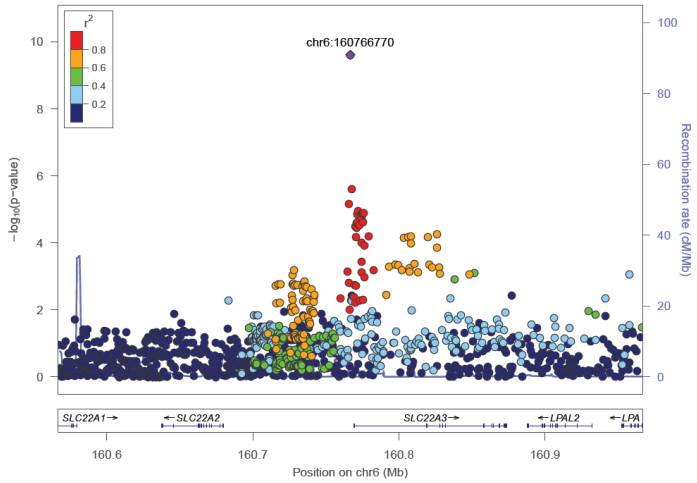
rs2706785, *TMEM155*



rs329122, *PHF15*



rs622217, *SLC22A1*



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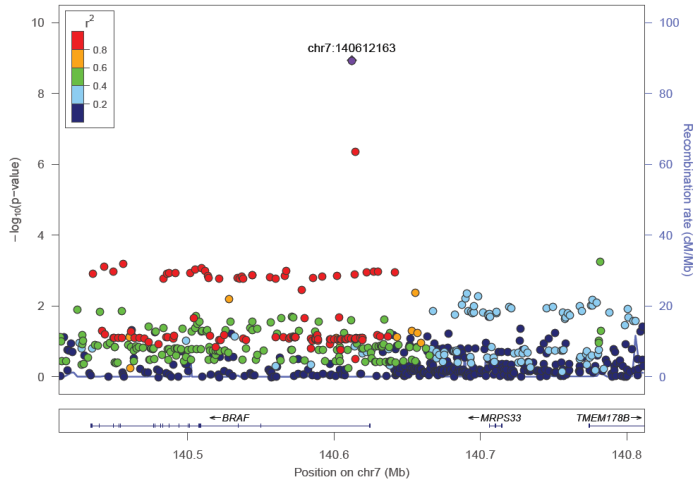

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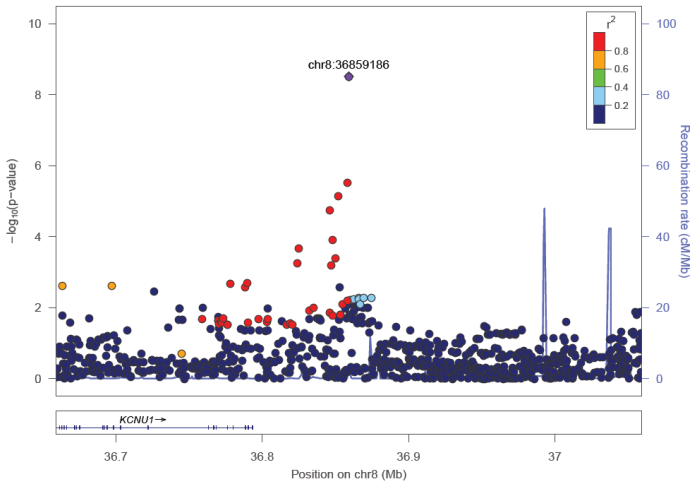
rs12681990. *KCNU1*



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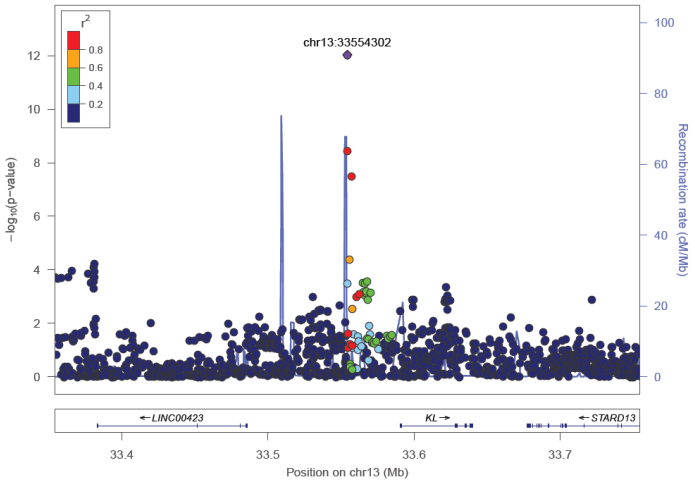
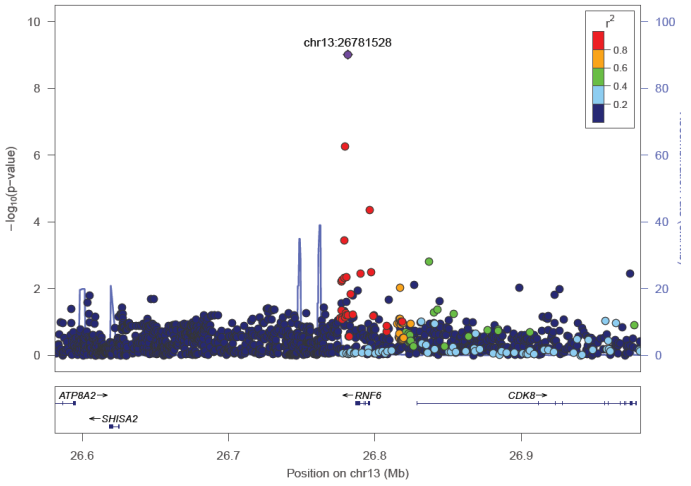


rs10507349, *RNF6*



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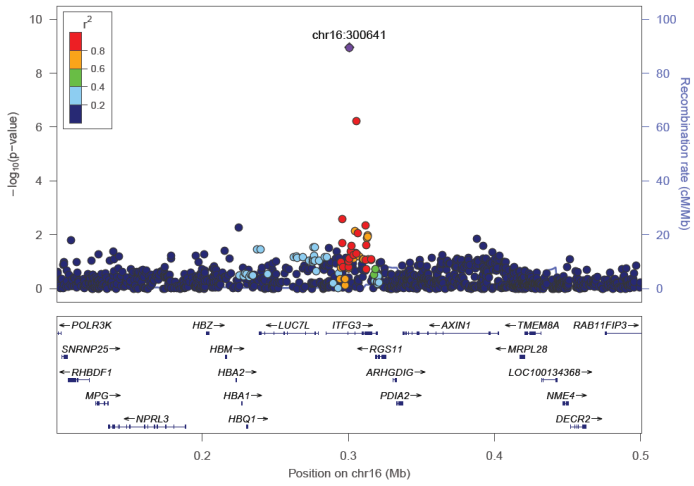

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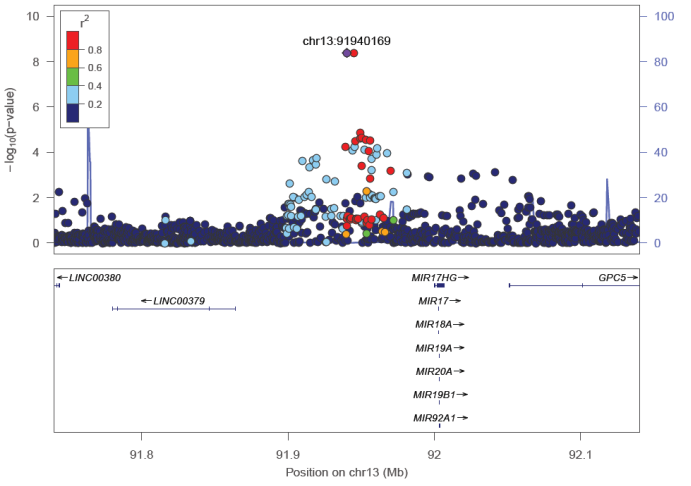
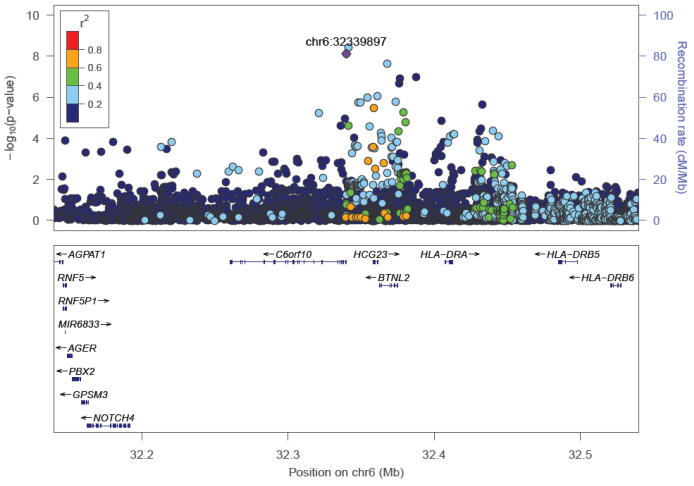
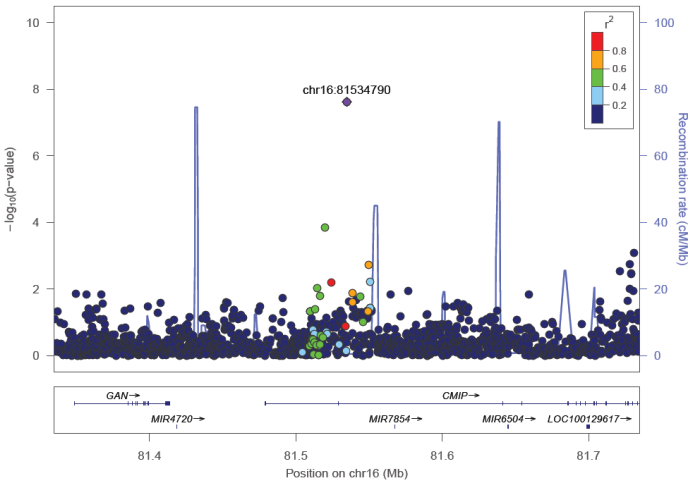


rs2050188, *HLA-DRB5*

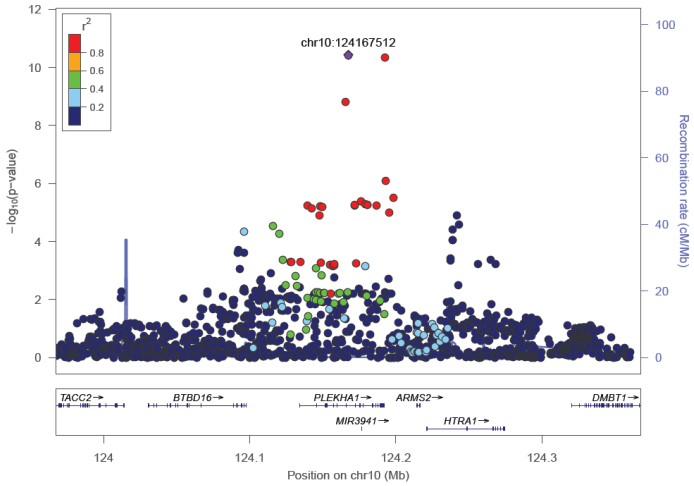


Nature Genetics: doi:10.1038/ng.3943

rs2925979, *CMIP*

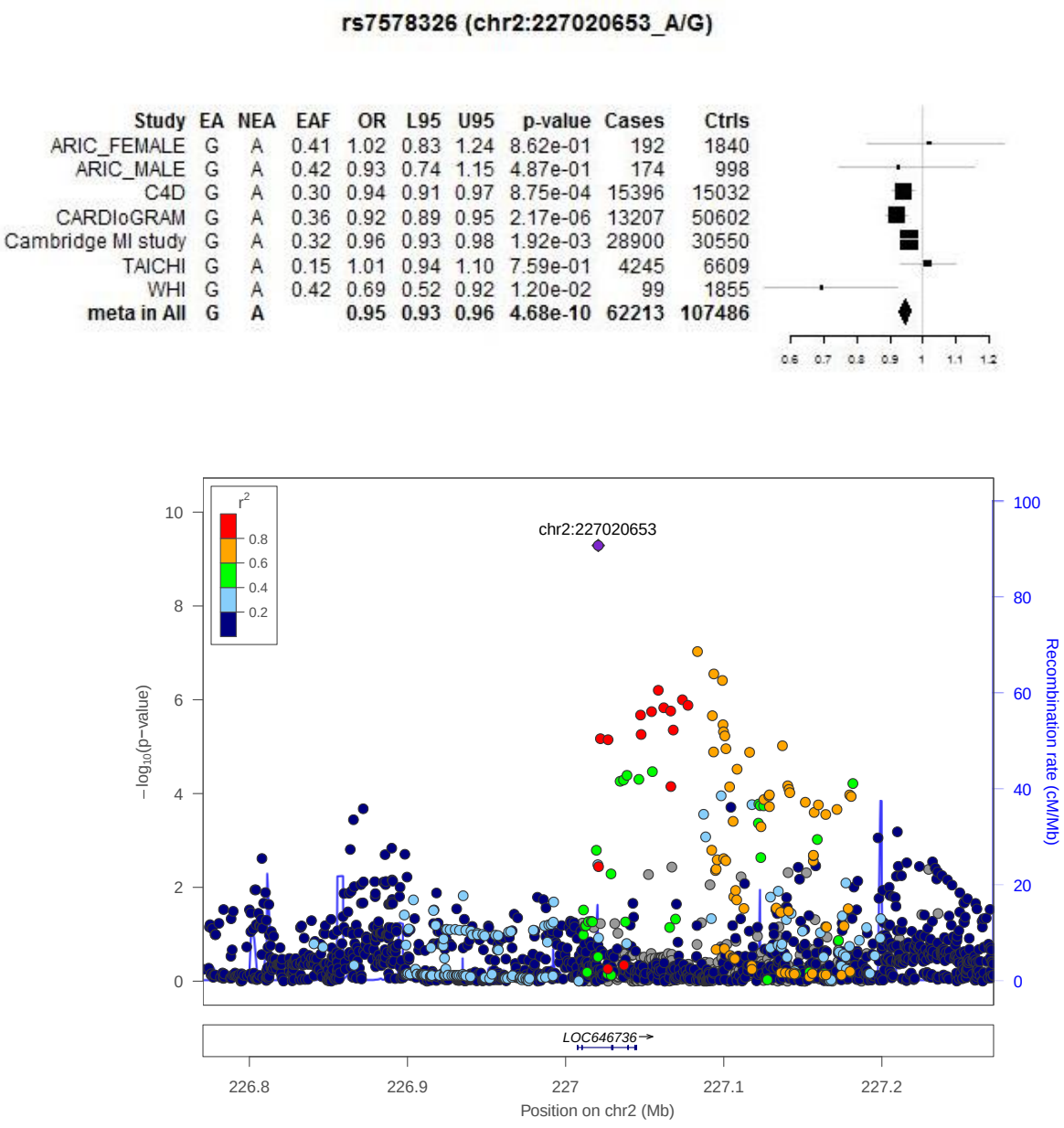


rs2421016, *PLEKHA1*



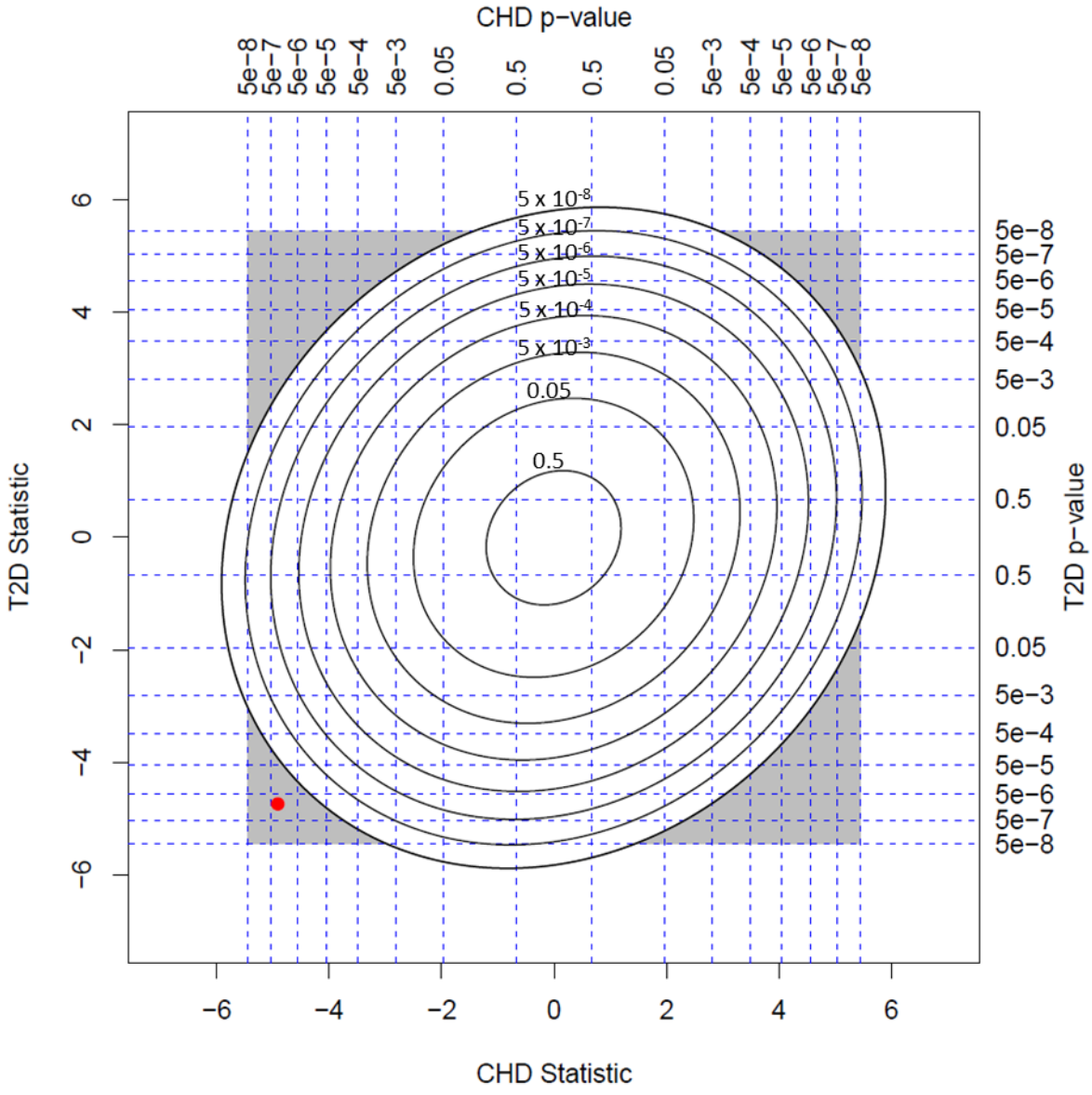
Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 4. Regional association and forest plots of the novel association of rs7578326 with CHD risk. For regional association, patterns of LD were taken from 1000 Genomes CEU (i.e., European ancestry is the predominant ancestry in the meta-analyzed samples). Description about the CHD meta-analyses are provided in Supplementary Methods section of this note under "Details on studies contributing to the CHD meta-analysis".



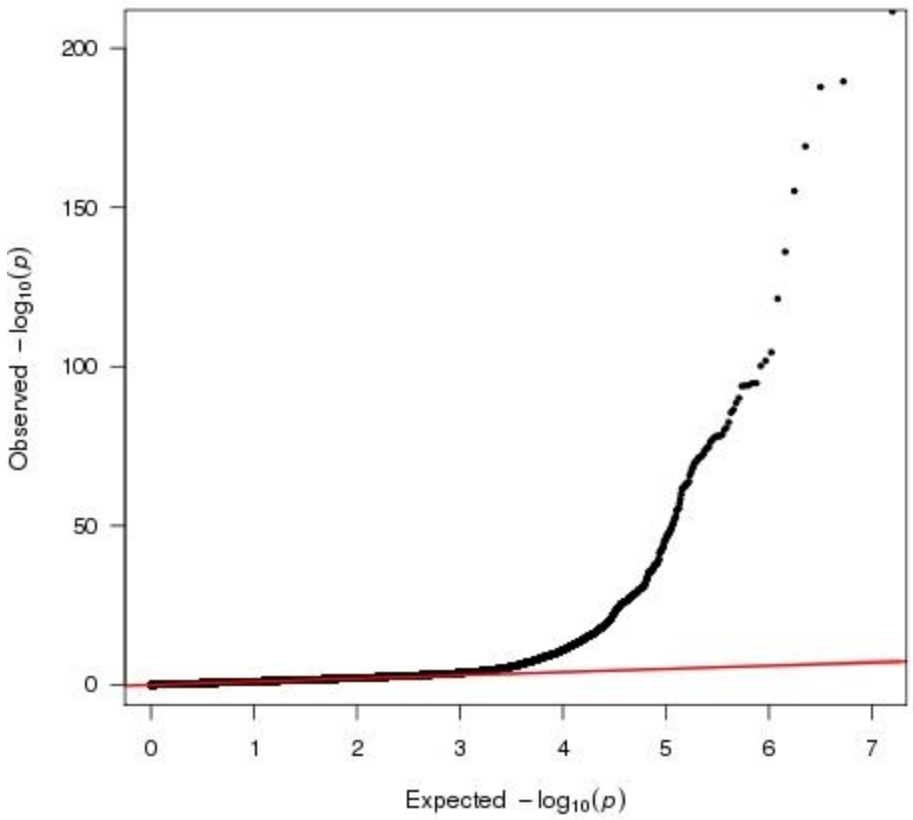
Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 5. Rejection region for a two-degree-of-freedom test in the bivariate-normal GWAS-scan of T2D and CHD. The ellipses and the numbers show the rejection region in the bivariate-normal GWAS-scan of T2D and CHD: SNPs fall into the region outside each ellipse has the level of significance in indicated. The shaded regions denotes the region where SNPs are not associated with either T2D or CHD at a GWAS-level of significance ($P < 5 \times 10^{-8}$) but have a $P < 5 \times 10^{-8}$ in the bivariate-normal test for T2D and CHD. The red dots show the position for the *CCDC92* SNP rs825476.



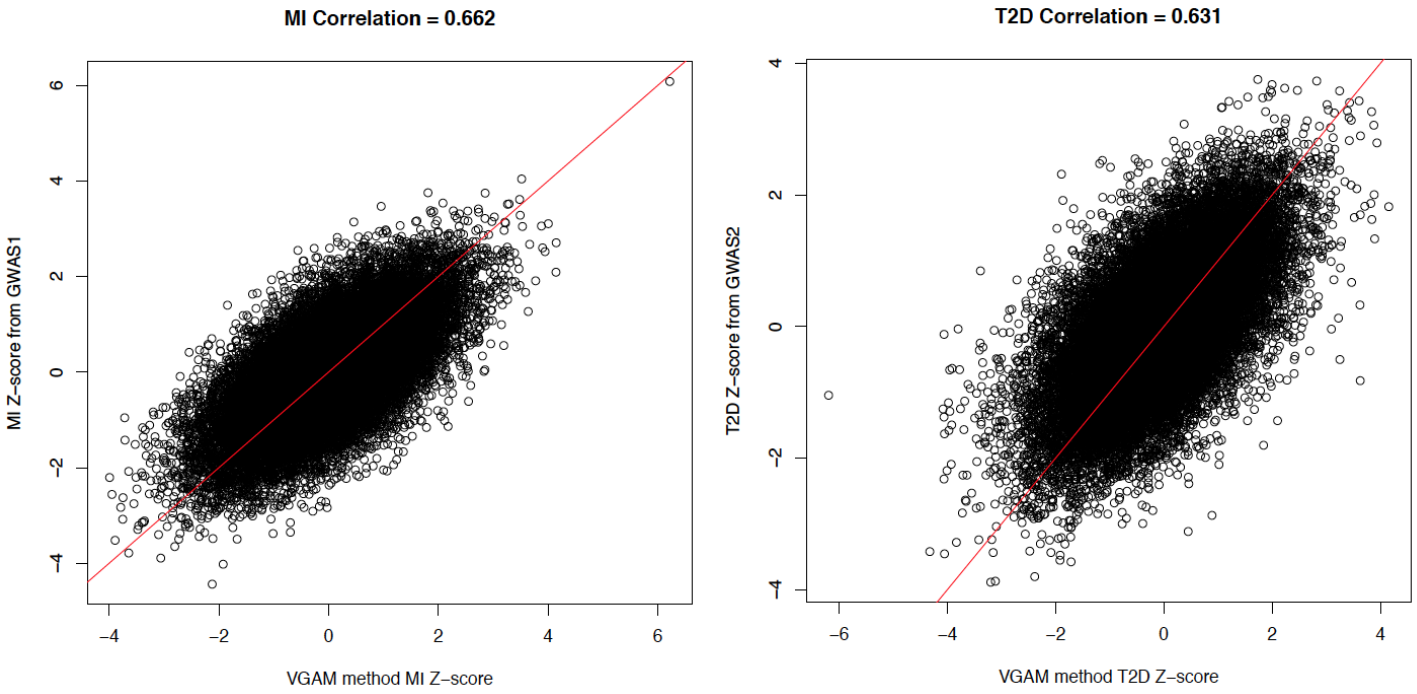
Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 6a. QQ plot for the T2D-CHD bivariate scan.



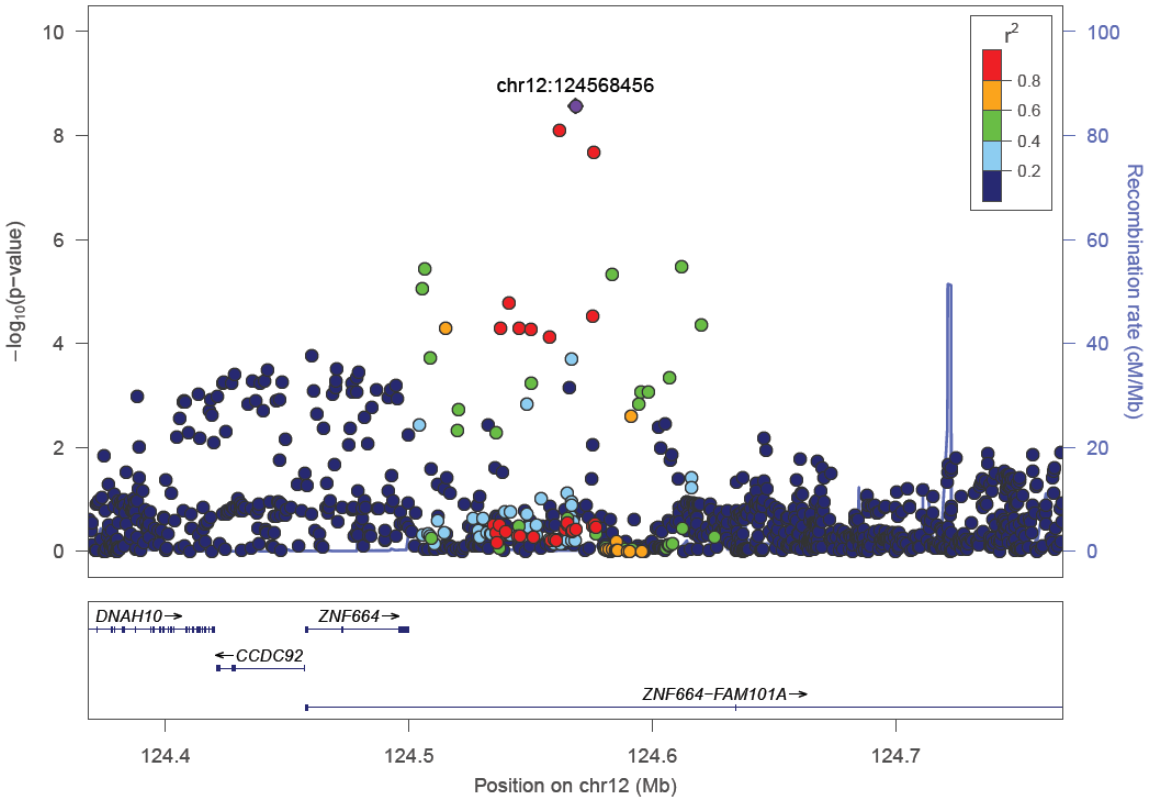
Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 6b. Correlation in bivariate Z-score based on multivariable regression analysis vs. joint analysis of univariate summary statistics.



Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 7a. Regional association plot at *CCDC92* locus discovered through T2D-CHD bivariate scan analyses.

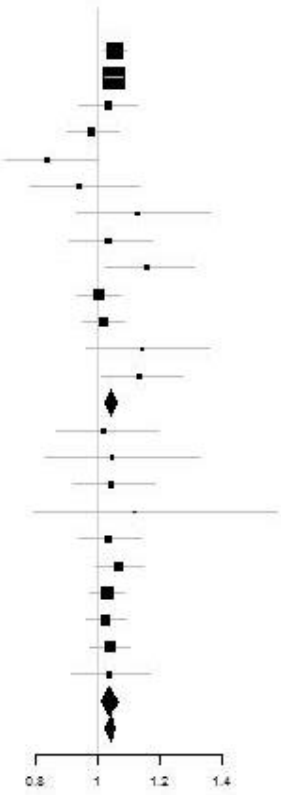


Nature Genetics: doi:10.1038/ng.3943

Supplementary Figure 7b. Forest plot detailing the discovery and replication studies for rs825476 (CCDC92), with respect to T2D association.

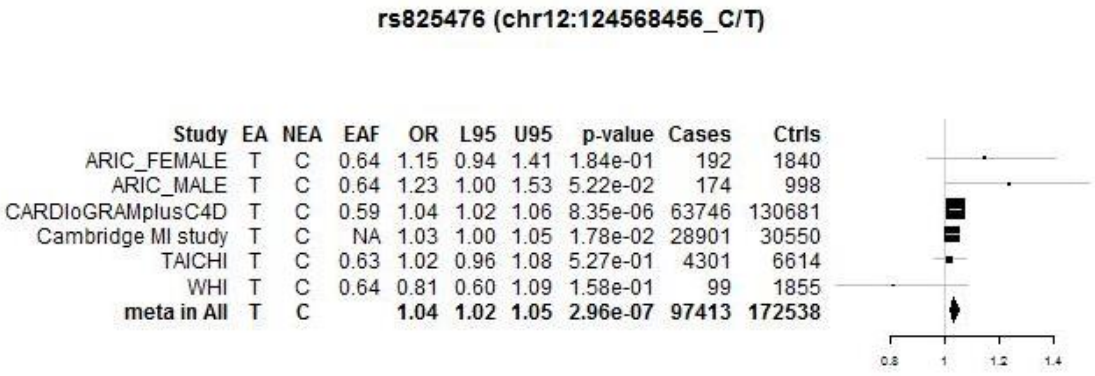
rs825476 (chr12:124568456_C/T)

Group	Study	EA	NEA	EAF	OR	L95	U95	p-value	Cases	Ctrls
DISCOVERY	DIAGRAMv3	T	C	0.57	1.05	1.02	1.09	4.10e-03	9495	53076
DISCOVERY	DIAGRAM metabo	T	C	0.57	1.05	1.02	1.08	3.15e-04	22669	58119
DISCOVERY	FINRISK	T	C	0.58	1.03	0.94	1.13	4.85e-01	1563	7553
DISCOVERY	MDC	T	C	0.59	0.98	0.90	1.07	6.37e-01	1418	5722
DISCOVERY	MEDSTAR	T	C	0.42	0.84	0.70	1.00	5.36e-02	358	964
DISCOVERY	PENNCATH	T	C	0.42	0.94	0.78	1.14	5.32e-01	278	1113
DISCOVERY	BRAVE	T	C	0.58	1.13	0.93	1.36	2.08e-01	250	2189
DISCOVERY	EPIDREAM	T	C	0.57	1.03	0.91	1.18	6.08e-01	612	2039
DISCOVERY	PROMIS GWAS1	T	C	0.60	1.16	1.02	1.31	2.03e-02	737	1804
DISCOVERY	PROMIS GWAS2	T	C	0.61	1.00	0.94	1.07	9.43e-01	3930	3250
DISCOVERY	PROMIS metabo	T	C	0.61	1.02	0.95	1.09	6.03e-01	2439	7088
DISCOVERY	RACE GWAS1	T	C	0.61	1.14	0.97	1.36	1.21e-01	602	598
DISCOVERY	RACE GWAS2	T	C	0.59	1.13	1.01	1.27	3.08e-02	1084	1527
	meta in DISCOVERY	**T**	**C**		**1.04**	**1.03**	**1.06**	**2.21e-06**	**45435**	**145042**
REPLICATION	LOLIPOP-IA317	T	C	0.59	1.02	0.87	1.20	8.04e-01	465	1393
REPLICATION	LOLIPOP-IA610	T	C	0.62	1.05	0.83	1.33	6.93e-01	326	453
REPLICATION	SINDI	T	C	0.57	1.04	0.92	1.18	5.05e-01	974	1168
REPLICATION	SHARP	T	C	0.62	1.12	0.80	1.58	5.15e-01	77	981
REPLICATION	Penn Bio Bank	T	C	0.58	1.04	0.94	1.14	4.62e-01	1047	5917
REPLICATION	Michigan Bio Bank	T	C	0.59	1.07	1.00	1.14	5.85e-02	1987	14906
REPLICATION	INTERACT1	T	C	0.57	1.03	0.98	1.09	2.76e-01	7269	5121
REPLICATION	INTERACT2	T	C	0.57	1.03	0.96	1.09	4.32e-01	4254	4187
REPLICATION	TAICHI	T	C	0.63	1.04	0.98	1.11	2.06e-01	4535	4800
REPLICATION	PROMIS Exomechip	T	C	0.61	1.04	0.92	1.17	5.52e-01	626	3888
	meta in REPLICATION	**T**	**C**		**1.04**	**1.01**	**1.07**	**5.54e-03**	**21560**	**42814**
	meta in ALL	**T**	**C**		**1.04**	**1.03**	**1.06**	**4.33e-08**	**66995**	**187856**



Nature Genetics: doi:10.1038/ng.3943

Supplmentary Figure 7c. Forest plot detailing the discovery and replication studies for rs825476 (CCDC92), with respect to CHD association. Description about the CHD meta-analyses are provided in Supplementary Methods section of this note under "Details on studies contributing to the CHD meta-analysis".



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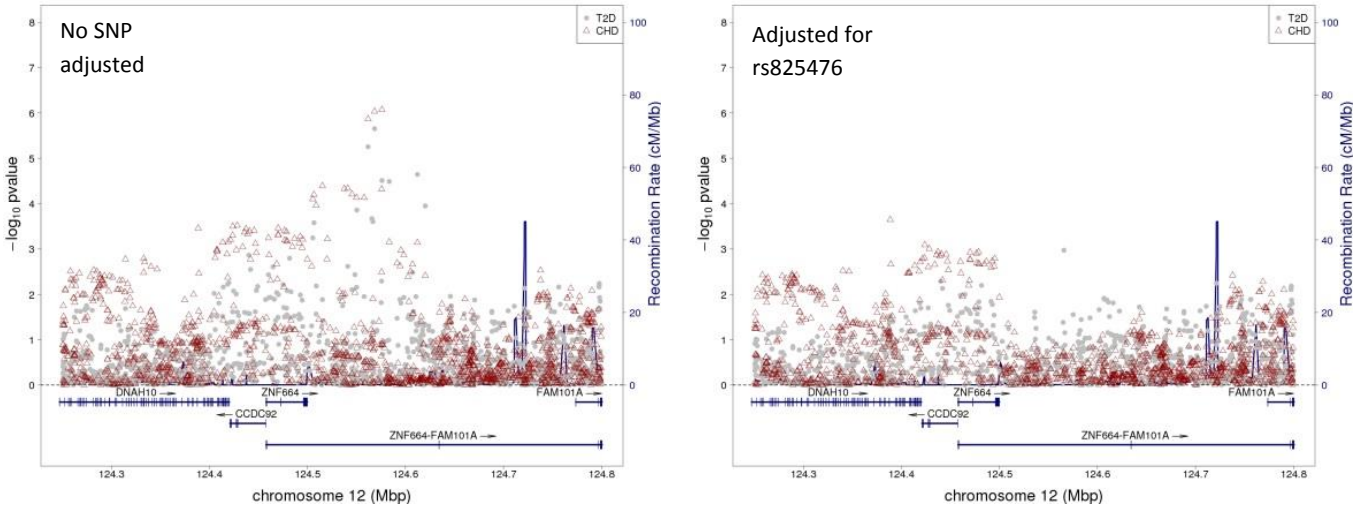
Supplementary Figure 8. Analyses of the CCDC92 signal, conditioning on rs825476, to indicate co-localize the genetic signal for T2D and CHD.

CCDC92



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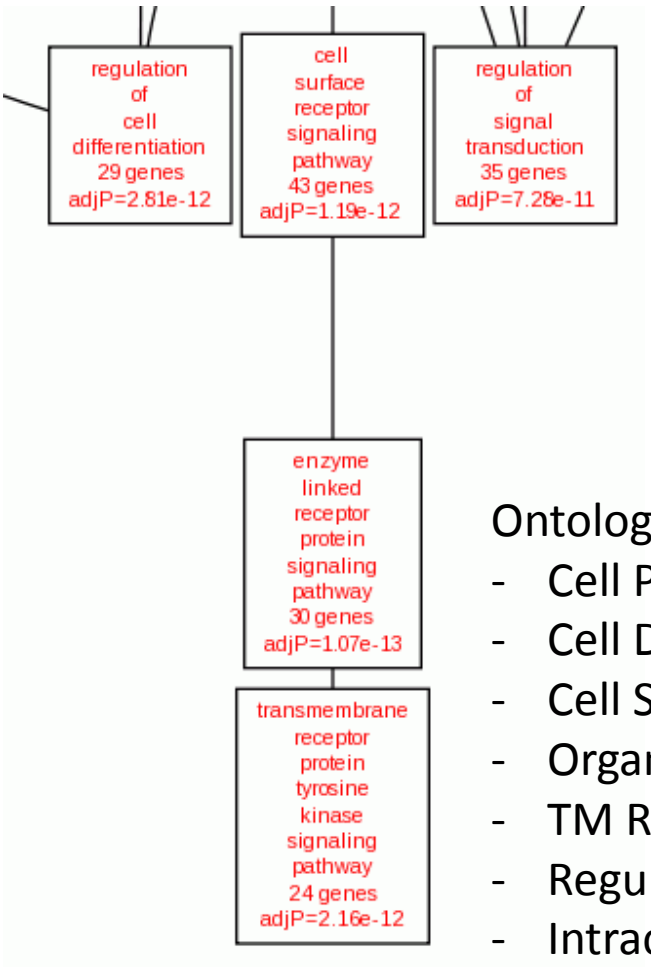
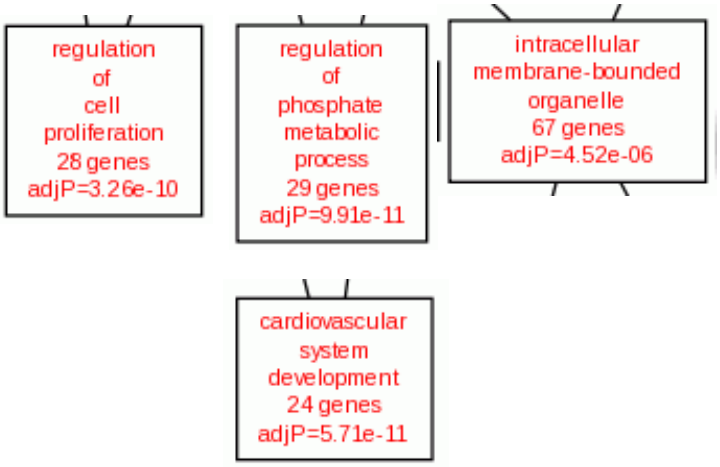
Supplementary Figure 9. Ontology analysis on the set of 79 loci that emerged from T2D-CHD bivariate scan for connectivity.





Ontology analysis Enrichment:

- Cell Proliferation
- Cell Differentiation
- Cell Signaling
- Organ development
- TM Receptor Protein Kinase
- Regulation of Phosphate metabolism
- Intracellular membranes
- Cardiovascular system development

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