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Supplemental Data

Whole-Genome Sequencing Coupled to Imputation Discovers Genetic Signals for Anthropometric Traits

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This research has been conducted using the UK Biobank Resource.

Supplemental Note

Cohort Descriptions

Cohorts contributing to the discovery phase: Whole-genome sequencing datasets

The Avon Longitudinal Study of Parents and Children (ALSPAC)

ALSPAC is a long-term health research project. More than 14,000 mothers enrolled during pregnancy in 1991 and 1992, and the health and development of their children has been followed in great detail ever since[1,2]. The ALSPAC families have provided a large amount of genetic and environmental information during the course of this longitudinal study. The study website contains details of all the data that is available through a fully searchable data dictionary. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Study participants were selected to maximise phenotypic coverage, previous genome-wide array genotyping, coverage with other "-omic" datasets (transcriptomic, metabolomic) and consent to whole genome sequencing, but were otherwise representative of the original population samples. For ALSPAC, the sequenced and imputed samples were combined for phenotype preparation.

The St Thomas' Twin Registry (TwinsUK)

The Department of Twin Research and Genetic Epidemiology (DTR) is the UK's only twin registry of 12,000 identical and non-identical twins between the ages of 16 and 85 years[3]. The database is used to study the genetic and environmental aetiology of age-related complex traits and diseases. Study participants were selected to maximise phenotypic coverage, previous genome-wide array genotyping, coverage with other "-omic" datasets (transcriptomic, metabolomic) and consent to whole genome sequencing, but were otherwise representative of the original population samples.

ALSPAC and TwinsUK WGS data quality control:

Of the 4,030 samples (1,990 TwinsUK and 2,040 ALSPAC) that were submitted for sequencing, 3,910 samples (1,934 TwinsUK and 1,976 ALSPAC) were sequenced and went through the variant calling procedure. Low quality samples were removed for any of the following reasons: high overall discordance to GWAS genotype data, high heterozygosity, no GWAS genotype data available, or sample below 4x mean read-depth. Overall, 3,798 samples (1,870 TwinsUK and 1,928 ALSPAC) were brought forward to the genotype refinement step. After the genotype refinement further samples were removed for any of the following reasons, post-refinement non-reference discordance with GWAS data, multiple relations to other samples, or discordance with manifest gender. This left a final set of 3,781 samples (1,854 TwinsUK and 1,927 ALSPAC). Details on production and quality control of ALSPAC and TwinsUK WGS are described in [4].

TwinsUK anthropometric traits:

Total body and regional fat mass was measured using a dual-energy x-ray absorptiometry (DXA) scanner (Hologic Discovery X-Ray Bone Densitometer; Hologic Model QDR-4500W). Participants were placed with light clothes and without metal objects in a recumbent position on the DXA table.

ALSPAC anthropometric traits:

A Lunar prodigy narrow fan beam densitometer was used to perform a whole body DXA scan where bone content, lean and fat masses are measured. The procedure was clearly explained to the child and parent and parental consent was obtained before proceeding. The child was asked to lie on the Prodigy couch (in light clothing without any metal fastenings), with the parent sitting at least a metre away to comply with the IRMER legislation. The child's height, weight, date of birth, gender and ethnicity (if appropriate) were entered into the computer and the machine was started. The arm of the machine moved over the child and two sources of X-ray scan the child. The child was reassured throughout the scan and encouraged to keep as still as possible. A daily QA was performed using the calibration block in accordance with the

manufacturers recommendations. The radiation protection supervisor or deputy scanned a spine phantom weekly.

FINRISK

The FINRISK study is a series of population-based cardiovascular risk factor surveys carried out every five years in five (or six in 2002) geographical areas of Finland, including North Karelia, Northern Savo (former Kuopio), Southwestern Finland, Oulu Province, Lapland province (in 2002 only) and the region of Helsinki and Vantaa[5]. A stratified random sample was drawn for each survey from the national population register; the age-range was 25-74 years. All individuals enrolled in the study received a physical examination, a self-administered questionnaire, and a blood sample was drawn. The Coordinating Ethical Committee of the Helsinki and Uusimaa Hospital District has approved the FINRISK surveys, which followed the declaration of Helsinki.

Anthropometric traits:

At the study sites, specially trained nurses measured weight, height, waist circumference, and hip circumference using standardized international protocols. All anthropometric measures were assessed with the participant in light clothing and with bare feet. The measurement of weight was rounded to the nearest 0.1 kg and height to the nearest 0.1 cm. BMI was calculated as the weight in kilograms divided by the squared height in meters (kg/m^2). Waist circumference was measured midway between the lower rib margin and iliac crest. Hip circumference was measured at the level of the widest circumference over the buttocks. The measurements of waist and hip circumferences were rounded to the nearest 0.5 cm. Waist to hip ratio was calculated as waist circumference divided by hip circumference.

Cohorts contributing to the discovery phase: GWAS imputed on the 1000 Genomes and UK10K haplotype panels

ALSPAC and TwinsUK GWAS

Additional GWAS data were used for each cohort. For ALSPAC, there were another 6,557 samples available, which were measured on Illumina HumanHap550 arrays 20. For TwinsUK, there were another 2,575 samples that were unrelated to the sequence dataset (IBS>0.125) with genotypes on Illumina HumanHap300 or Illumina Human610 arrays 21.

ALSPAC and TwinsUK GWAS data quality control:

Both datasets passed QC criteria (gender check, heterozygosity, European ancestry, relatedness (ALSPAC) and zygosity (TwinsUK). Variants discovered through WGS of the TwinsUK and ALSPAC cohorts were imputed into the full GWAS genotyped cohorts increasing the sample size for single point association analysis up to 9,132 subjects. The combined UK10K and 1000 Genomes Project reference panel and imputation of it into ALSPAC and TwinsUK GWAS arrays are discussed in [4,6].

TwinsUK anthropometric traits:

Total body and regional fat mass was measured using a dual-energy x-ray absorptiometry (DXA) scanner (Hologic Discovery X-Ray Bone Densitometer; Hologic Model QDR-4500W). Participants were placed with light clothes and without metal objects in a recumbent position on the DXA table.

ALSPAC anthropometric traits:

A Lunar prodigy narrow fan beam densitometer was used to perform a whole body DXA scan where bone content, lean and fat masses are measured. The procedure was clearly explained to the child and parent and parental consent was obtained before proceeding. The child was asked to lie on the Prodigy couch (in light clothing without any metal fastenings), with the parent sitting at least a metre away to comply with the IRMER legislation. The child's height, weight, date of birth, gender and ethnicity (if appropriate) were entered into the computer and the machine was started. The arm of the machine moved over the child and two sources of X-ray scan the child. The child was reassured throughout the scan and encouraged to keep as still as possible. A daily QA was performed using the calibration block in accordance with the manufacturers recommendations. The radiation protection supervisor or deputy scanned a spine phantom weekly.

United Kingdom Household Longitudinal Study (UKHLS)

The UKHLS, also known as Understanding Society is a longitudinal panel survey of 40,000 UK households (England, Scotland, Wales and Northern Ireland) representative of the UK population[7]. Participants are surveyed annually since 2009 and contribute information relating to their socioeconomic circumstances, attitudes, and behaviours via a computer assisted interview. The study includes phenotypical data for a representative sample of participants for a wide range of social and economic indicators as well as a biological sample collection encompassing biometric, physiological, biochemical, and haematological measurements and self-reported medical history and medication use. The UKHLS has been approved by the University of Essex Ethics Committee and informed consent was obtained from every participant.

UKHLS data quality control:

In total, 10,484 samples were genotyped on the Illumina HumanCoreExome chip (v1.0) at the Wellcome Trust Sanger Institute. Genotype calling was performed using GenCall and zCall. We excluded samples with a call rate <98% and <99% for Gencall and zCall respectively, or that were heterozygosity outliers, had sex discrepancies, were duplicates or that were ethnic outliers. Variants were excluded with a call rate below 95% and 99% for GenCall and zCall respectively, with a Hardy-Weinberg equilibrium *P-value* < 10^{-4} or with a cluster separation score < 0.4. Prior to phasing we compared the variants to the 1000 Genomes Project and the UK10K haplotypes and we excluded any variant for which the alleles differed for the same variant at the same position. In addition variants were excluded if they were a duplicate, monomorphic, a singleton or known to have poor clustering after inspecting the intensity data. Samples were phased using SHAPEITv2 and imputed using IMPUTE v2. Unrelated samples were determined by performing identity by descent using the autosomal directly genotyped variants with MAF≥1% and filtered so that variants with a linkage-disequilibrium r^2 <0.2 remained, in total 9175 unrelated samples were included in the analysis.

Rotterdam Study cohort I (RS-I)

The Rotterdam Study is an ongoing prospective population-based cohort study, focused on chronic disabling conditions of the elderly. The study comprises an outbred ethnically homogenous population of Dutch Caucasian origin. The rationale of the study has been described in detail elsewhere[8]. In summary, 7,983 men and women aged 55 years or older, living in Ommoord, a suburb of Rotterdam, the Netherlands, were invited to participate in the first phase. Fasting blood samples were taken during the participant's third visit to the research center.

Rotterdam Study cohort II (RS-II)

The Rotterdam Study cohort II prospective population-based cohort study comprises 3,011 residents aged 55 years and older from the same district of Rotterdam. The rationale and study design of this cohort is similar to that of the RS-I[8]. The baseline measurements took place during the first visit. The Rotterdam Study has been approved by the Medical Ethics Committee of the Erasmus MC and by the Ministry of Health Welfare and Sport of the Netherlands, implementing the "Wet Bevolkingsonderzoek: ERGO (Population Studies Act: Rotterdam Study)". All participants provided written informed consent to participate in the study and to obtain information from their treating physicians.

Rotterdam Study cohort III (RS-III)

The Rotterdam Study is an ongoing prospective population-based cohort study, focused on chronic disabling conditions of the elderly. The study comprises an outbred ethnically homogenous population of Dutch Caucasian origin. In 2006 all residents of Ommoord aged 45 years and over and who had not been invited before to RSI or RSII, were asked to participate following the same rationale that in these studies. A total of 3,932 out 6,057 of men and women entered the study. All participants provided written informed consent to participate in the study and to obtain information from their treating physicians.

Anthropometric traits for Rotterdam Study cohorts I-III:

For all participants dual-energy x-ray absorptiometry (DXA) based bone mineral density (BMD) measurements of the lumbar spine, dual hip and total body BMD, as well as determination of body composition parameters are assessed with a ProdigyTM total body fan-beam densitometer (GE Lunar Corp, Madison, WI, USA). From the total body scan, we measure lean mass and fat mass body composition, including total body, trunk, arm, legs, and android and gynoid regions of interest[9].

The Ludwigshafen Risk and Cardiovascular Health (LURIC) study - controls

The LURIC study is a prospective study of more than 3,300 individuals of German ancestry in whom cardiovascular and metabolic phenotypes (CAD, MI, dyslipidaemia, hypertension, metabolic syndrome and diabetes mellitus) have been defined or ruled out using standardised methodologies in all study participants. A 10-year clinical follow-up for total and cause specific mortality has been completed[10]. From 1997 to 2002 about 3,800 patients were recruited at the Heart Center of Ludwigshafen (Rhein). Inclusion criteria were: German ancestry, clinical stability (except for acute coronary syndromes) and existence of a coronary angiogram. Exclusion criteria were: any acute illness other than acute coronary syndromes, any chronic disease where non-cardiac disease predominated and a history of malignancy within the last five years. The study was approved by the ethics review committee at the Landesarztekammer Rheinland-Pfalz in Mainz, Germany, and written informed consent was obtained from the participants.

1958 Birth Cohort

Participants to the cohort have been followed-up regularly since birth with prospective information collected on a wide range of indicators related to health, health behaviour, lifestyle, growth and development. There have been 9 contacts with the participants since their birth (ages 7, 11, 16, 23, 33, 41, 45, 47, and 50 years). The biomedical survey at age 45 years included collection of blood samples and DNA from about 8000 participants. The survey was approved by the South East multicentre research ethics committee (MREC). There was an informed consent process conducted by the National Centre for Social Research[11].

TEENs of Attica: Genes and Environment (TEENAGE)

Participants were drawn from the TEENAGE study. A random sample of 857 adolescent students attending public secondary schools located in the wider Athens area of Attica in Greece were recruited in the study from 2008 to 2010. Our sample comprised 707 (55.9% females) adolescents of Greek origin aged 13.42 ± 0.88 years. Details of recruitment and data collection have been described elsewhere[12]. Prior to recruitment all study participants gave their verbal assent along with their parents'/guardians' written consent forms. The study was approved by Harokopio University Bioethics Committee and the Greek Ministry of Education, Lifelong Learning and Religious Affairs. DNA samples were genotyped using Illumina HumanOmniExpress BeadChips (Illumina, San Diego, CA, USA) at the Wellcome Trust Sanger Institute, Hinxton, UK. Genotyping and data quality control have been described previously[12].

HELIC MANOLIS

The HELIC (Hellenic Isolated Cohorts) MANOLIS (Minoan Isolates) collection focuses on Anogia and surrounding Mylopotamos villages. Recruitment of this population-based sample was primarily carried out at the village medical centres. All individuals were older than 17 years and had to have at least one parent from the Mylopotamos area. The study includes biological sample collection for DNA extraction and lab-based blood measurements, and interview-based questionnaire filling. The phenotypes collected include anthropometric and biometric measurements, clinical evaluation data, biochemical and haematological profiles, self-reported medical history, demographic, socioeconomic and lifestyle information. The study was approved by the Harokopio University Bioethics Committee and informed consent was obtained from every participant.

HELIC Pomak

The HELIC (Hellenic Isolated Cohorts) Pomak collection focuses on the Pomak villages, a set of isolated mountainous villages in the North of Greece. Recruitment of this population-based sample was primarily carried out at the village medical centres. The study includes biological sample collection for DNA extraction and lab-based blood measurements, and interview-based questionnaire filling. The phenotypes collected include anthropometric and biometric measurements, clinical evaluation data, biochemical and haematological profiles, self-reported medical history, demographic, socioeconomic and lifestyle information. The study was approved by the Harokopio University Bioethics Committee and informed consent was obtained from every participant.

HELIC MANOLIS and HELIC Pomak data quality control:

The HELIC samples were genotyped on both the Illumina HumanOmniExpress and Illumina HumanExome chip at the Wellcome Trust Sanger Institute. For the genotype calling we used Illuminus for OmniExpress and GenCall followed by zCall for the exome chip. We excluded samples with sex discrepancies, that were duplicates or ethnic outliers, that were heterozygosity outliers or that had a call rate <98% for OmniExpress and call rate <98% and <99% for Exome chip for GenCall and zCall respectively. We excluded variants with call rate <95%, if they had a MAF≥5%, and <99%, if they had a MAF<5% for OmniExpress and call rate <95% and <99% for Exome chip for GenCall and zCall respectively or that had a Hardy-Weinberg equilibrium *P-value* $<10^{-4}$. We also excluded variants with a cluster separation score <0.4 for the Exome chip. We combined the genotypes for the OmniExpress and Exome chip into a single dataset. If a variant was present in both the OmniExpress and Exome array then the genotypes for those variants with MAF≥5% were taken from the OmniExpress whilst those with MAF <5% were taken from the Exome chip. Prior to phasing we compared the variants to the 1000 Genomes Project data and the UK10K haplotypes and we excluded any variant for which the alleles differed for the same variant at the same position. Variants were also excluded if they had MAF <5% and were genotyped on the OmniExpress, were monomorphic, a duplicate, a singleton or that were known to have poor clustering after inspecting the intensity data. We phased using SHAPEITv2 and imputed using IMPUTE v2.

INGI-Val Borbera (INGI-VB)

The INGI-Val Borbera population is a collection of 1,785 genotyped samples collected in the Val Borbera Valley, a geographically isolated valley located within the Appennine Mountains in Northwest Italy[13]. The valley is inhabited by about 3,000 descendants from the original population, living in 7 villages along the valley and in the mountains. Participants were healthy people 18-102 years of age that had at least one grandfather living in the valley. A standard battery of tests was performed by the laboratory of ASL 22 - Novi Ligure (AL), on sera from fasting blood collected in the morning. The project was approved by the Ethical committee of the San Raffaele Hospital and of the Piemonte Region. All participants signed an informed consent.

INGI-Friuli Venezia Giulia (INGI-FVG)

The Friuli Venezia Giulia population represents a collection of six villages covering a total area of 7858 km^2 in a hilly part of Friuli-Venezia Giulia (FVG) county located in north-eastern Italy. A recent study[14] characterized this population as a genetic isolate with high level of genomic homozygosity and elevated linkage disequilibrium. The cohort accounts for 1,590 genotyped samples. Participants were randomly selected people 3-92 years of age. Genotyping and phenotyipic data for 1,590 samples are available. People with age <18 were excluded from analyses. A written informed consent for participation was obtained from all subjects. The project was approved by the Ethical committee of the IRCCS Burlo-Garofolo.

INGI-Carlantino (INGI-Carl)

Carlantino is a small village in the Province of Foggia in southern Italy. Genetic analyses of chromosome Y haplotypes as well as mitochondrial DNA show that Carlantino is a genetically homogeneous population and not only a geographically isolated village[14]. Participant were randomly selected in a range of 15 – 90 years of age. Genotyping and phenotypic data are available for 630 individuals. People with age <18 were

excluded from analyses. Subjects gave their written informed consent for participating in these studies. The project was approved by the local administration of Carlantino, the Health Service of Foggia Province, Italy, and ethical committee of the IRCCS Burlo-Garofolo of Trieste.

Arthritis Research UK Osteoarthritis Genetics (arcOGEN)

arcOGEN is a collection of unrelated, UK-based individuals of European ancestry with knee and/or hip osteoarthritis (OA) from the arcOGEN Consortium[15,16]. Cases were ascertained based on clinical evidence of disease to a level requiring joint replacement or radiographic evidence of disease (Kellgren–Lawrence grade ≥2). The arcOGEN study was ethically approved, and all subjects used in this study provided written, informed consent.

INCIPE

For the INCIPE study, 6200 randomly chosen individuals, all of European descent and at least 40 years of age as of 1 January 2006, received a letter inviting them to participate in the study. A total of 3870 subjects (62%) accepted and were enrolled. The ethics committees of the involved institutions approved the study protocol. Two studies were included in the analysis:

1. INCIPE1: Individuals genotyped on HumanOmniExpress-12v1-Multi_B
2. INCIPE2: Individuals genotyped on HumanCoreExome-12v1

London Life Sciences Prospective Population Study (LOLIPOP)

LOLIPOP is an ongoing community prospective cohort of 17,606 Indian Asian and 7,766 European men and women aged 35-75 years, recruited in West London, UK, to study the environmental and genetic factors that contribute to cardiovascular disease among UK Indian Asians[17,18]. Indian Asian participants reported having all four grandparents born on the Indian subcontinent, while European participants are self-classified whites born in Europe. For the current study, only white individuals were included in the primary meta-analysis. All participants provided written consent including for genetic studies. The LOLIPOP study is approved by the local Research Ethics Committees.

Three studies were included in the analysis:

1. LOLIPOP_EW_A: European whites from the general population, genotyped on Affymetrix 500K arrays.
2. LOLIPOP_EW_P: European whites from the general population, enriched by subjects with metabolic syndrome, genotyped on Perlegen custom array.
3. LOLIPOP_EW610: European whites from the general population, genotyped on Illumnia Human610 array.

Cohorts contributing to the follow-up effort: *In silico* follow-up

SardiNIA

The SardiNIA study is a longitudinal population-based cohort study started in 2001 to study quantitative traits of biomedical relevance with a special emphasis on those influencing aging. In a first survey, the project recruited individuals from four towns in the Lanusei Valley (east-central Sardinia) and assessed 98 quantitative traits including over 62% of the eligible population living in the region (age 14-102 years), and at least 96% of the initial cohort have all grandparents born in the same province. The initial group of 6,148 individuals included 4,933 phenotyped sib pairs, 4,266 phenotyped parent-child pairs, >4,069 phenotyped cousin pairs, and >6,459 phenotyped avuncular pairs. Recently, the study recruited 773 additional individuals, involving a total of 6,921 subjects. The longitudinal study, now in its 14th year and in its fourth phase, collected the longitudinal information on more than 1000 quantitative traits, including inflammatory markers and immuno-related traits, that can be scored on a continuous scale[19,20]. A written informed consent was obtained from all participants.

<u>Quality control:</u>

Samples having sex discordance or with call rate lower than 98% were removed from the analyses.

SNPs with call rate lower than 98%, HWE *P-value* $<10^{-6}$, at least 1 mendelian errors in more than 1% of the available families, monomorphic and with more than 1 discordance in 13 twin pairs were removed from the analyses.

GenerationR (GenR)

This study was embedded in the Generation R Study, a population-based prospective cohort study from fetal life onwards in Rotterdam, the Netherlands. The Medical Ethics Committee of the Erasmus MC, University Medical Center, Rotterdam, has approved the study and written informed consent was obtained for all participants. All children were born between April 2002 and January 2006. Enrollment was aimed at early pregnancy, but was allowed until birth of the child. In total, 9,778 mothers and their children were included in the study. Details of recruitment and data collection have been described in detail elsewhere[21,22]. The current analysis includes those children with genome-wide scan data that had a DXA scan around the age of six years.

Anthropometric traits:

Total body and regional fat mass was measured using a dual-energy x-ray absorptiometry (DXA) scanner (iDXA, 2008; GE-Lunar) and analyzed with the enCORE software, version 12.6 (GE-Healthcare). DXA can accurately detect whole-body fat mass within less than 0.25% coefficient of variation. Children were placed without shoes, heavy clothing, and metal objects in supine position on the DXA table. Total fat mass (kilograms) was calculated as a percentage of total body weight (kilograms) measured by DXA. The fat mass index (body fat mass/height^2), and lean mass index (body lean mass/height^2) calculated[23].

Quality Control:

Cord blood for DNA isolation was available in 58% of all live-born participating children. Sex-mismatch rate between genome based sex and midwife-record based sex was low (<0.5%), indicating that possible contamination of maternal DNA was extremely low. Missing cord blood samples were mainly due to logistical constraints at the delivery. GWAS scans were run using the Illumina 610 Quad and 660 platforms. IMPUTE2 software was used to impute genotypes to the combined UK10K-1000 genomes panel. Before imputation, SNPs were excluded if they had high levels of missing data (SNP call rate <98%), strong departures from Hardy-Weinberg equilibrium (*P-value* $<1x10^{-6}$), or low MAF (<0.1%).

UK Biobank

500,000 participants aged 40-69 years were recruited between 2006 and 2010 in 22 assessment centres throughout the UK[24]. The assessment visit included electronic signed consent; a self-completed touch-screen questionnaire; brief computer-assisted interview; physical and functional measures; and collection of biological samples and genetic data.

Anthropometric traits:

BMI was calculated (kg/m^2) using measured height and weight. Weight (kg) was measured using the Tanita BC-418 MA body composition analyser (accurate to within 0.1kg) after removal of heavy clothing and shoes. Standing height (cm) was measured without shoes using a Seca 202 height measure. Waist circumference (cm) at the level of the umbilicus and hip circumference was measured using a Wessex non-stretchable sprung tape measure.

Data Quality Control:

All the analyses were carried out in Europeans. Subjects with high heterozygosity, low call rate, related participants, and pregnant women were further excluded from analyses. SNP genotypes were called by Affymetrix, and any SNPs failed by Affymetrix batch-specific QC thresholds were set to missing in all subjects from that batch. Additional SNP QC steps were carried out by the UK Biobank team, in which SNPs at certain batch/plates were set to missing if their genotype distributions were significantly different from other batches/plates (*P-value* $<10^{-12}$), or there were significant deviations of genotype frequencies from those expected under Hardy-Weinberg equilibrium (*P-value* $<10^{-12}$). Imputation was carried out, with the combined reference panel of 1000 Genomes phase 3 and UK10K data. Any variants imputed, with minor allele frequency of <0.001% were filtered. Association results from SNPs with imputation quality score <0.3 were discarded.

Cohorts contributing to GoT2D:

WGS

Diabetes Genetics Initiative (DGI)
Details of the samples have been described elsewhere[25]. For sequencing, we selected individuals from the phenotypic extremes using T2D liability scores calculated based on disease status, age, BMI, and sex[26]. We chose individuals from the studies used for the DGI GWAS, the Scania Diabetes Registry[27], and the Malmö Preventive Project[28]. We prioritized early-onset cases with low BMI and older controls with high BMI; we excluded cases with age of diagnosis<35 years to minimize inclusion of individuals with type 1 diabetes (T1D).

Finland-United States Investigation of NIDDM Genetics (FUSION)
Details of the samples have been described elsewhere[29]. For sequencing, we chose T2D cases from FUSION families with ≥2 first-degree relatives with T2D and selected one individual per family with either available GWAS data or earliest age at diagnosis. Remaining cases were chosen from the FUSION replication set, selecting those with earlier age at diagnosis from among those with Metabochip data and age at diagnosis≥35 years. Unrelated normal glucose tolerant (NGT) controls with age≤80 years were frequency matched to the cases by birth province and, within each birth province, controls with the highest age (in years) + 2×BMI (in kg/m^2) were prioritized. All selected individuals had BMI≥18.5 kg/m^2.

Cooperative Health Research in the Region of Augsburg (KORA)
Details of the samples have been described elsewhere[30-32]. For sequencing, we prioritized cases with ≥1 first-degree relative with T2D (self-reported). We then chose individuals with BMI≤30 kg/m^2 and age of diagnosis<65 years, or BMI≤33 kg/m^2 and age of diagnosis≤60 years. We selected controls from KORA F4 who were either >60 years of age with BMI>32 kg/m^2, or >65 years of age with BMI>31 kg/m^2.

United Kingdom T2D Genetics consortium (UKT2D)
Details of the samples have been described elsewhere[33-35]. For sequencing, we chose cases from the Wellcome Trust Case Control Consortium (WTCCC) and controls from the TwinsUK study. For cases, we excluded females with age of diagnosis≥66 years or BMI≥32 kg/m^2, and males with age of diagnosis≥62 years or BMI≥31 kg/m^2. We ranked the remaining samples by age and BMI; we multiplied the two ranks and selected individuals with the lowest product of ranks. For controls, we considered twin pairs (a) with no recorded family history of diabetes; (b) with neither twin ever recorded as impaired glucose tolerant (fasting glucose [FG]>6.1mmol/l); and (c) who had available quantitative trait and GWAS data and no evidence of admixture in analysis of the GWAS data. From qualifying twin pairs, we chose the twin with the lowest ratio of FG level to BMI across all readings, giving priority to unrelated individuals with the lowest FG/[BMI×age] ratio. We performed pairwise sample matching between cases and possible controls using the first two principal components from an analysis of previously available genome-wide genotyping data, with the best control for each case selected.

Imputed GWAS

Diabetes Genetics Initiative (DGI)
Details of the samples and GWAS have been described elsewhere[25]. The current analysis included 899 T2D cases and 1,057 NGT controls from Sweden or Finland. The Finnish samples were predominantly from the Botnia region of Finland and the Swedish samples from Southern Sweden and Skara. T2D cases from both countries met WHO 1999 criteria with FG≥7.0 mmol/l or 2-hour glucose≥11.1 mmol/l during an oral glucose tolerance test. Cases had age of diagnosis >35 years and no detectable anti-GAD antibodies (defined as anti-GAD antibody levels <32 IU/ml in the Finnish samples and <1.3 anti-GAD relative units in

the Swedish). Controls had no first-degree relatives with T2D. Cases and controls were matched on age (within 5 years), sex, BMI, and geographic region. Samples were genotyped using the Affymetrix Human Mapping 500K array.

Estonian Genome Center of the University of Tartu (EGCUT)
Details of the samples have been described elsewhere[36]. The current analysis included 469 T2D cases and 7,781 population-based controls from the Estonian Biobank cohort, a volunteer-based sample of the Estonian resident adult population aged ≥18 years. T2D diagnosis was based on standardized health examination together with questionnaires on health-related topics as described in WHO ICD-10. Data are regularly updated through linkage to national databases and registries. Controls represent a random subset of the Estonian population. Participants were genotyped with either the Illumina HumanHap 370K array (EGCUT-370K, 80 cases and 1,768 controls) or the Illumina OmniExpress array (EGCUT-OMNI, 389 cases and 6,013 controls). GWAS analysis was performed separately in the two subsets.

Finland-United States Investigation of NIDDM Genetics (FUSION)
Details of the samples and GWAS have been described elsewhere[29]. The GWAS sample for imputation included 1,060 T2D cases and 1,090 NGT controls of Finnish origin. 688 T2D cases were selected one per family from T2D affected sibling pairs; 372 were from the population-based Finrisk 2002 study. NGT controls included 272 spouses of FUSION study subjects, 188 individuals who were NGT at ages 65 and 70, and individuals from Finrisk 2002. Cases were defined by WHO 1999 criteria of FG≥7.0 mmol/l or 2-hour plasma glucose≥11.1 mmol/l, by reported diabetes medication use, or based on medical record review. FUSION cases were excluded if they had known or probable T1D among first-degree relatives. Controls were NGT as defined by WHO 1999 criteria. Cases and controls were approximately frequency matched by 5-year age category, sex, and birth province. Samples were genotyped using the Illumina HumanHap300 array.

METabolic Syndrome In Men (METSIM)
The cross-sectional METSIM Study includes 10,197 men, aged from 45 to 73 years, randomly selected from the population register of the Kuopio town, Eastern Finland, and examined in 2005-2010. The aim of the study is to investigate genetic and non-genetic factors associated with the risk of type 2 diabetes (T2D), cardiovascular disease (CVD), and insulin resistance –related traits in a cross-sectional and longitudinal setting[37,38]. Study protocol includes e.g. collection of data on CVD risk factors (smoking, exercise, diet, history of chronic diseases including coronary heart disease, stroke, cardiac failure, medication, history of diabetes or early onset coronary heart disease in the family), questionnaire on the FINDISC Score, measurement of height, weight, waist circumference, hip circumference, blood pressure (3 times), and bioimpedance for the evaluation of fat percentage.

Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS)
Details of the samples and GWAS have been described elsewhere[39,40]. Participants were randomly sampled from all men and women aged 70 years living in Uppsala County in 2001. This analysis included 111 T2D cases and 838 non-T2D controls of Swedish descent. T2D status was defined by fasting blood glucose>6.1 mmol/l or known diabetes. Controls were non-T2D individuals. All samples were genotyped with the Illumina Metabochip and Illumina OmniExpress array.

Uppsala Longitudinal Study of Adult Men (ULSAM)
All men born between 1920 and 1924 in Uppsala, Sweden were invited to participate at age 50 years in this longitudinal cohort study that was started in 1970. Participants were reinvestigated at ages 60, 70, 77, 82, and 88 years[41]. Our analysis included 166 T2D cases and 953 non-T2D controls of Swedish descent. T2D status was defined as hospital discharge register-defined diabetes before 2002. Controls were non-T2D individuals. All samples were genotyped with the Illumina Metabochip and Illumina HumanOmni2.5 array.

Cohorts contributing to the follow-up effort: *De novo* follow-up

Fenland

The Fenland Study is an ongoing, population-based cohort study (started in 2005) designed to investigate the association between genetic and lifestyle environmental factors and the risk of obesity, insulin sensitivity, hyperglycemia and related metabolic traits in men and women aged 30 to 55 years[42]. Potential volunteers were recruited from General Practice sampling frames in the Fenland, Ely and Cambridge areas of the Cambridgeshire Primary Care Trust in the UK. Exclusion criteria for the study were: prevalent diabetes, pregnant and lactating women, inability to participate due to terminal illness, psychotic illness, or inability to walk unaided. All participants had measurements done at the MRC Epidemiology Unit Clinical Research Facilities in Ely, Wisbech and Cambridge. Participants attended after an overnight fast for a detailed clinical examination, and blood samples were collected. The Local Research Ethics Committee granted ethical approval for the study and all participants gave written informed consent.

Sequenom genotyping:

Genotyping was performed using the iPLEX® Assay and the MassARRAY® System (Agena Bioscience, Inc.). Assays for all SNPs were designed using the eXTEND suite and MassARRAY Assay Design software version 4.0.0.2 (Agena Bioscience, Inc.). Amplification was performed in a total volume of 5µL containing ~10ng genomic DNA, 100nM of each PCR primer, 500µM of each dNTP, 1.25 x PCR buffer (Qiagen), 1.625mM $MgCl_2$ and 1U HotStar Taq® (Qiagen). Reactions were heated to 94 °C for 15 min followed by 45 cycles at 94°C for 20 s, 56°C for 30 s and 72°C for 1 min, then a final extension at 72°C for 3 min. Unincorporated dNTPs were SAP digested prior to iPLEX™ allele specific extension with mass-modified ddNTPs using an iPLEX reagent kit (Agena Bioscience, Inc.). SAP digestion and extension were performed according to the manufacturer's instructions with reaction extension primer concentrations adjusted to between 0.7-1.8µM, dependent upon primer mass. Extension products were desalted and dispensed onto a SpectroCHIP using a MassARRAY Nanodispenser prior to MALDI-TOF analysis with a MassARRAY Analyzer Compact mass spectrometer. Genotypes were automatically assigned and manually confirmed using MassARRAY TyperAnalyzer software version 4.0 (Agena Bioscience, Inc.).

Sequenom Data Quality Control:

Samples were removed if their call rate was <80%. SNPs were removed if their call rate was <80%, HWE *P-value* $<10^{-4}$ and if the gender in the manifest was discordant with the gender in the Sequenom iPLEX assay.

Anthropometric traits:

Body composition measurements of fat mass were measured by total body DXA scans (GE Lunar Prodigy Advanced, GE Medical Systems, Hatfield, UK). Results were acquired and analysed within the enCORE software (Version 10.51.006 to 16, GE Medical Systems) under basic analysis settings. Participants were positioned according to the total body measurement and analysis protocol recommended by the manufacture. Participants body composition results were recalculated by the symmetry and ½ body method when appropriate (replacing omitted left arm or body with right arm or body data). Volunteers were excluded if pregnancy could not be ruled out and if weight exceeded 136kg.

Copenhagen General Population Study (CGPS)

This general population study was initiated in 2003 with ongoing enrolment[43,44]. BMI and ischemic heart disease endpoints have been collected from 1976 to May 2009. Individuals were selected on the basis of the national Danish Civil Registration System to reflect the adult Danish population aged 20–100 y. All participants were white and of Danish descent; this information is available through the national Danish Central Person Registry. Data were obtained from a questionnaire, a physical examination, blood samples, and from DNA. At the time of genotyping 59,883 participants had been included; of these, 5,270 were used as controls in the Copenhagen Ischemic Heart Disease Study, leaving 54,613 for analyses in the CGPS. The study was approved by Danish ethical committees and Herlev Hospital.

Dataset used for mQTL analyses

ARIES Data

The Accessible Resource for Integrative Epigenomic Studies (ARIES) dataset represents genome-wide DNA methylation levels on ALSPAC samples selected from 1,018 mother-child pairs at three time points in children and two time points in their mothers[45]. A DNA sample was extracted from cord blood drawn from the umbilical cord upon delivery or peripheral blood according to standard procedures. Written informed consent has been obtained from all ALSPAC participants. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Samples were bisulfite converted using the Zymo EZ DNA Methylation^{TM} kit and genome-wide methylation was measured using the Illumina HumanMethylation450 BeadChip. Methylation data were normalized in R with the wateRmelon package[46] using the Touleimat and Tost[47] algorithm to reduce the non-biological differences between probes. Data were then rank-normalized to remove outliers, and regressed on all covariates, plus bisulphite-converted DNA plate batch to remove potential batch effects (with missing values set to probe mean). Children were genotyped using the Illumina HumanHap550 quad genome-wide SNP genotyping platform by the Wellcome Trust Sanger Institute and the Laboratory Corporation of America. Mothers were genotyped using the Illumina human660W-quad genome-wide SNP genotyping platform at the Centre National de Génotypage. Genotypes were phased together using SHAPEIT, and then imputed against the 1000 Genomes reference panel (phase 1 version 3) using Impute. The final imputed dataset contained 8,074,398 SNPs keeping SNPs that have Hardy-Weinberg equilibrium *P-value* $>5\times10^{-7}$, MAF>1% and imputation quality score >0.8. Each SNP in the imputed datasets was analysed against all CpG sites in the Illumina HM450 with the exception of those failing QC, and those reported to map to more than one location (N 19,834) or to contain a genetic variant at the CpG site (N 74,182)[48]. Association analysis of SNPs with CpG sites was performed using an additive model (rank-normalized CpG methylation on SNP allele count) using Matrix eQTL[49]. SNP effects from this analysis that were *P-value* $<10^{-7}$ were then taken forward for re-analysis in PLINK to perform exact linear regression including covariates. Covariates included in all analyses were age (excluding birth), sex (children only), the top 10 ancestry principal components, bisulfite conversion batch and estimated white blood cell counts (using an algorithm based on differential methylation between cell types[50]).

Annotations of newly reported variants

Variants associated with height:

rs61734601 (stage 1 and 2 weighted effect allele frequency [WEAF] 8.2%, beta=-0.113, *P-value*=$1.38\text{x}10^{-101}$) is 359kb away from the physically closest positive control variant (Table S14). It is located in the intron of *PPP1CA* and a non-coding exon of *CARNS1*, but is reported as significantly associated with expression of *RAD9A,* a DNA repair gene 20kb downstream, in several different tissues in the GTEx[51] portal. DNA repair genes have previously been linked to growth disorders[52]. rs61734601 is in high LD (r^2=0.82) with rs553917782, a 6-nucleotide insertion 10bp upstream of *RAD9A*. The 8 following nucleotides are conserved (mean GERP[53] score 2.2) and occur near the centre of a DNase hypersensitivity peak that coincides with nucleosome depletion in multiple tissues from the Roadmap Epigenomics[54] project, indicating likely transcription factor binding (Figure S15).

rs41271299 (WEAF 5.5%, beta=0.123, *P-value*=$1.90\text{x}10^{-71}$) resides in the intron of *ID4*, in a highly conserved region (the flanking 20 bases are completely conserved in a 17-way mammalian alignment[55] and the GERP score[53] at the variant site is 5.8) (Table S16). The variant resides 23bp from the final acceptor splice site in the gene, therefore potentially disrupting splicing, and the region is annotated as open chromatin in diverse tissues[56] (Figure S15).

rs114976626 (WEAF 2.7%, beta= -0.096, *P-value*=$5.00\text{x}10^{-20}$) is a missense variant in *SSC5D*. *SSC5D* and its secreted protein product are poorly characterized. rs114976626 causes a conservative alanine to valine

mutation in a linker sequence connecting two scavenger receptor cysteine-rich (SRCR) domains[57]. The expression of *SSC5D* can be detected in many tissues[51], and the presence of the protein product throughout the entire body[58]. Proteins belonging to the scavenger receptor family are involved in the innate immune response[59].

rs6930571 (WEAF 17.9%, beta=0.038, *P-value*=6.01x10^{-18}) is a regulatory region variant that overlaps with a CTCF binding site, and has been identified as eQTL for 13 genes in 26 tissues[51]. rs6930571 is associated with the expression of *RNF5*[51], a E3 ubiquitine ligase gene located 231kb downstream. Animal models show that the mutation of this gene causes abnormal muscle regeneration[60]. Aberrant expression of *RNF5* is observed in various human myopathies[60]. rs6930571 is also associated with the expression of *CYP21A2*[51]. The protein product of this gene catalyzes the 21-hydroxylation of steroids, involved in adrenal synthesis of mineralocorticoids and glucocorticoids[61]. Abnormalities of this gene cause congenital adrenal hyperplasia, a common recessive disease due to defective synthesis of cortisol, characterized by androgen excess leading to ambiguous genitalia in affected females, rapid somatic growth during childhood in both sexes with premature closure of the epiphyses and short adult stature. The minor allele of rs6930571 is associated with lower plasma cortisol in the CORNET GWAS meta-analysis[62], although the association is not significant (EAF=18%, beta= -0.023, standard error=0.016, *P-value*=0.168, sample size 12,592).

rs202238847 (WEAF 2.23%, beta=0.095, height *P-value*=3.76x10^{-17}) causes a single base pair deletion in an intron of *CCDC36*, which is expressed in skin/skeletal muscle and testis/ovary in the fetal and adult body, respectively[51]. *LAMB2* is located 93kb upstream of rs202238847 and is involved in growth retardation and decreased body weight in mice[63].

rs4360494 (WEAF 44.7%, beta=0.024, *P-value*=8.98x10^{-13}) is captured by rs4072980 (r^2=0.84) in [64] with *P-value*=3.1x10^{-6}. rs4360494 has an effect on the expression on multiple genes[51]: *FHL3, SF3A3, INPP5B, RP11-109P14.10, UTP11L, MTF1*. The cytoskeleton associated protein product of *FHL3* plays an important role in myogenesis through its binding partner *MyoD*[65]. Overexpression of this gene in mouse myoblast cells results in the retarded myotube formation and decreases the expression of muscle-specific regulatory genes such as myogenin[65]. *INPP5B* is a protein coding gene 43kb upstream involved in PI3K signaling pathway. *INPP5B* might play a role in Lowe's syndrome which is characterized by short stature[66]. *MTF* ,located 130kb upstream from rs4360494, has been associated with hypothyroidism[67], often characterized by slow growth rate and its protein product activates metal response genes.

rs13059073 (WEAF 45.5%, beta=0.022, *P-value*=3.23x10^{-11}) is captured by rs1047898 (r^2=0.98) in [64] with *P-value*=4.6x10^{-6}. rs13059073 is an intergenic variant located 7kb downstream of *WNT5A*, whose secreted product (Wnt-5a) is the primary ligand in the non-canonical Wnt signalling pathway, and a regulator of chondrogenesis[68]. Mutations within this gene were shown to cause the autosomal dominant Robinow syndrome, which is characterized by skeletal dysplasia, limb shortening and other abnormalities[69]. Shortened body length, and various skeletal abnormalities were also described in animal models[70]. Members from the non-canonical Wnt signalling pathway have already implicated in the determination of height (eg. *ROR2*). rs17711489 is associated with the expression of *WNT5A*[51] and is in LD with our signal (r^2=0.25).

rs4303473 (WEAF 38.0%, beta=0.022, *P-value*=4.08x10^{-11}) is an intronic variant in *CRISPLD2*, which is involved in the assembly of the extracellular matrix and has been linked with abnormal embryo size in mice[71].

rs16888802 (WEAF 17.6%, beta=0.028, *P-value*=5.49x10^{-11}) is located 4kb downstream of *NKX3-2*, which encodes a transcription factor with an important role in development and chondrocyte regulation[72]. Rare

frameshift mutations of this gene are observed in spondylo-megaepiphyseal-metaphyseal dysplasia, a skeletal dysplasia characterized by disproportionate short stature [73].

rs183677281 (WEAF 2.4%, beta= 0.071, *P-value*=1.24x10^{-10}) is an intron of the principal[74] transcript of *TGFB2* and a promoter flanking region (ENSR00001598375) active in skeletal muscle myotubes, umbilical vein endothelial cells, astrocytes, fibroblasts[75]. The protein coded by *TGFB2* is a transforming growth factor involved in various developmental processes[76]. Animal models of this gene show diverse phenotypes including defects of musculoskeletal system and morphology[76]. *TGFB2* has already been linked to height by several studies[64,77,78] but the reported associations are independent of our signal (Table S14).

rs1848053 (WEAF 24.8%, beta= -0.024, *P-value*=2.00x10^{-10}) is associated with the expression of *FBN1*[51], which is involved in a series of developmental disorders affecting the musculoskeletal system[79-81].

rs62038850 (WEAF 2.7%, beta= 0.071, *P-value*=2.45x10^{-10}) overlaps with the 3' untranslated region of the principal transcript of the ubiquitously expressed gene *PGP*. Phosphoglycolate phosphatase, the protein product of this gene, regulates the cellular levels of glycerol-3-phosphate a metabolic intermediate of glucose, lipid and energy metabolism[57]. rs62038850 is 1kb away from *BRICD5*, whose integral membrane protein product is mainly found in prostate, pancreas, salivary gland, gastric chief cells, glandular cells in cervix and endometrium[82]. rs62038850 is also 3kb away from *MLST8*, whose protein product is part of the mTOR complex, therefore involved in the regulation of cell growth and survival[57]. The highest levels of the broadly expressed protein product can be detected in skeletal muscle, heart and kidney[83]. Animal models of *MLST8* show growth/body-size phenotypes including embryotic growth retardation and decreased embryo size[84]. *CASKIN1* is located 16kbp away coding a scaffolding protein and is expressed mainly in brain[58]. *MLST8* and *CASKIN1* have already been associated with height[77], but the reported signals are independent from rs62038850 (Table S14). *E4F1* is a ubiquitously expressed protein coding gene 10kb away from rs62038850, the protein product of this gene is a transcriptional repressor regulating cell proliferation and survival[57]. Animal models show mutation of *E4F1* can cause decreased embryo size[85].

rs142854193 (WEAF 2.3%, beta=0.071, *P-value*=1.31x10^{-9}) is a novel height variant overlapping with the 3' untranslated region of the principal[74] transcript of the protein coding gene *FKBP9* and an intron of protein coding gene *AVL9*. *AVL9* is a poorly characterized gene, its protein product is a single pass membrane protein potentially involved in cell migration, endosome trafficking[86]. Misregulation of the expression of this protein causes secretory defects in yeast[86]. *FKBP9* is a chaperone: it mediates the isomerization of peptide bonds during protein synthesis[57]. Mutations of *FKBP9* in mice causes behavioral abnormalities[87] its protein product is expressed throughout the entire body[58].

rs2808290 (WEAF 50%, beta=0.0198, *P-value*=1.34x10^{-9}) is located in an intergenic region, but overlaps with a regulatory feature (ENSR00001421990), a predicted enhancer, which is predicted to be active in osteoblast, myoblast and fibroblast cell lines[75]. The closest gene is protein coding *MKX* located 60kb downstream. The protein product of *MKX* is a transcription factor and regulates collagen expression and tendon development. Animal models of this gene show abnormal tendon and tail morphology[88].

rs116878242 (WEAF 7.5%, beta=0.033, *P-value*=3.14x10^{-8}) resides in an intergenic region flanked by several non-coding genes. rs116878242 overlaps with an annotated promoter flanking region (ENSR00001537939) shown to be active in various cell types including fibroblasts[89]. The nearest protein-coding gene is *SOX9* over 100kb upstream, which is involved in sex determination, and is associated with height (intergenic rs10083886[64], r^2=0.061 with rs116878242, Table S14). *SOX9* is also implicated in various monogenic diseases (Table S25) including campomyelic dysplasia, which includes a skeletal development phenotype[90]. 400bp away from rs116878242, there is a NF-κB transcription binding site, which has been shown to affect the expression of *SOX9*[91].

Variants associated with BMI:

rs62107261 (WEAF 4.7%, beta=-0.075, *P-value*=1.27x10^{-27}) resides in the exon of a long intergenic non-coding RNA (*AC105393.2*). The closest protein-coding gene is *TMEM18*, over 200kb upstream, which has previously been associated with BMI and obesity (Table S14).

rs2003476 (WEAF 40.4%, beta= -0.025, *P-value*=5.89x10^{-13}) resides in an intron of the transcription factor-coding gene *CRTC1*. *Crtc1*-null mice are hyperphagic, obese, and infertile, and the *Creb1- Crtc1* pathway mediates the central effects of hormones and nutrients on energy balance and fertility[92]. rs2003476 is associated with the expression of *CRLF1*[51], a protein coding gene 88kb upstream. *CRLF1* expression changes significantly during human adipogenesis[93]. *CRLF1* also shows differential expression levels in gluteal and abdominal subcutaneous adipose tissue in humans[94].

rs765876 (WEAF 48.8%, beta= -0.020, BMI *P-value*=9.64x10^{-10}) resides in an intron of *HIVEP2*, which codes for a transcription factor that binds to the enhancer sequences of various genes including somatostatin receptor II[95]. Mouse models of this gene show smaller body, with reduced fat mass[96].

Variants associated with hip circumference adjusted for BMI:

rs10044000 (WEAF 39%, beta=0.0157, *P-value*=6.45x10^{-13}) variant overlaps with the coding region of the gene *CATSPER3* , where it causes a synonymous mutation. rs10044000 has been previously associated with height and *CATSPER3* is a known locus for height[78,97] and bulimia[98]. rs10044000 has been shown to be an eQTL for *PITX1*[51] gene located 20kb upstream. The protein product of this gene is a transcription factor and involved in skeletal development[99]. Various congenital diseases are associated to this gene and all characterized by skeletal abnormalities[100,101]. Animal models also highlight the effect of this gene on skeletal development[102].

rs35874463 (WEAF 58.2%, beta=0.0374, *P-value*=9.26x10^{-17}) results in an isoleucine to valine substitution in *SMAD3*. The substitution caused by this variant is predicted to be benign (Polyphen score = 0.007). Position 65 is directly adjacent to the metal binding site, which is required for the RNA binding function of the MH1 domain, valine is frequently found in the homolog position. Mutations of this gene were implicated in the aneurysms-osteoarthritis syndrome[103], characterized by early onset osteoarthritis in the knees, hands and spine. Animal models of this gene shows a series of skeletal phenotypes[104] highlighting the gene's role in ossification and skeletal development. rs35874463 is also associated with height[64] and heart developmental failures[105].

Variants associated with waist circumference adjusted for BMI:

rs28610092 (WEAF 17%, beta= -0.021, *P-value*=8.92x10^{-16}) resides in the promoter flanking region of *PKD1*, which has been found to be active in myoblasts, fibroblasts and osteoblasts[75]. rs28610092 is associated with the expression of *PKD1*[51]. Although the primary function of this gene is the regulation of the development of the renal tubulogenesis[106] and is the primary causal gene for adult type-1 polycystic kidney disease[107], animal models show diverse phenotypes including defects in the myoskeletal development[108].

rs577721086 (WEAF 5.1%, beta=0.056, *P-value*=2.54x10^{-39}) is located in the 5' untranslated region of *RSPO3*, its position is highly conserved (GERP score=3.77) and has a number of epigenetic marks indicative of being an active promoter in several tissues[55], GWAVA[109] score=0.63. Intronic variation at this locus has previously been associated with waist circumference and waist to hip ratio adjusted for BMI (Table S14) and whilst collider bias might have complicated the interpretation of this signal[110], it appears

to be a genuine contributor to variance in waist circumference relative to trunk and not BMI (stage 1 *P-value*=0.14) (Figure S27). rs577721086 has been previously associated with waist to hip ratio adjusted for BMI (Table S14).

Variants associated with other anthropometric traits:

rs11042397 is associated with hip circumference (WEAF 56.4%, beta= 0.047, *P-value*=5.20x10^{-11}) and is located in an intron of *ZNF143*, which codes for a transcription factor involved in early developmental processes in animal models[111]. rs11042397 is tagged in HapMap by rs2290424 (r^2=0.963) with *P-value*=0.02[112]. rs11042397 is located 161kb upstream of *SWAP70* , known for affecting bone mass and osteoclast function through modulating f-actin[113] and 187kb away from *TMEM49B*, implicated in metabolic processes in animal models[114].

rs62065847 is associated with waist circumference (WEAF 48.6%, beta= -0.022, *P-value*=2.86x10^{-11}). This intergenic variant resides in a reported enhancer[115] and is associated with the expression of many genes in close proximity including *HOXB2*, which is involved in skeletal abnormalities in animal models[116,117].

rs2082881 is a novel TRFM signal (WEAF 24.4%, beta=0.0834, *P-value*=9.91x10^{-9}), but it is a known variant for BMI and height. rs2082881 overlaps with an intron of *CENPO*, which has been associated with height[64]. Animal models of this gene shows increased body length[71]. rs2082881 is an eQTL for other genes including *NCOA1* and *ADCY3*[51]. *NCOA1* is a nuclear receptor coactivator, involved in the coactivation of steroid hormone receptors and activates the expression of a series of genes involved in development. Mouse model of this gene shows diverse phenotypes including obesity[118]. Several obesity and obesity related signals were associated to *ADCY3*, whose protein product, through its adenyl-cyclase activity, is an important regulator of energy balance.

rs6901225 is a novel association for weight (WEAF 12%, beta=-0.0377, *P-value*=4.20x10^{-13}) and is a known variant for height. Although the variant is located in the intergenic region, it is associated with the expression of multiple transcription factors[51] such as *ZNF322* and *ABT1*. *ZNF322*, a zinc-finger protein, is responsible for the regulation of many embryonic genes[119]. *ABT1* interacts with *IGHMBP2*, which is important for skeletal phenotypes[120].

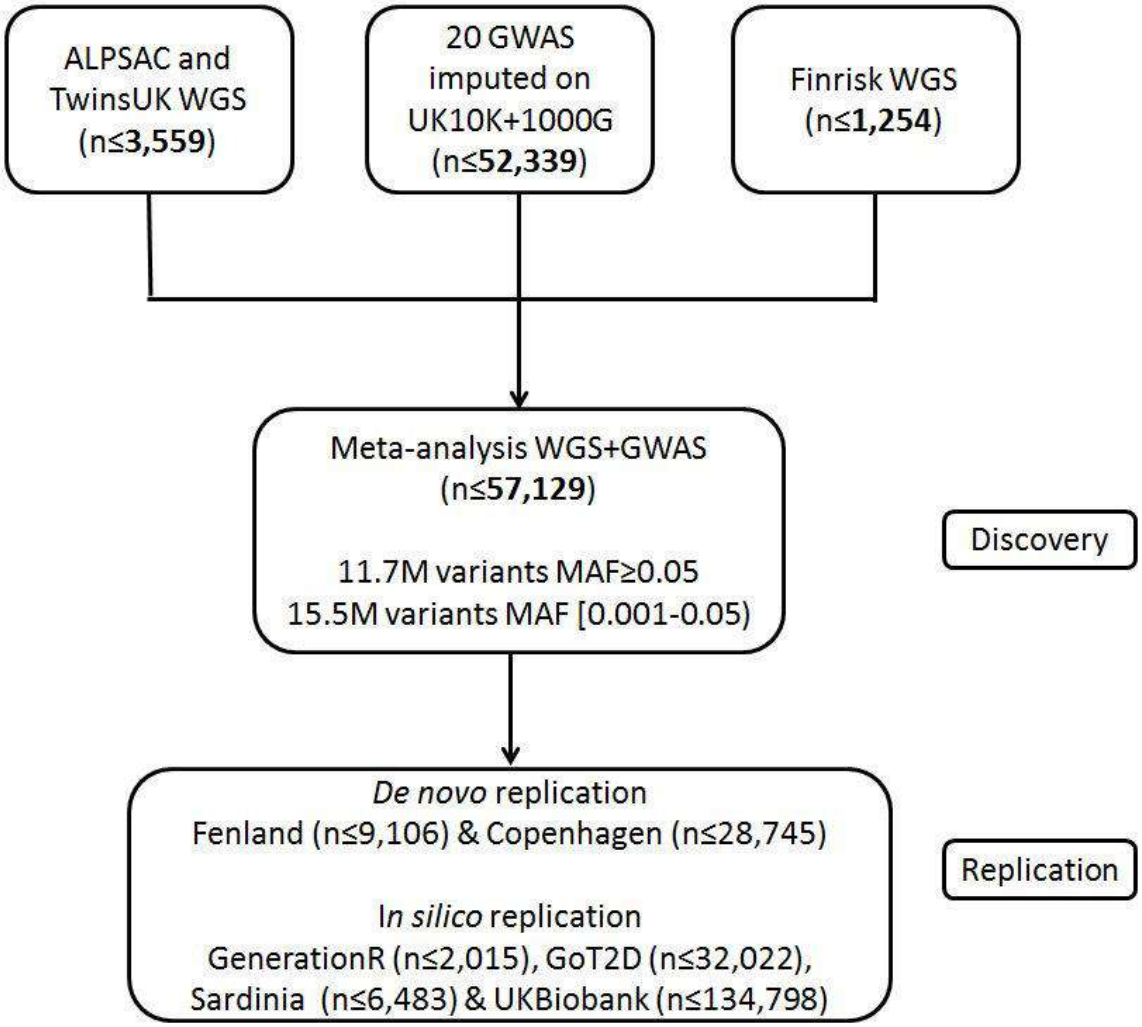


Figure S1: Study design for single marker tests.

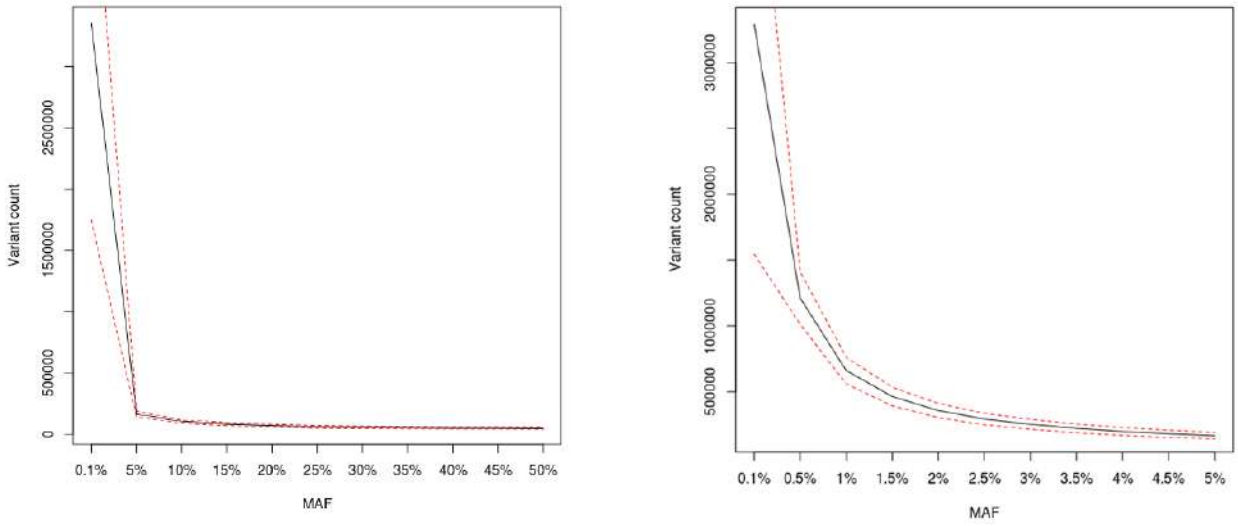


Figure S2: A minor allele frequency (MAF) histogram of variants that have passed the imputation quality threshold (0.4) across the imputed datasets that are available genome-wide.
In the left graph we plotted the whole MAF range (0.01% -50%) and in the right graph we zoomed in MAF between 0.01% -5%. The y-axis is the average number of variants across our genome-wide imputed datasets (arcOGEN, UKHLS, ALSPAC, TwinsUK, 1958 Birth Cohort, INGI-Carl, INGI-FVG, HELIC MANOLIS, HELIC Pomak, INCIPE1, INCIPE2, LURIC, Rotterdam Study-1, Rotterdam Study-2, Rotterdam Study-3, TEENAGE, INGI-VB and UK Biobank).

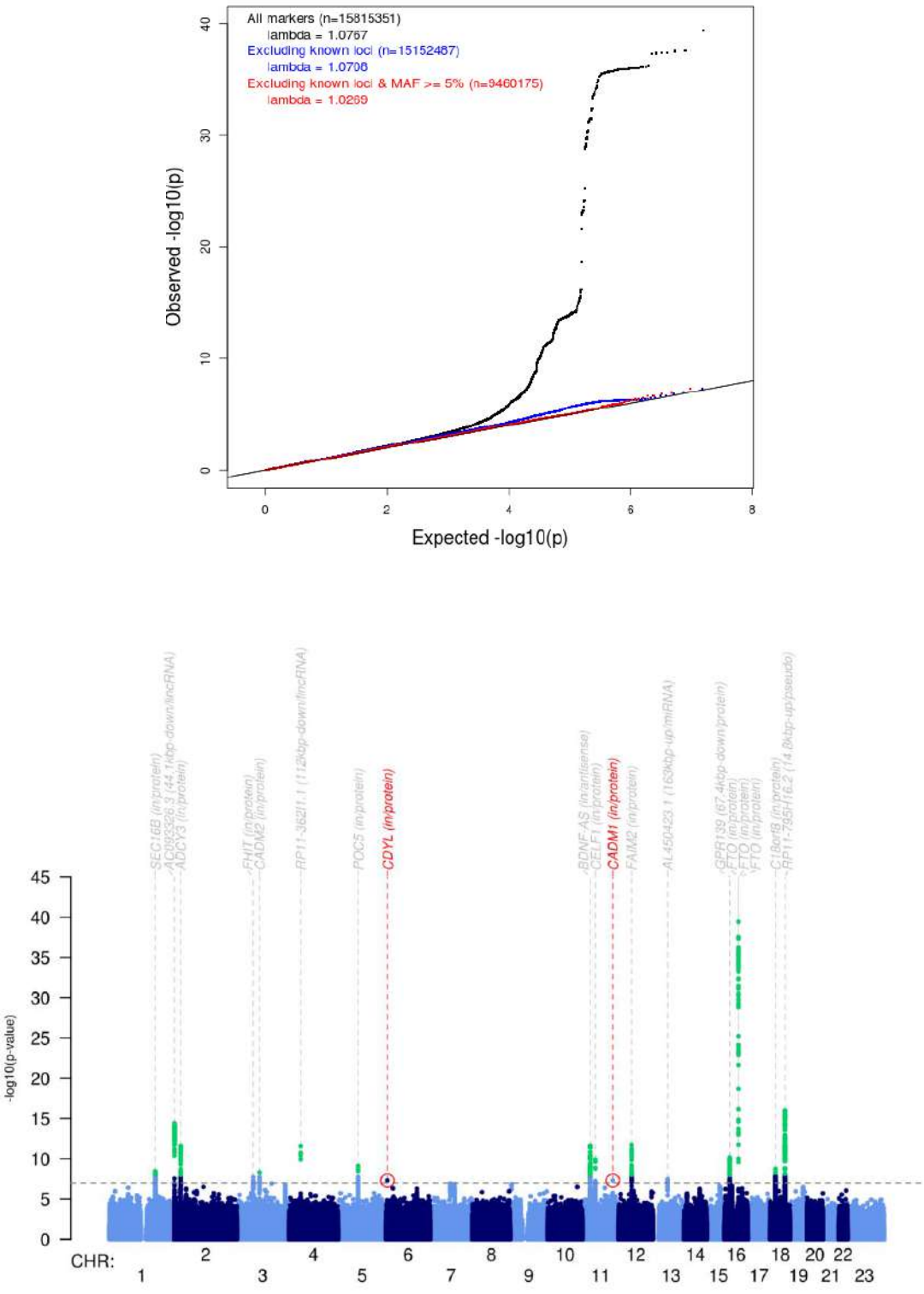


Figure S3: Summary plots of body mass index (BMI) sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

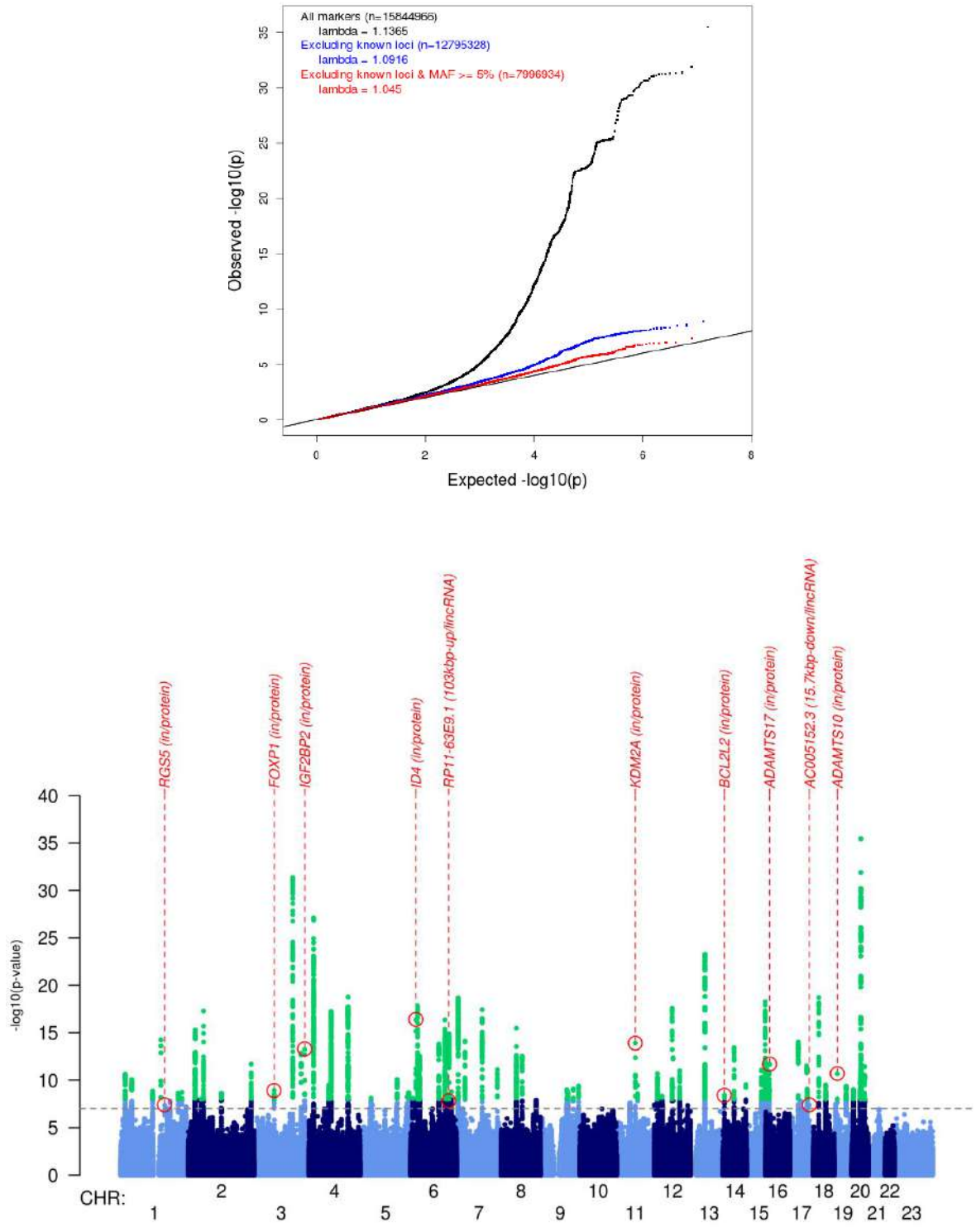


Figure S4: Summary plots of height sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}. Only novel signals are annotated for Height, to avoid overcrowding in the graph.

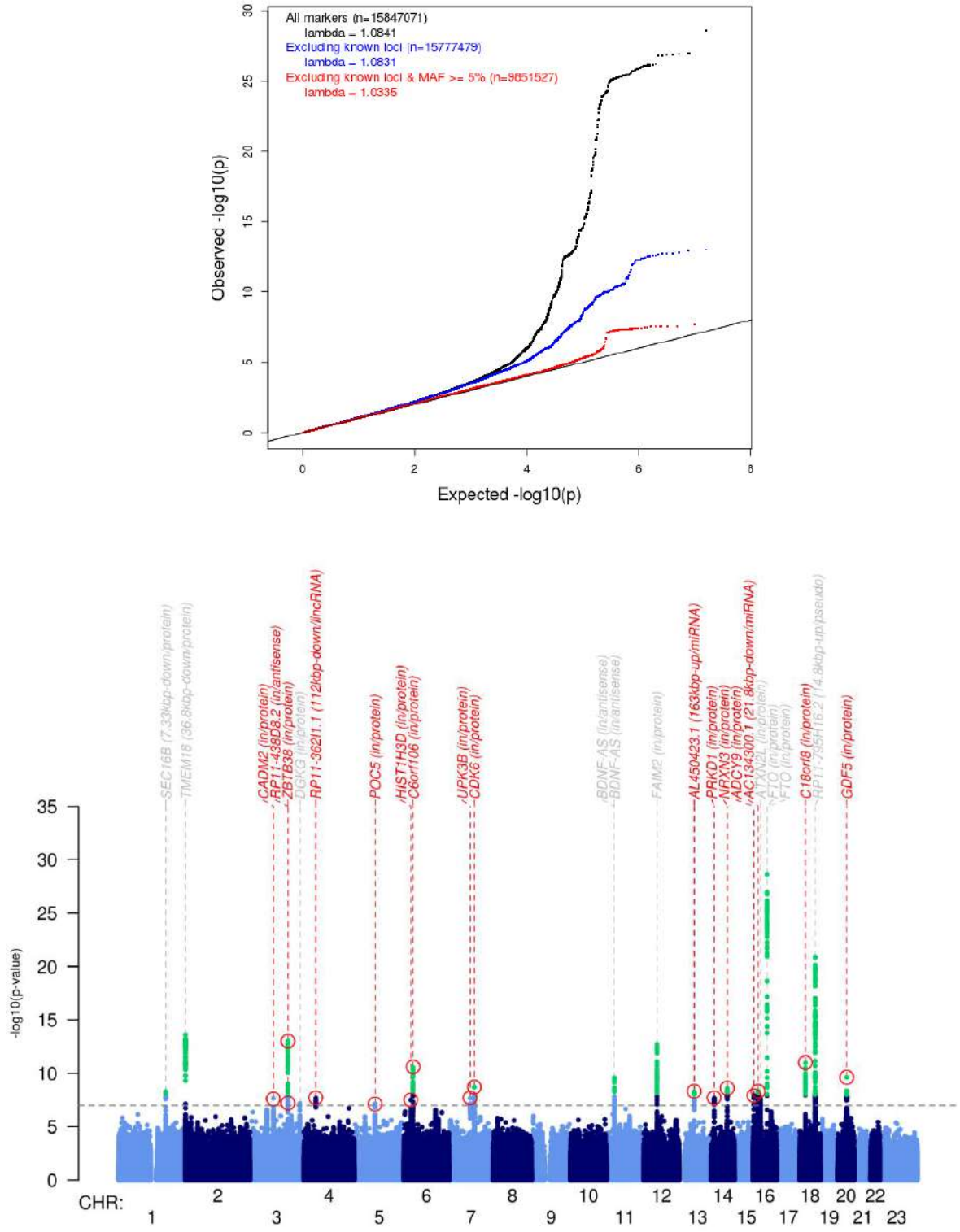


Figure S5: Summary plots of weight sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

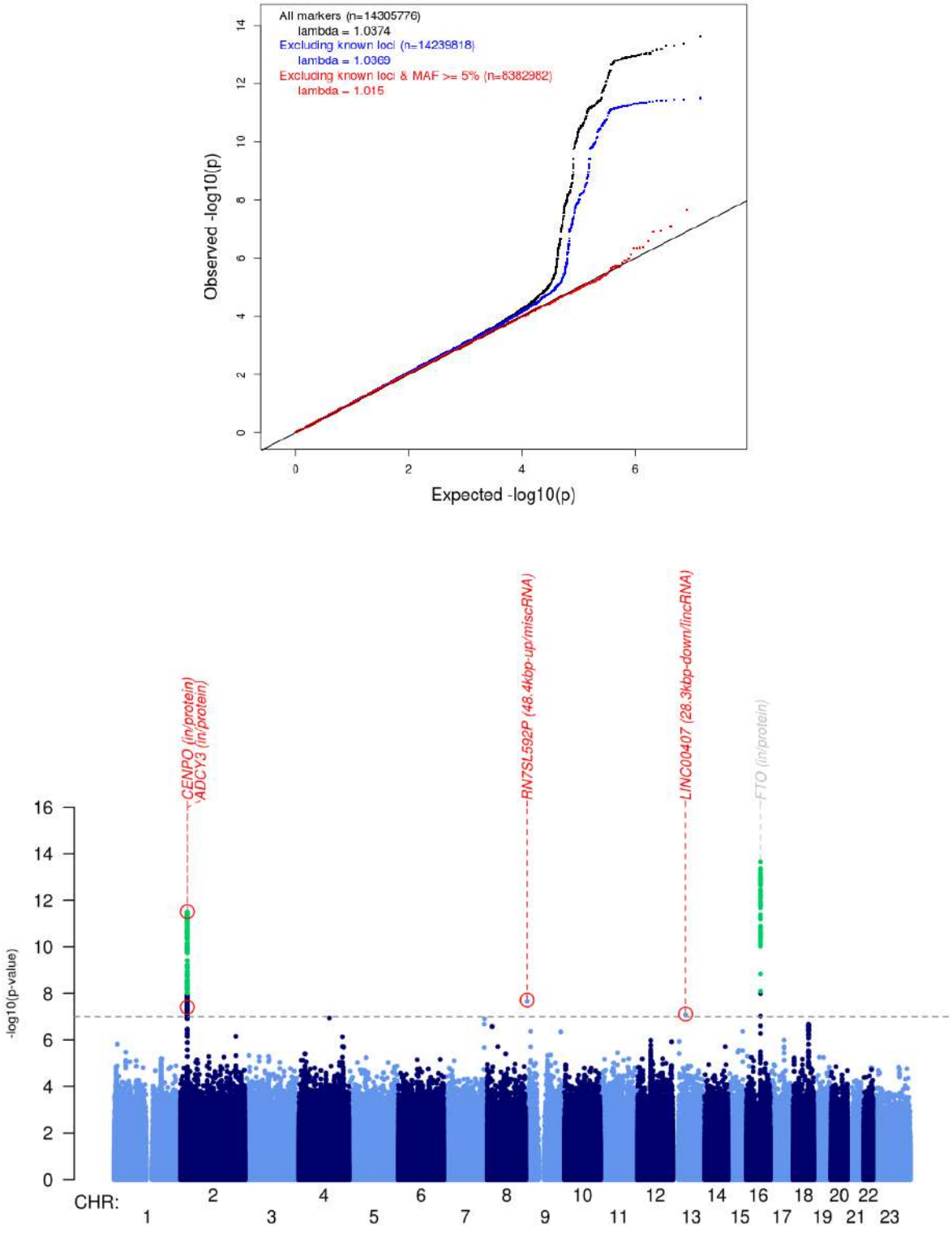


Figure S6: Summary plots of total fat mass (TFM) sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

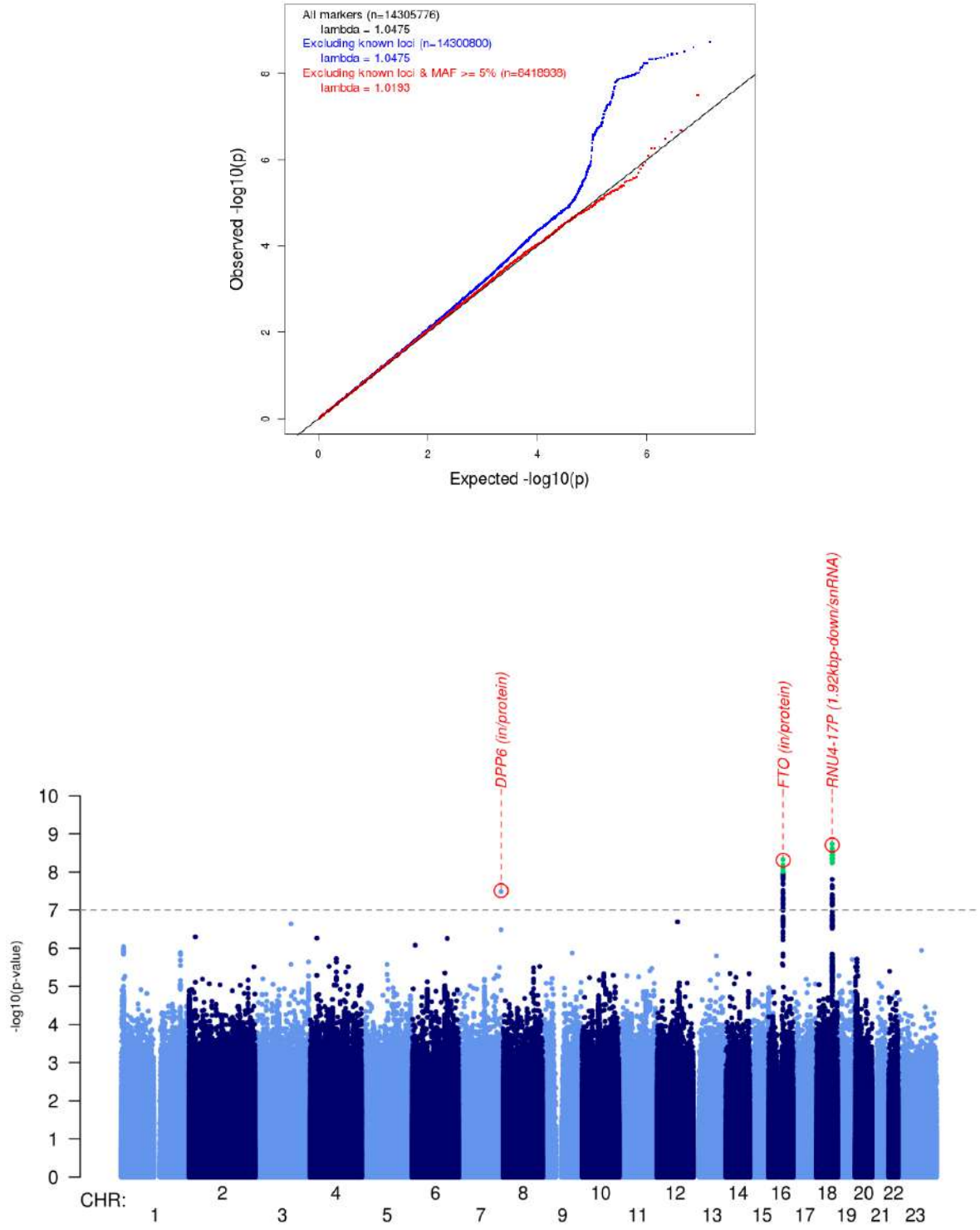


Figure S7: Summary plots of total lean mass (TLM) sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

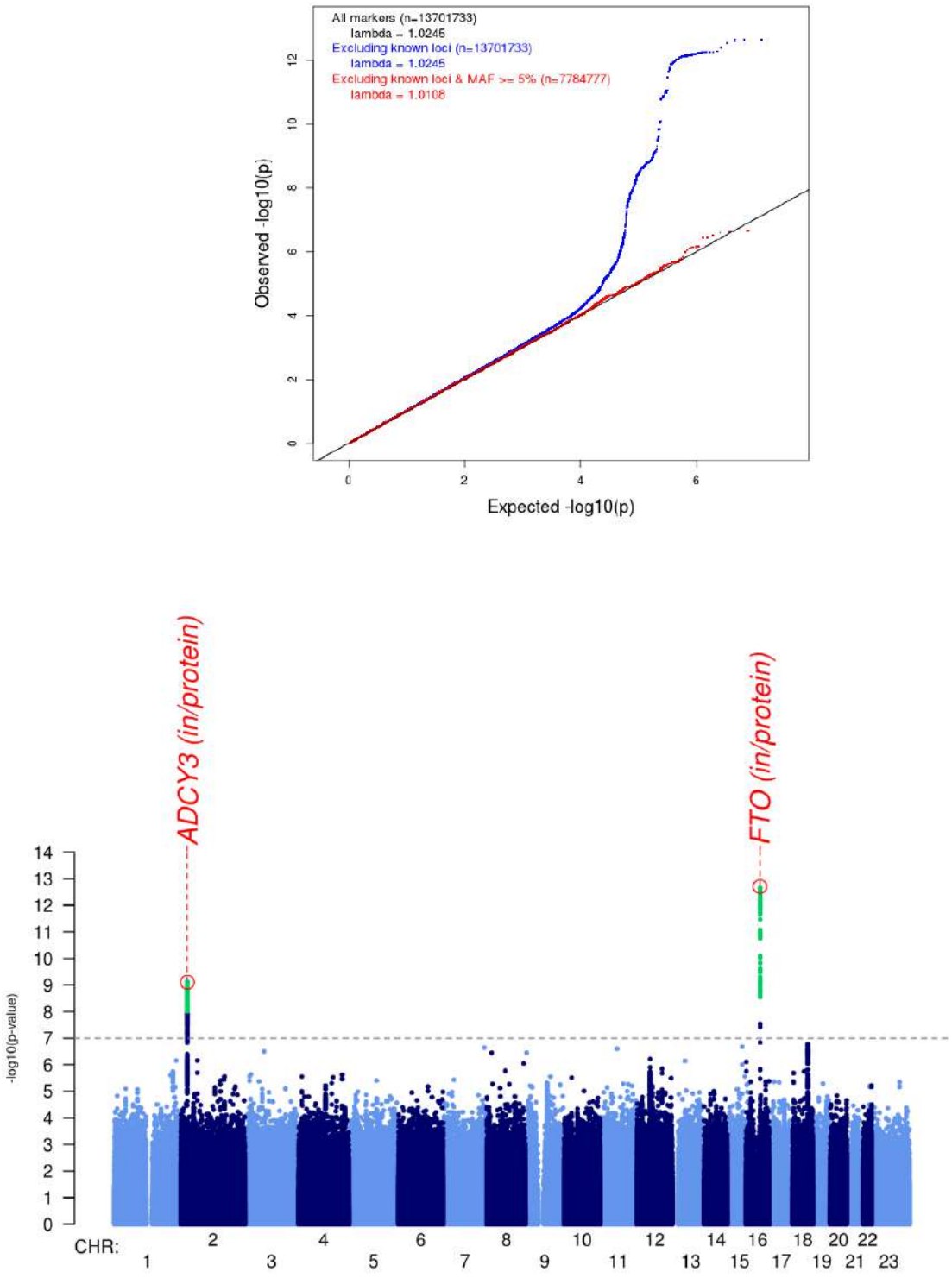


Figure S8: Summary plots of trunk fat mass (TRFM) sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

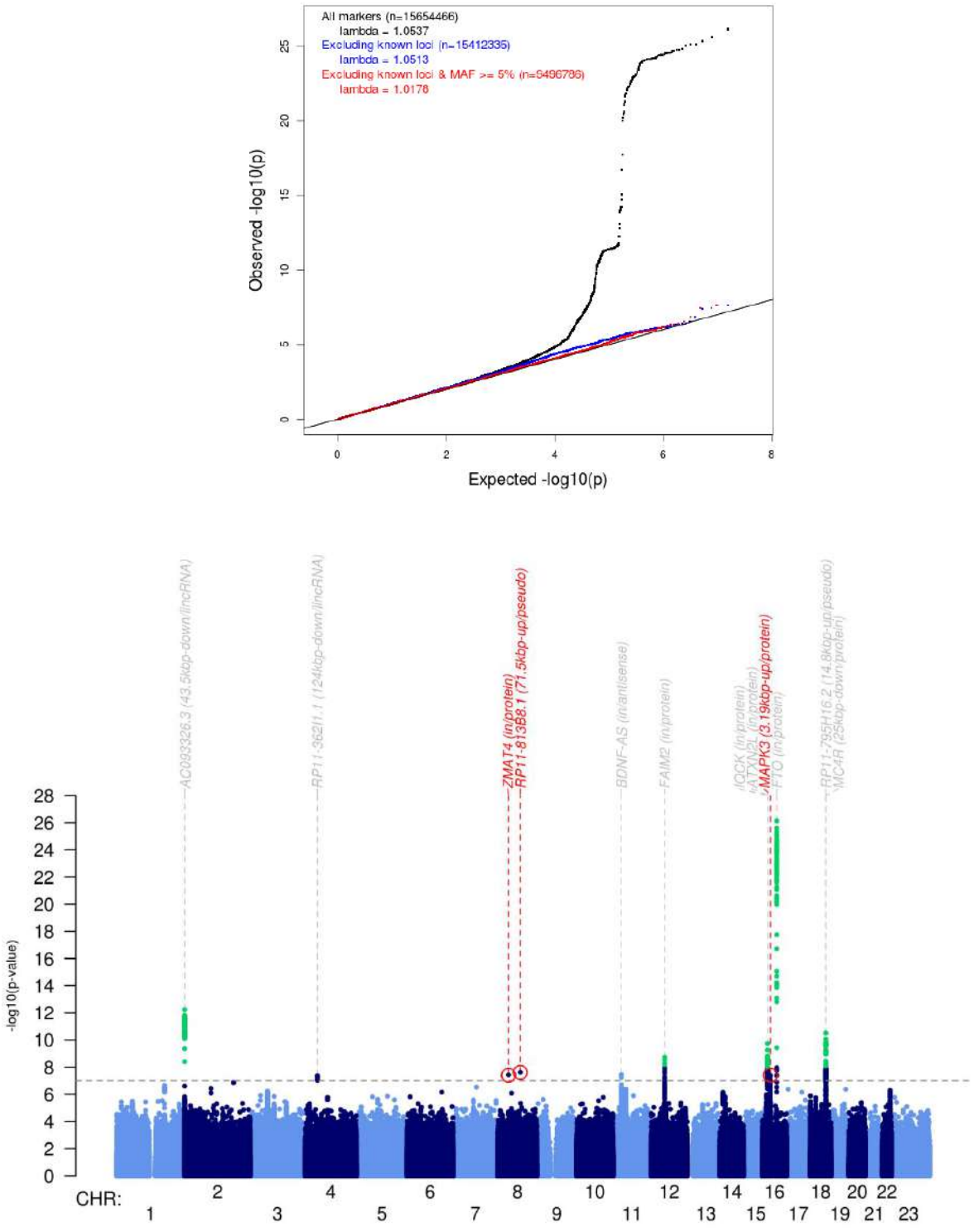


Figure S9: Summary plots of waist circumference sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

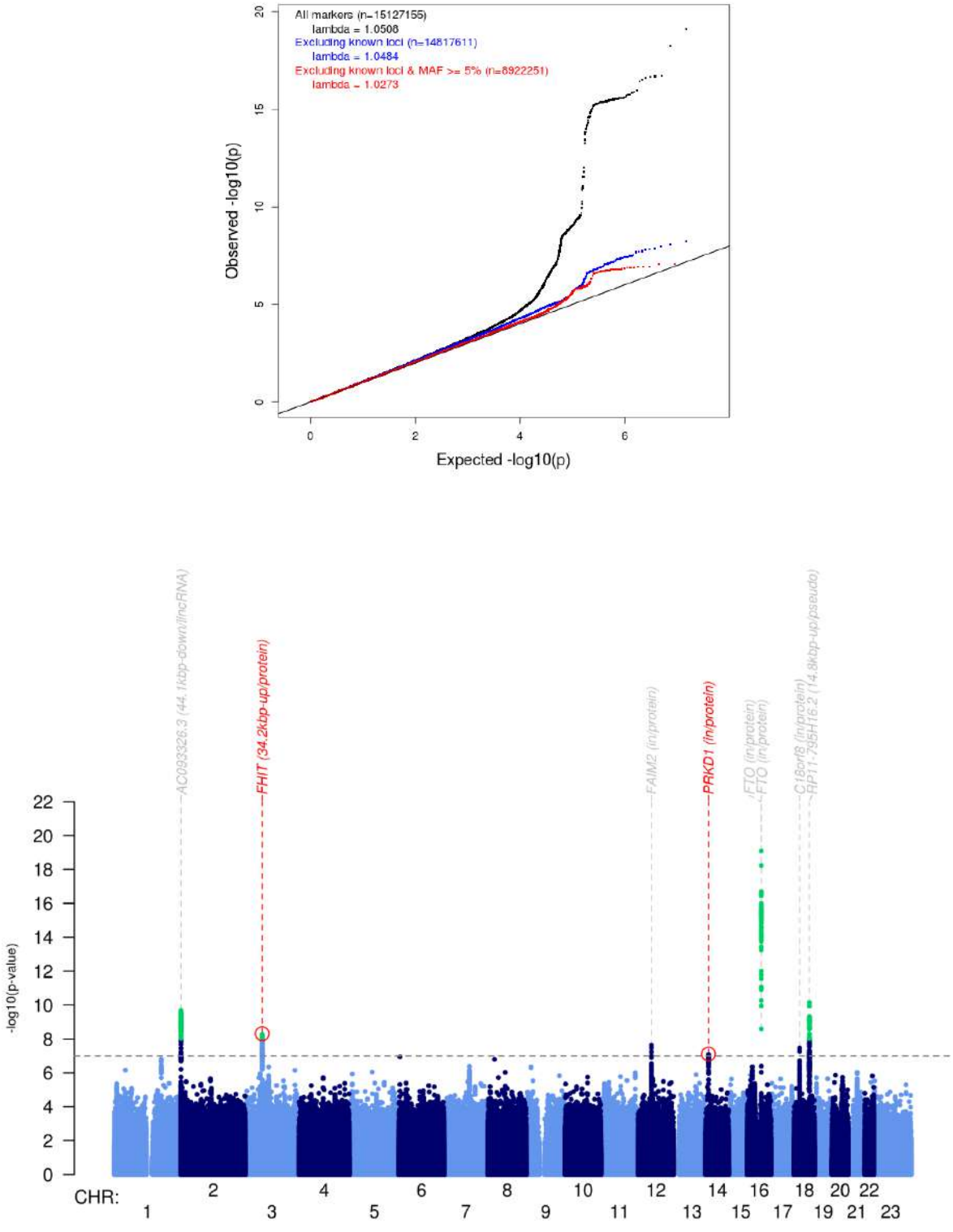


Figure S10: Summary plots of hip circumference sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

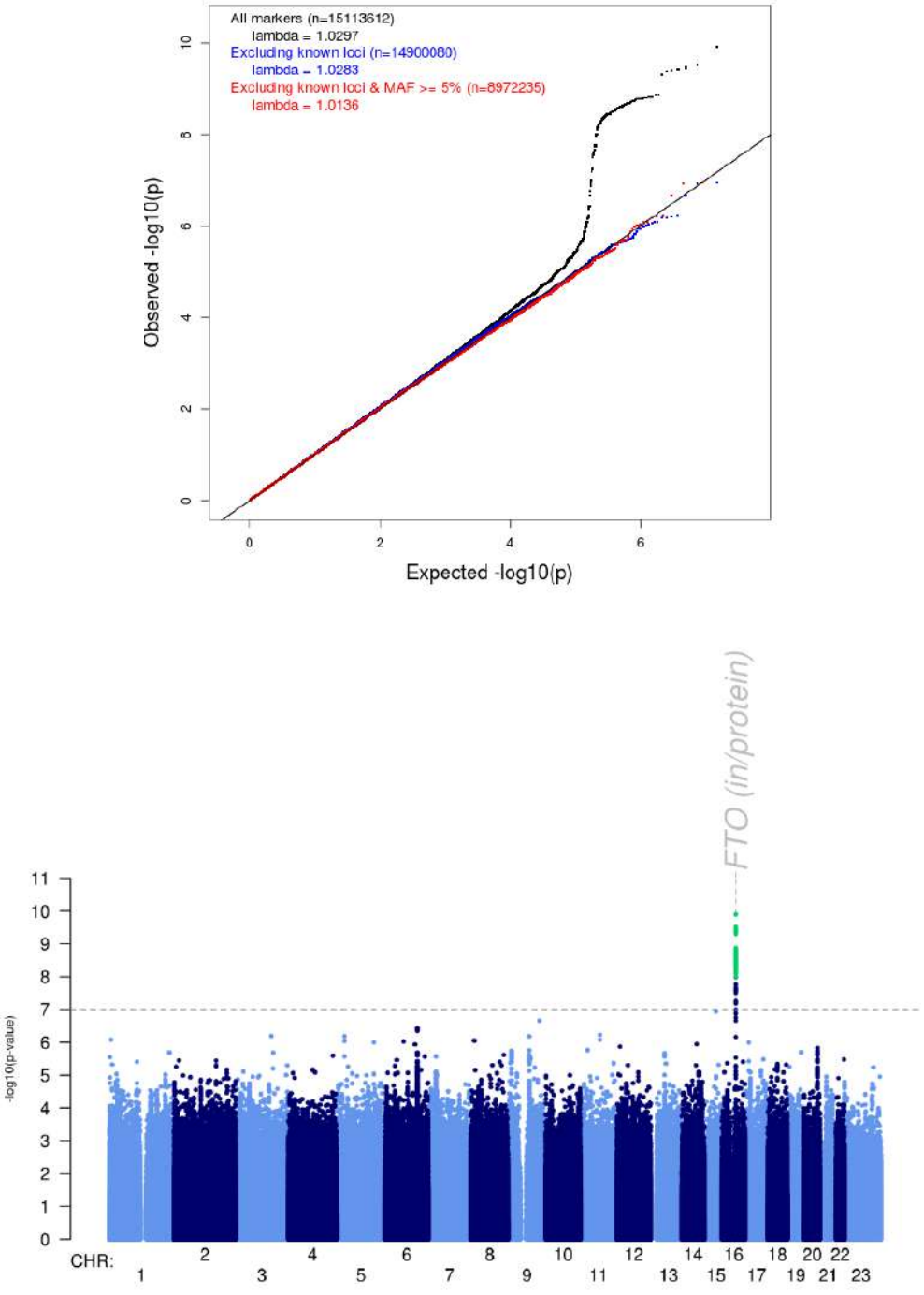


Figure S11: Summary plots of waist-to-hip ratio (WHR) sex-combined meta-analysis.
Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

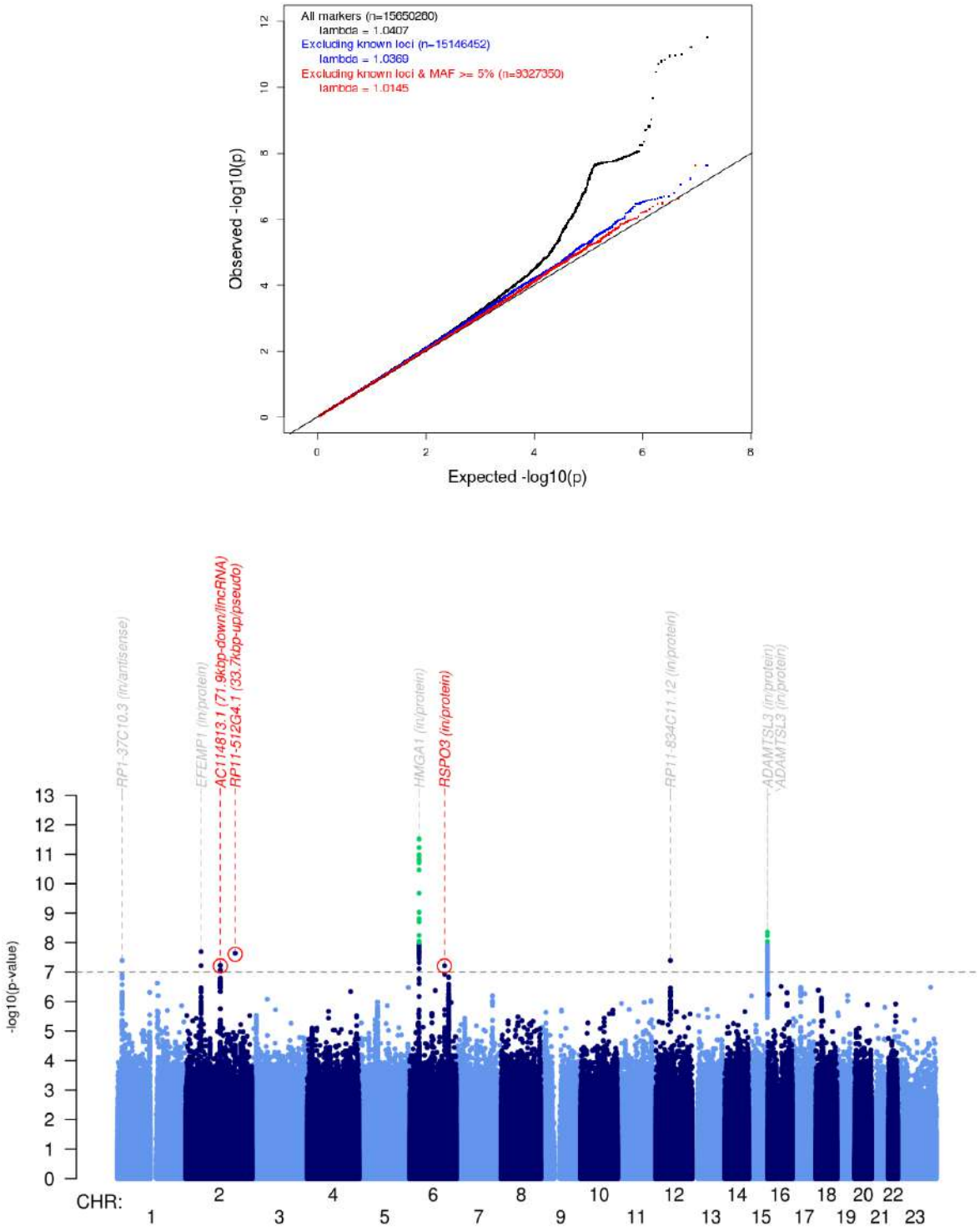


Figure S12: Summary plots of waist circumference adjusted for BMI sex-combined meta-analysis. Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

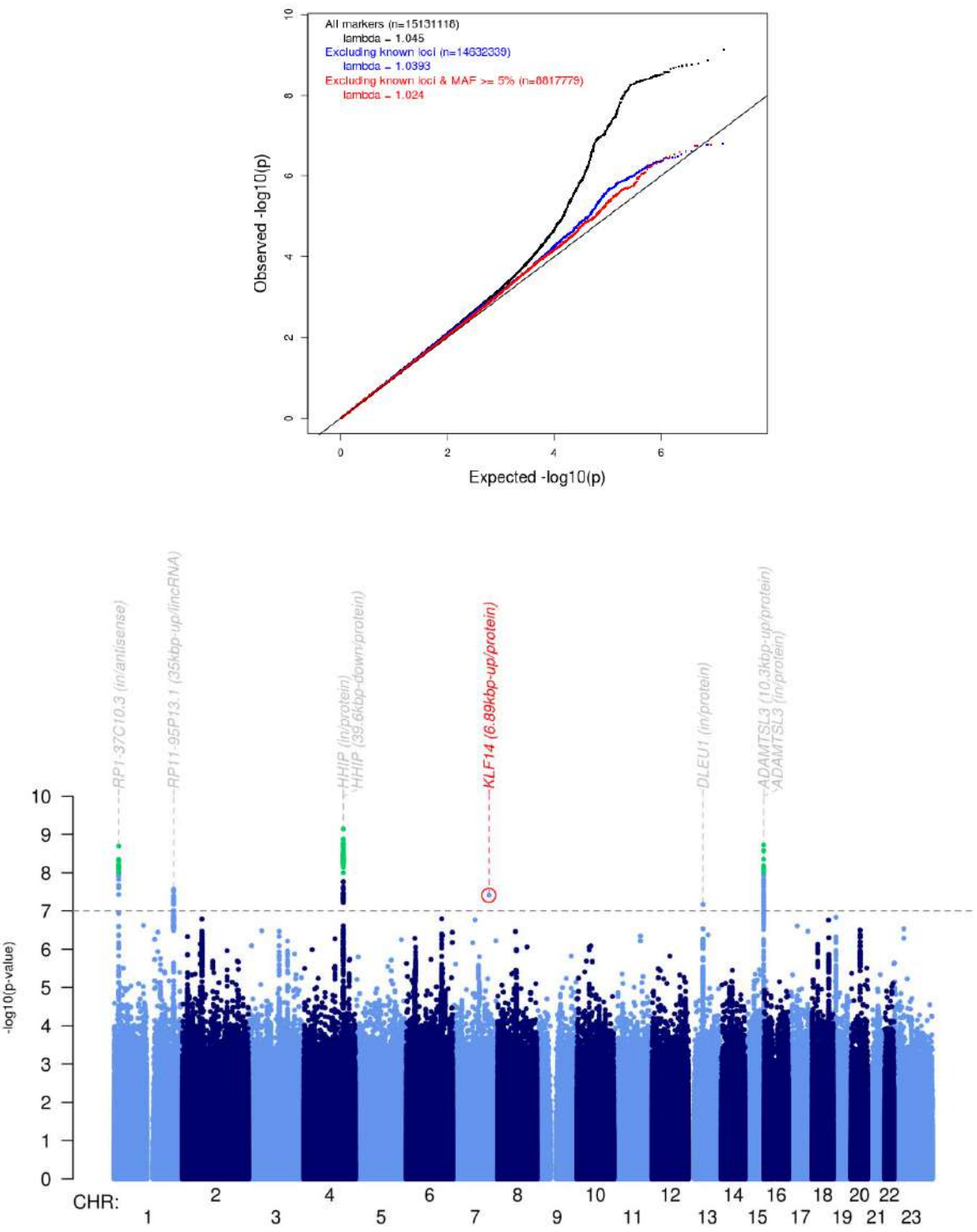


Figure S13: Summary plots of hip circumference adjusted for BMI sex-combined meta-analysis. Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.

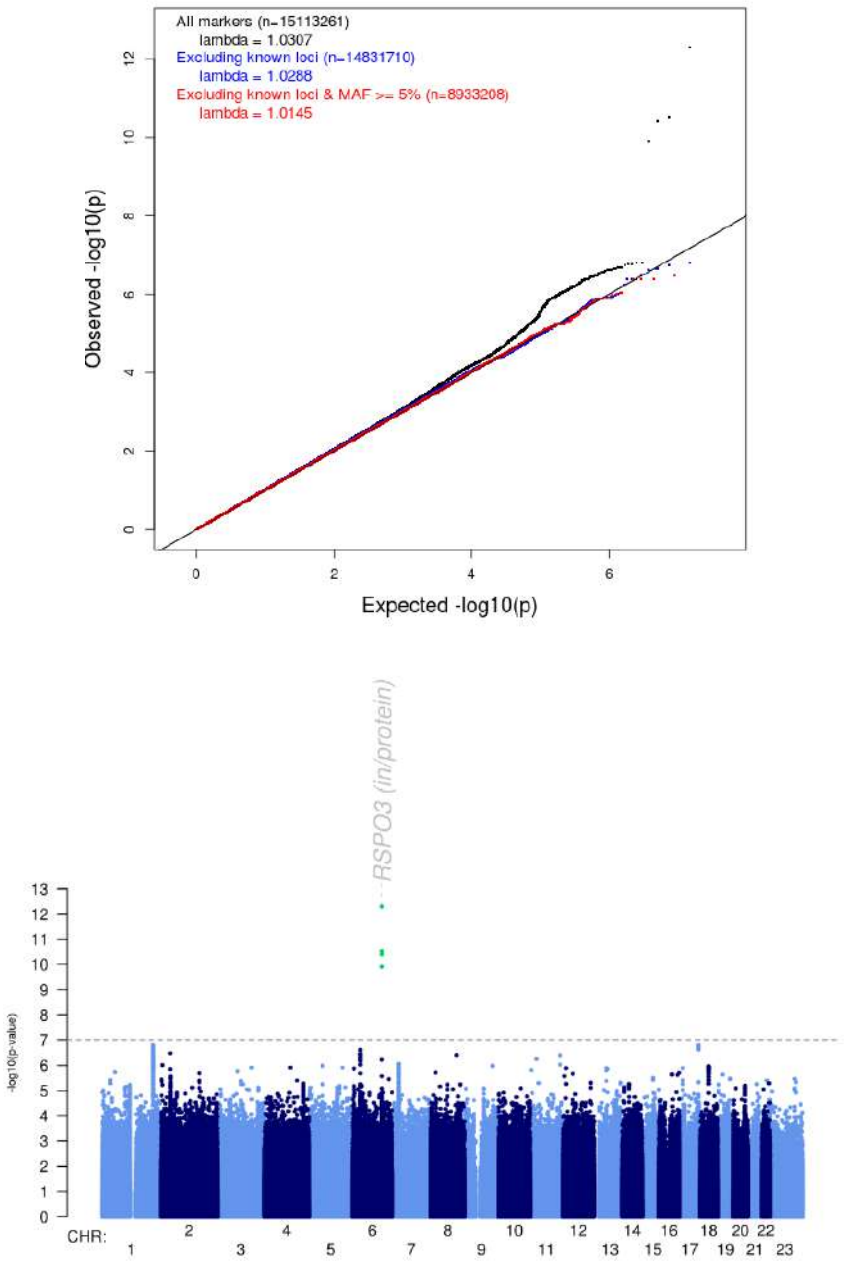
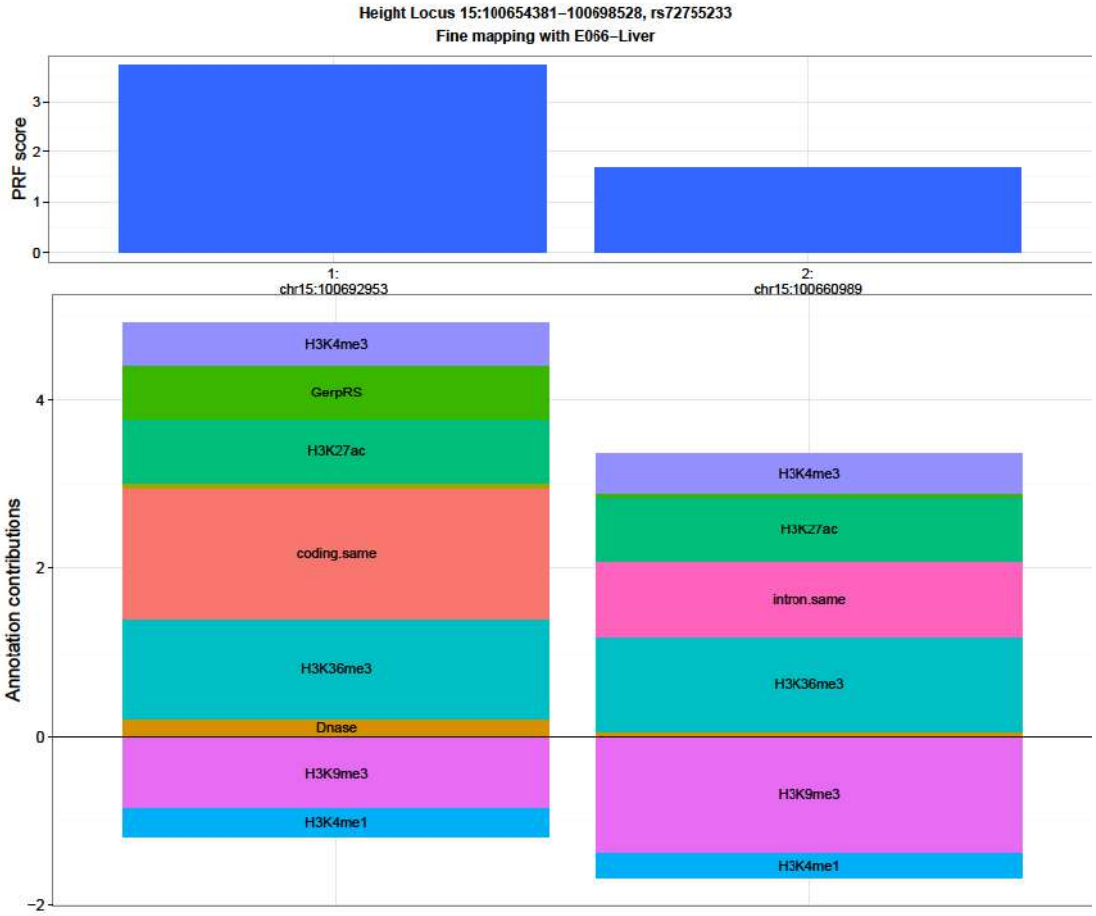
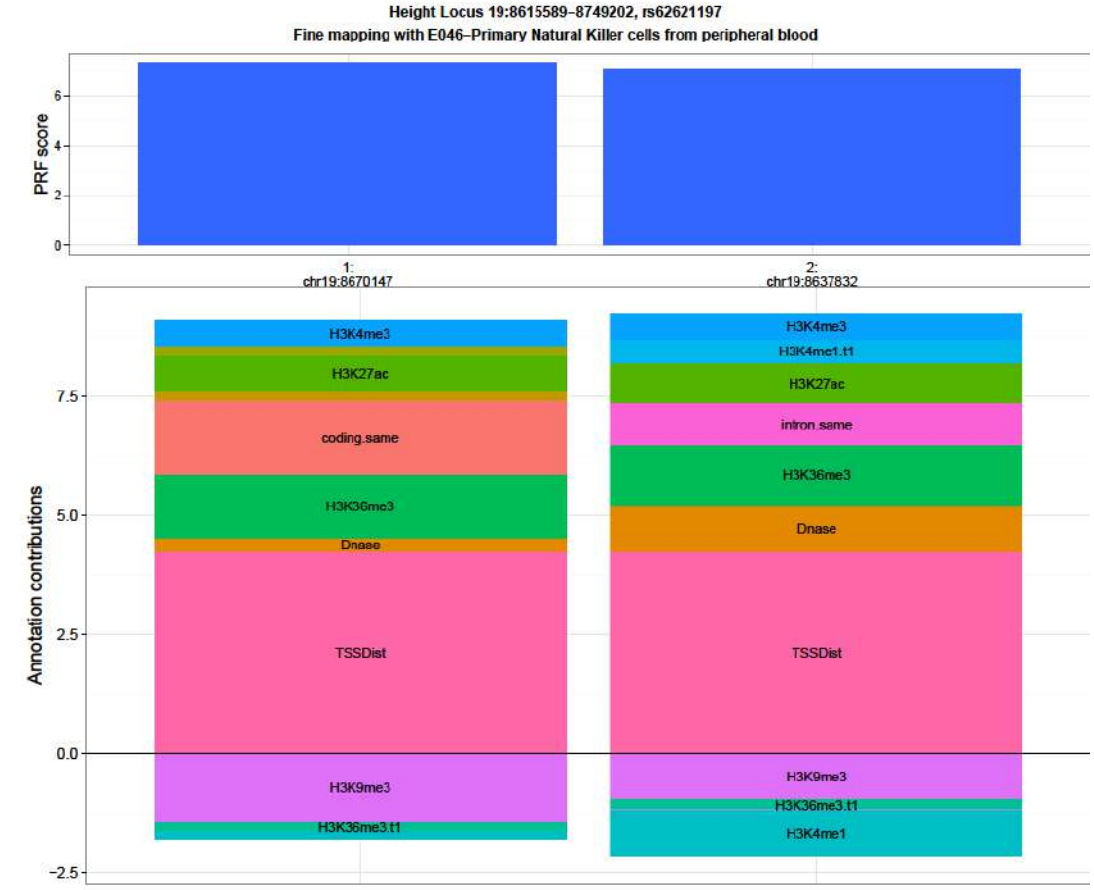
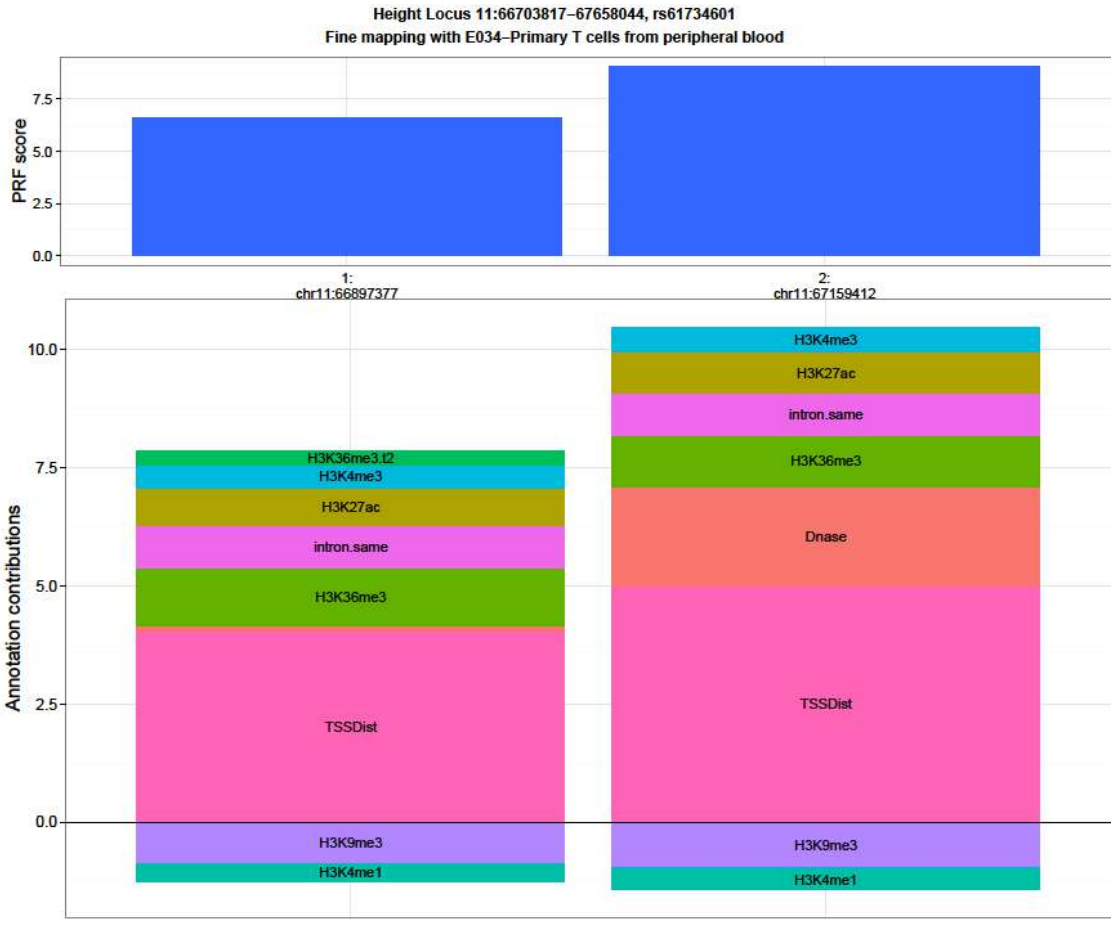
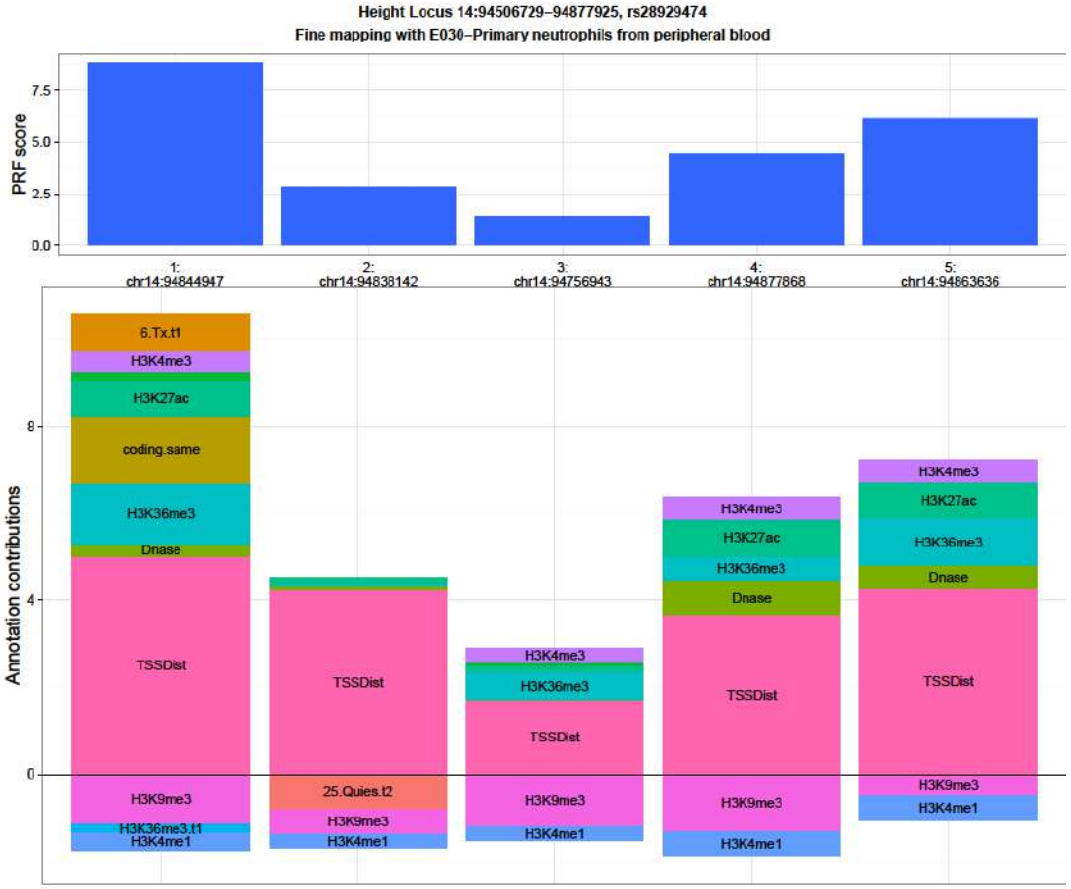


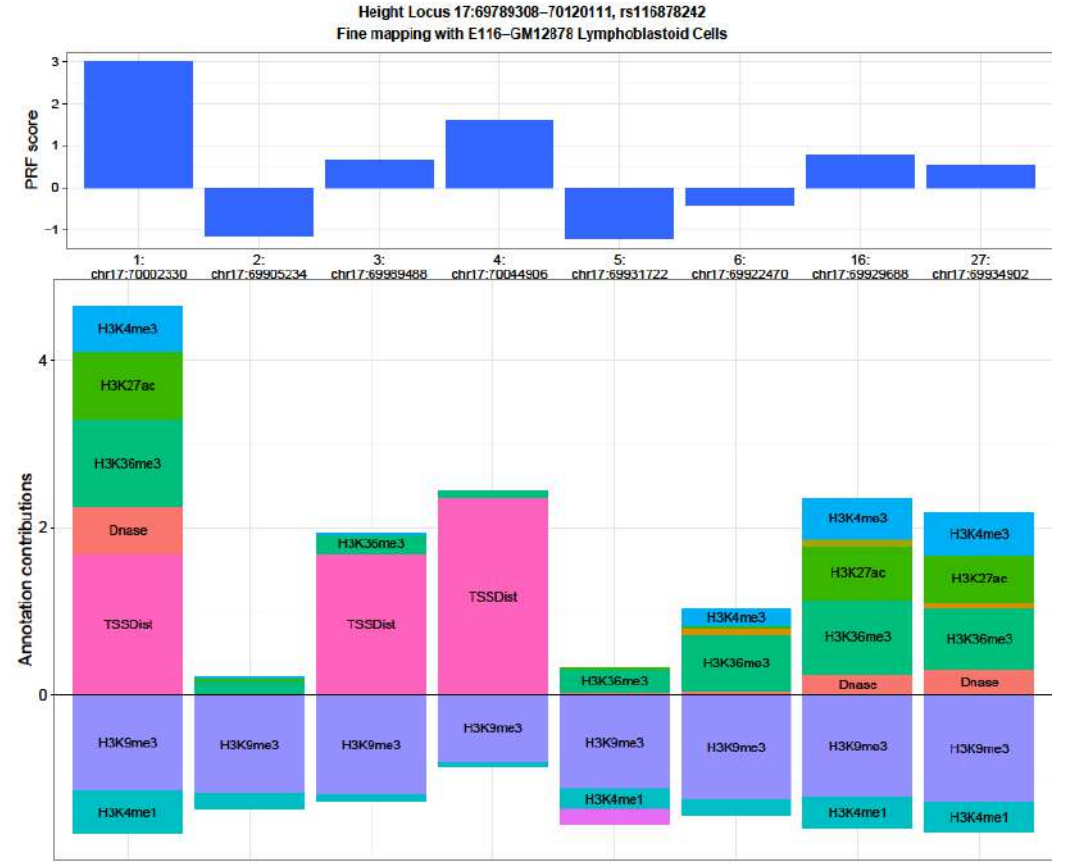
Figure S14: Summary plots of wait-to-hip ratio (WHR) adjusted for BMI sex-combined meta-analysis. Quantile-quantile plot of SNP associations. All SNPs are plotted in black, after excluding previously known loci (±500 kb) in blue, and after excluding previously known and common loci (±500 kb) in red. Manhattan plot showing in green loci with $P \leq 10^{-8}$. Loci with $P \leq 10^{-7}$ are labeled with the nearest protein coding gene in grey if they are known and in red if they are novel. The reported gene is the closest in physical distance. The horizontal line is drawn at 10^{-7}.


Height Locus 15:100654381–100698528, rs72755233
Fine mapping with E066–Liver
PRF score
0
1
2
3
1:
chr15:100692953
2:
chr15:100660989
Annotation contributions
−2
0
2
4
H3K4me3
GerpRS
H3K27ac
coding.same
H3K36me3
Dnase
H3K9me3
H3K4me1
H3K4me3
H3K27ac
intron.same
H3K36me3
H3K9me3
H3K4me1


Height Locus 19:8615589–8749202, rs62621197
Fine mapping with E046–Primary Natural Killer cells from peripheral blood
PRF score
1:
chr19:8670147
2:
chr19:8637832
Annotation contributions
H3K4me3
H3K27ac
coding.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K36me3.t1
H3K4me3
H3K4me1.t1
H3K27ac
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K36me3.t1
H3K4me1


Height Locus 11:66703817–67658044, rs61734601
Fine mapping with E034–Primary T cells from peripheral blood
PRF score
1:
chr11:66897377
2:
chr11:67159412
Annotation contributions
H3K36me3.t2
H3K4me3
H3K27ac
intron.same
H3K36me3
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K27ac
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1


Height Locus 14:94506729–94877925, rs28929474
Fine mapping with E030–Primary neutrophils from peripheral blood
PRF score
7.5
5.0
2.5
0.0
1: chr14:94844947
2: chr14:94838142
3: chr14:94756943
4: chr14:94877868
5: chr14:94863636
Annotation contributions
8
4
0
6.Tx.t1
H3K4me3
H3K27ac
coding.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K36me3.t1
H3K4me1
TSSDist
25.Quies.t2
H3K9me3
H3K4me1
H3K4me3
H3K36me3
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K27ac
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K27ac
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1


Height Locus 17:69789308–70120111, rs116878242
Fine mapping with E116–GM12878 Lymphoblastoid Cells
PRF score
3
2
1
0
−1
1: chr17:70002330
2: chr17:69905234
3: chr17:69989488
4: chr17:70044906
5: chr17:69931722
6: chr17:69922470
16: chr17:69929688
27: chr17:69934902
Annotation contributions
4
2
0
H3K4me3
H3K27ac
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K9me3
H3K36me3
TSSDist
H3K9me3
TSSDist
H3K9me3
H3K36me3
H3K9me3
H3K4me1
H3K4me3
H3K36me3
H3K9me3
H3K4me3
H3K27ac
H3K36me3
Dnase
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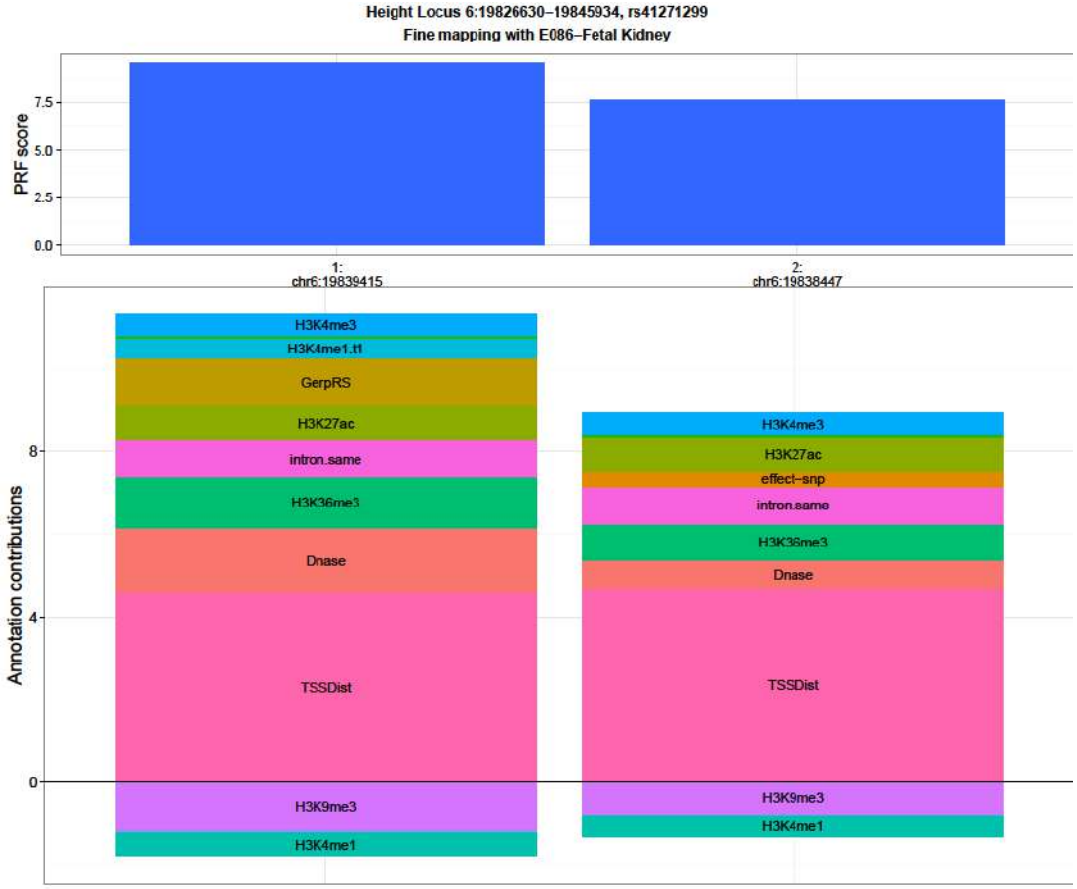
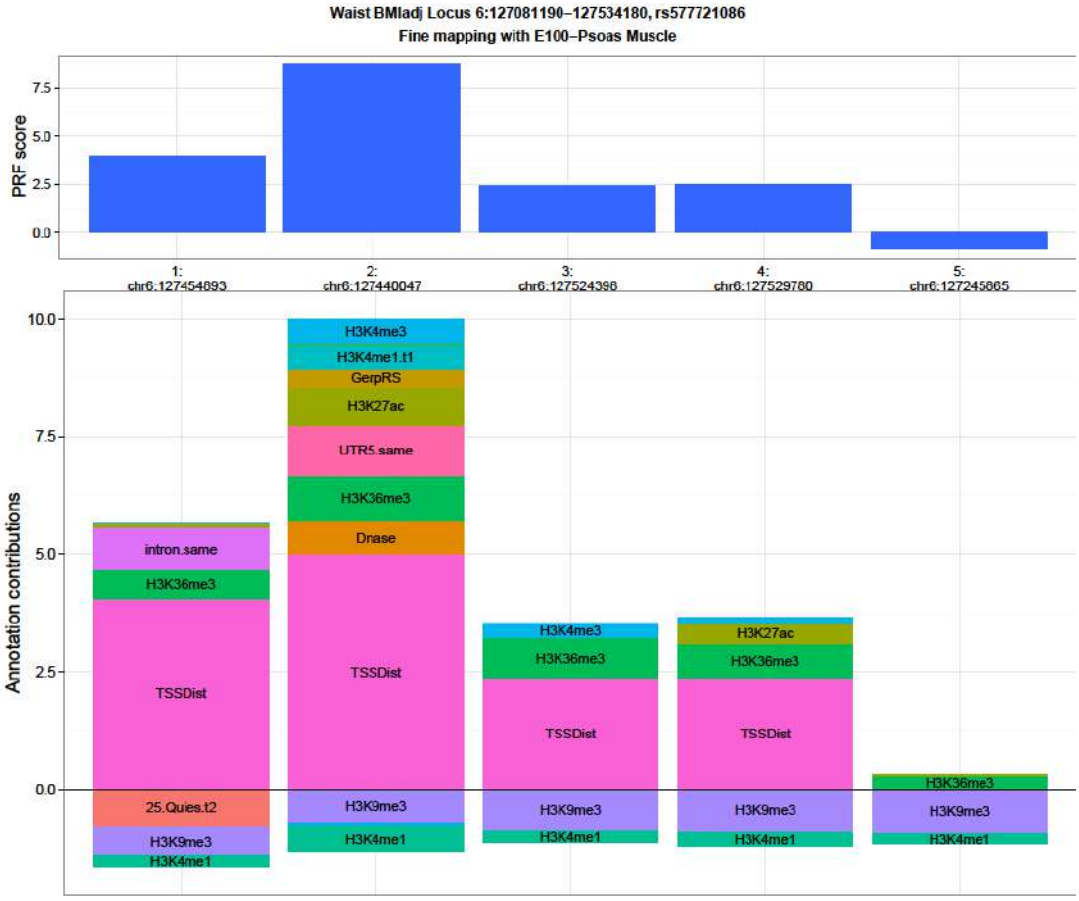
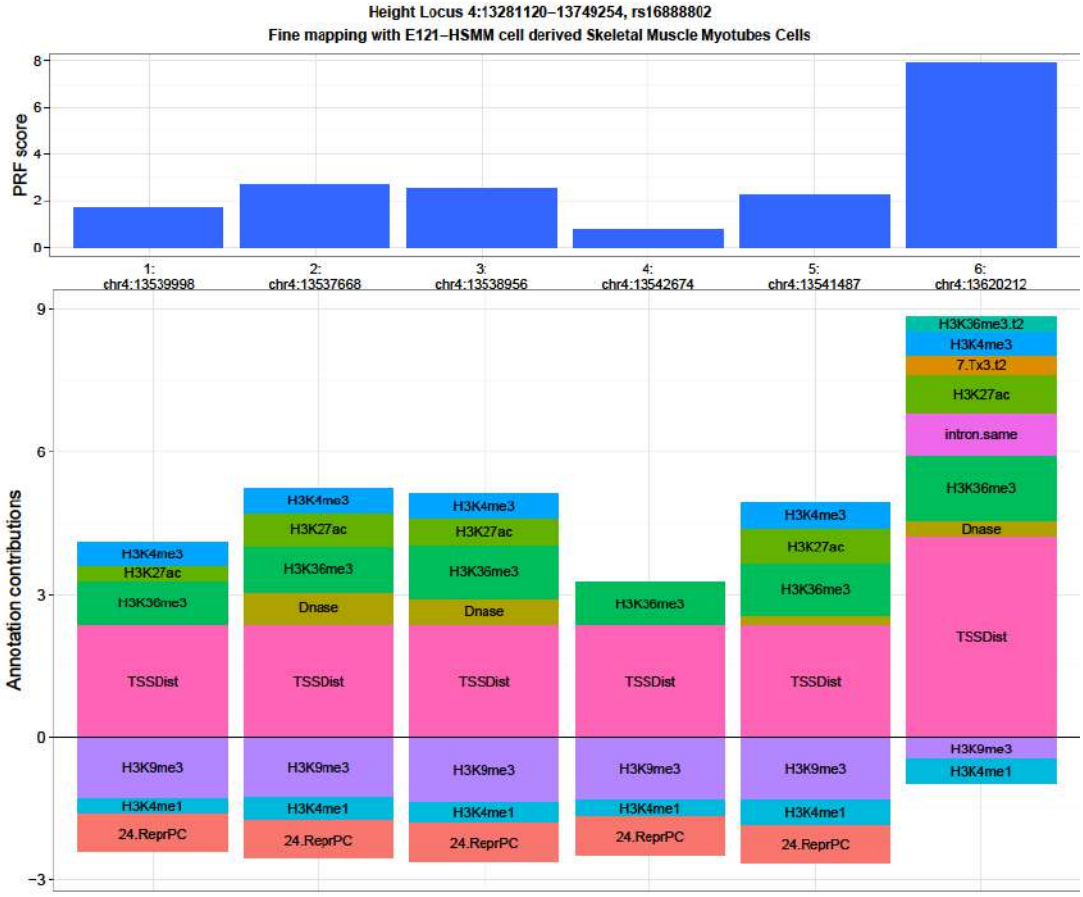
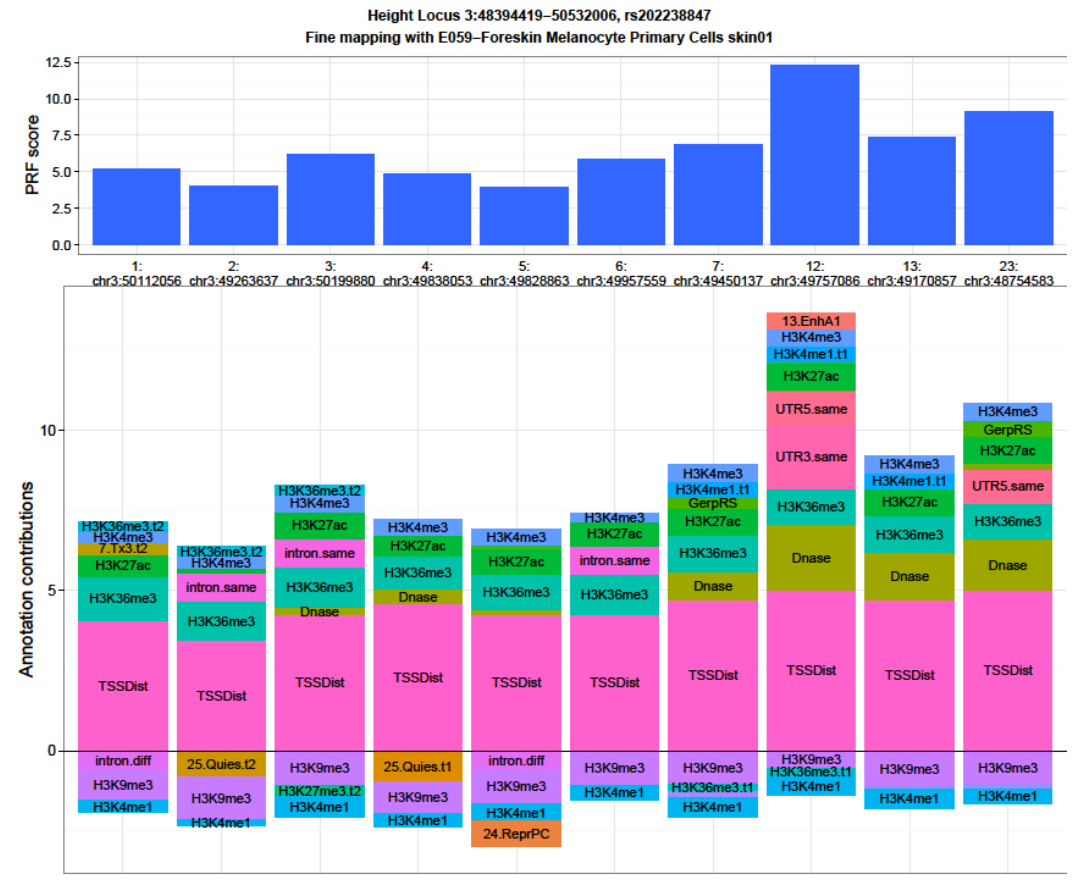
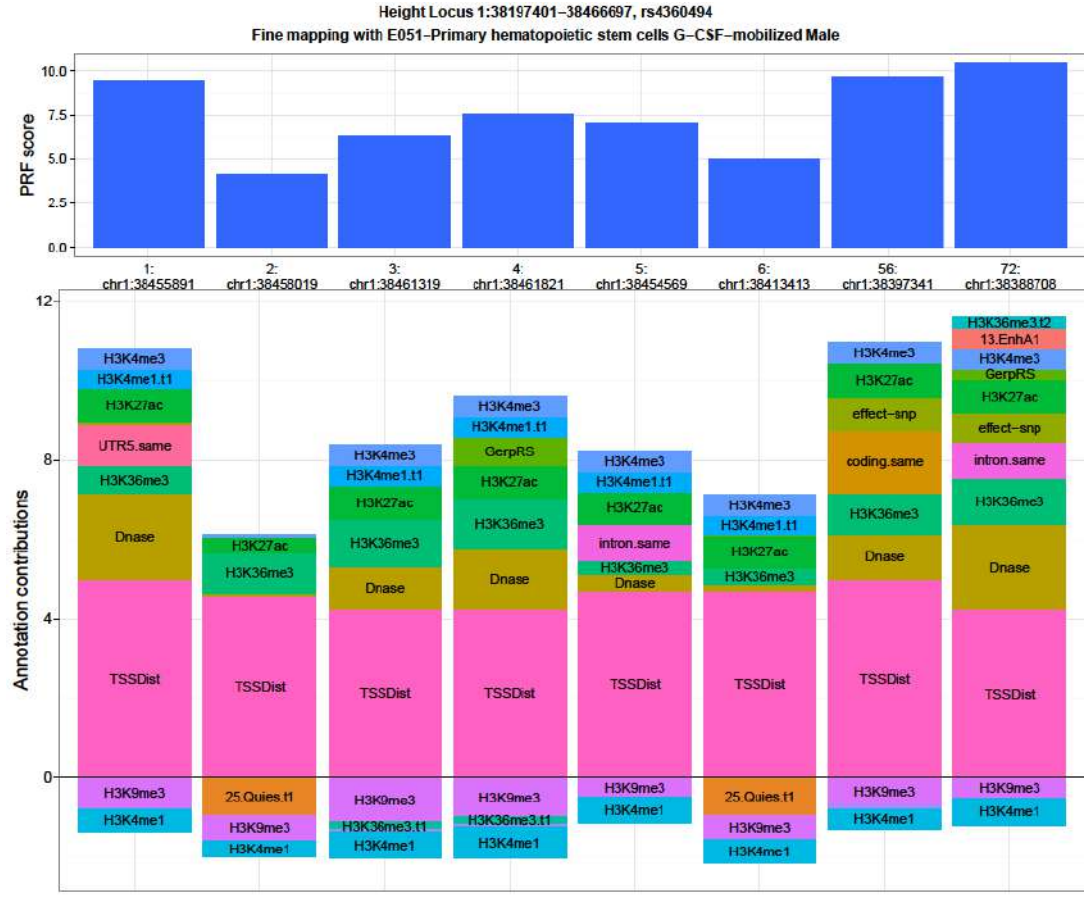
H3K4me3
H3K27ac
H3K36me3
Dnase
H3K9me3
H3K4me1

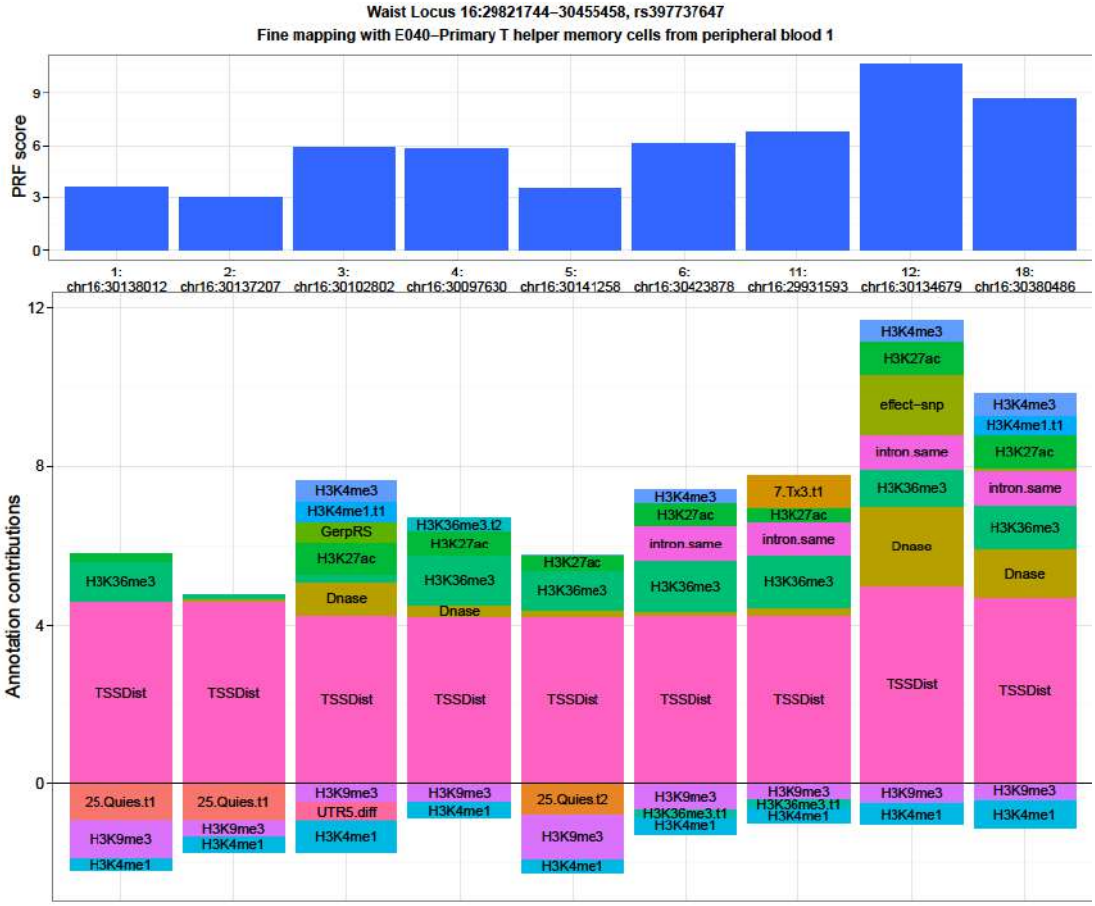

Height Locus 6:19826630–19845934, rs41271299
Fine mapping with E086–Fetal Kidney
PRF score
7.5
5.0
2.5
0.0
1:
chr6:19839415
2:
chr6:19838447
Annotation contributions
8
4
0
H3K4me3
H3K4me1.t1
GerpRS
H3K27ac
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K27ac
effect–snp
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1

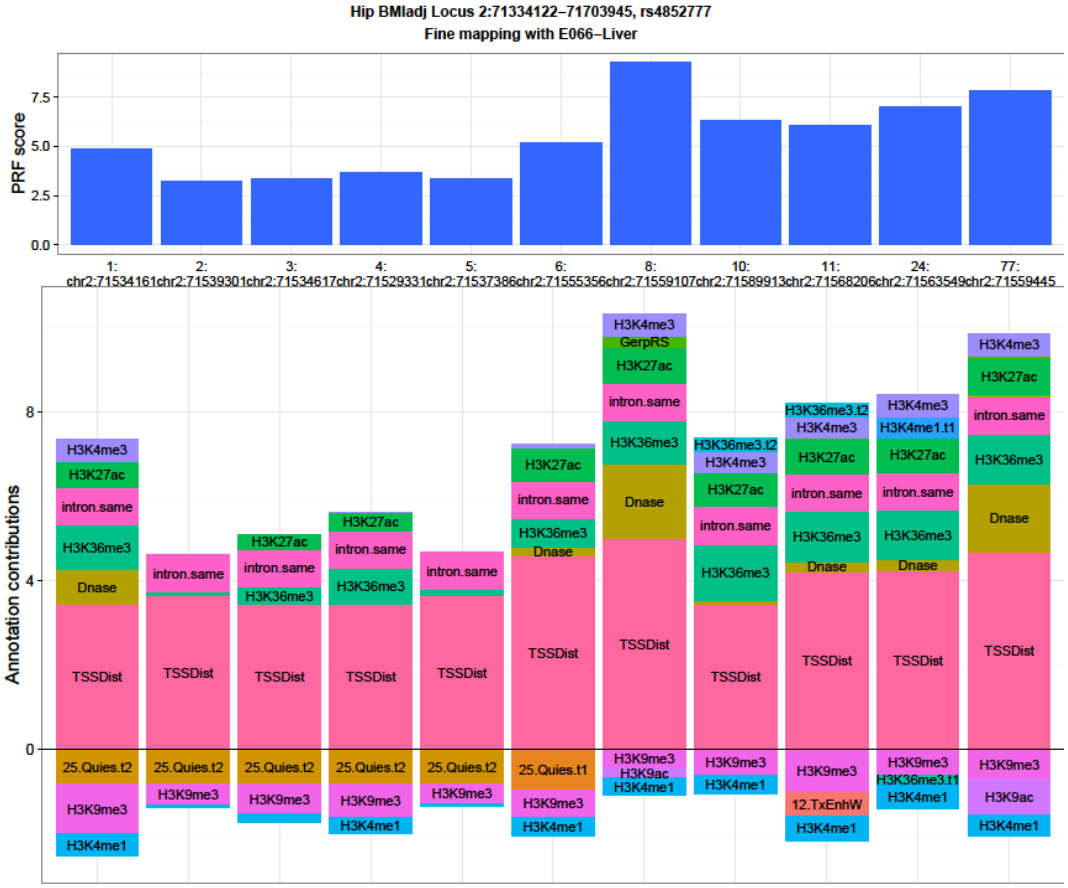

Waist BMIadj Locus 6:127081190–127534180, rs577721086
Fine mapping with E100–Psoas Muscle
PRF score
7.5
5.0
2.5
0.0
1:
chr6:127454893
2:
chr6:127440047
3:
chr6:127524398
4:
chr6:127529780
5:
chr6:127245865
Annotation contributions
10.0
7.5
5.0
2.5
0.0
intron.same
H3K36me3
TSSDist
25.Quies.t2
H3K9me3
H3K4me1
H3K4me3
H3K4me1.t1
GerpRS
H3K27ac
UTR5.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K36me3
TSSDist
H3K9me3
H3K4me1
H3K27ac
H3K36me3
TSSDist
H3K9me3
H3K4me1
H3K36me3
H3K9me3
H3K4me1

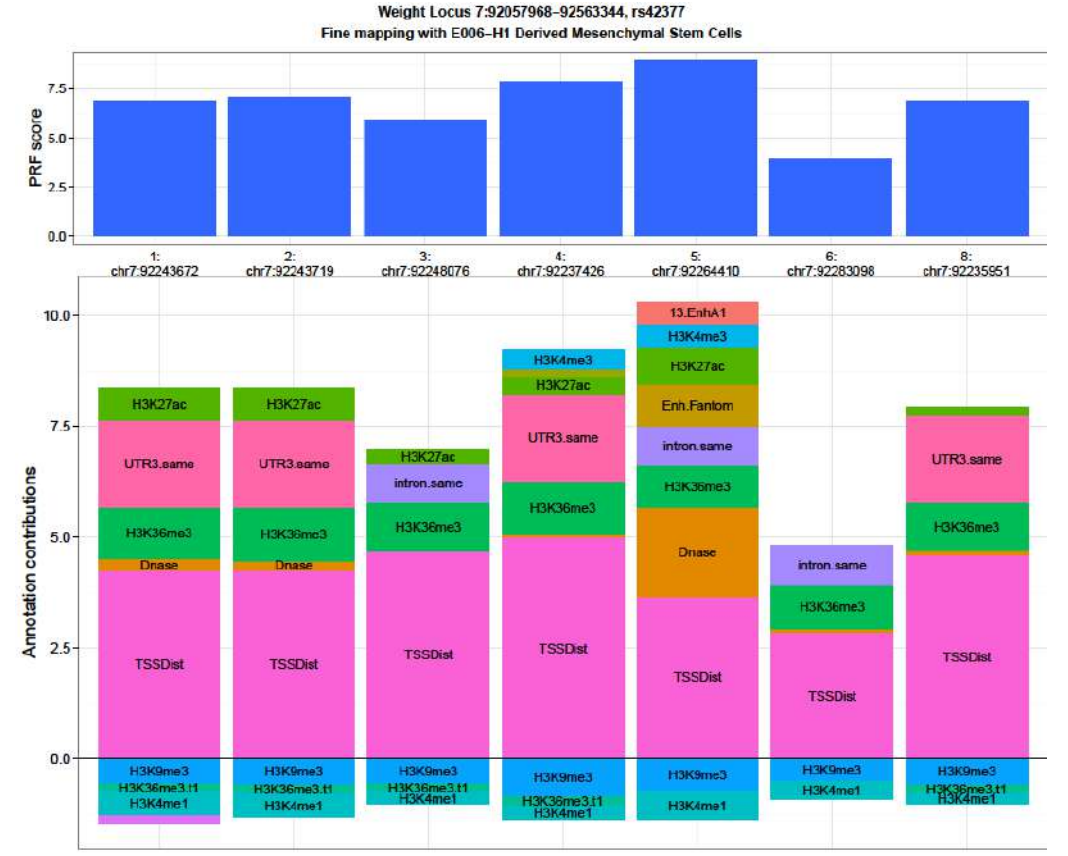

Height Locus 4:13281120–13749254, rs16888802
Fine mapping with E121–HSMM cell derived Skeletal Muscle Myotubes Cells
PRF score
1: chr4:13539998
2: chr4:13537668
3: chr4:13538956
4: chr4:13542674
5: chr4:13541487
6: chr4:13620212
Annotation contributions
H3K4me3
H3K27ac
H3K36me3
TSSDist
H3K9me3
H3K4me1
24.ReprPC
Dnase
H3K36me3.t2
7.Tx3.t2
intron.same


Height Locus 3:48394419–50532006, rs202238847
Fine mapping with E059–Foreskin Melanocyte Primary Cells skin01
PRF score
1: chr3:50112056
2: chr3:49263637
3: chr3:50199880
4: chr3:49838053
5: chr3:49828863
6: chr3:49957559
7: chr3:49450137
12: chr3:49757086
13: chr3:49170857
23: chr3:48754583
Annotation contributions
H3K4me3
H3K27ac
H3K36me3
TSSDist
H3K9me3
H3K4me1
Dnase
intron.same
H3K36me3.t2
7.Tx3.t2
intron.diff
25.Quies.t2
25.Quies.t1
24.ReprPC
H3K27me3.t2
13.EnhA1
H3K4me1.t1
UTR5.same
UTR3.same
GerpRS
H3K36me3.t1


Height Locus 1:38197401–38466697, rs4360494
Fine mapping with E051–Primary hematopoietic stem cells G–CSF–mobilized Male
PRF score
10.0
7.5
5.0
2.5
0.0
1: chr1:38455891
2: chr1:38458019
3: chr1:38461319
4: chr1:38461821
5: chr1:38454569
6: chr1:38413413
56: chr1:38397341
72: chr1:38388708
Annotation contributions
12
8
4
0
H3K4me3
H3K4me1.t1
H3K27ac
UTR5.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K27ac
H3K36me3
TSSDist
25.Quies.t1
H3K9me3
H3K4me1
H3K4me3
H3K4me1.t1
H3K27ac
H3K36me3
Dnase
TSSDist
H3K9me3
H3K36me3.t1
H3K4me1
H3K4me3
H3K4me1.t1
GerpRS
H3K27ac
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K4me1.t1
H3K27ac
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K4me1.t1
H3K27ac
H3K36me3
TSSDist
25.Quies.t1
H3K9me3
H3K4me1
H3K4me3
H3K27ac
effect–snp
coding.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K36me3.t2
13.EnhA1
H3K4me3
GerpRS
H3K27ac
effect–snp
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1


Waist Locus 16:29821744–30455458, rs397737647
Fine mapping with E040–Primary T helper memory cells from peripheral blood 1
PRF score
9
6
3
0
1: chr16:30138012
2: chr16:30137207
3: chr16:30102802
4: chr16:30097630
5: chr16:30141258
6: chr16:30423878
11: chr16:29931593
12: chr16:30134679
18: chr16:30380486
Annotation contributions
12
8
4
0
H3K36me3
TSSDist
25.Quies.t1
H3K9me3
H3K4me1
H3K4me3
H3K4me1.t1
GerpRS
H3K27ac
Dnase
TSSDist
H3K9me3
UTR5.diff
H3K4me1
H3K36me3.t2
H3K27ac
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K27ac
H3K36me3
TSSDist
25.Quies.t2
H3K9me3
H3K4me1
H3K4me3
H3K27ac
intron.same
H3K36me3
TSSDist
H3K9me3
H3K36me3.t1
H3K4me1
7.Tx3.t1
H3K27ac
intron.same
H3K36me3
TSSDist
H3K9me3
H3K36me3.t1
H3K4me1
H3K4me3
H3K27ac
effect–snp
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1
H3K4me3
H3K4me1.t1
H3K27ac
intron.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K4me1


Hip BMIadj Locus 2:71334122–71703945, rs4852777
Fine mapping with E066–Liver
PRF score
Annotation contributions
1: chr2:71534161
2: chr2:71539301
3: chr2:71534617
4: chr2:71529331
5: chr2:71537386
6: chr2:71555356
8: chr2:71559107
10: chr2:71589913
11: chr2:71568206
24: chr2:71563549
77: chr2:71559445
H3K4me3
H3K27ac
intron.same
H3K36me3
Dnase
TSSDist
25.Quies.t2
H3K9me3
H3K4me1
GerpRS
H3K36me3.t2
H3K4me1.t1
25.Quies.t1
H3K9ac
H3K36me3.t1
12.TxEnhW


Weight Locus 7:92057968–92563344, rs42377
Fine mapping with E006–H1 Derived Mesenchymal Stem Cells
PRF score
Annotation contributions
1: chr7:92243672
2: chr7:92243719
3: chr7:92248076
4: chr7:92237426
5: chr7:92264410
6: chr7:92283098
8: chr7:92235951
H3K27ac
UTR3.same
H3K36me3
Dnase
TSSDist
H3K9me3
H3K36me3.t1
H3K4me1
H3K4me3
13.EnhA1
Enh.Fantom
intron.same

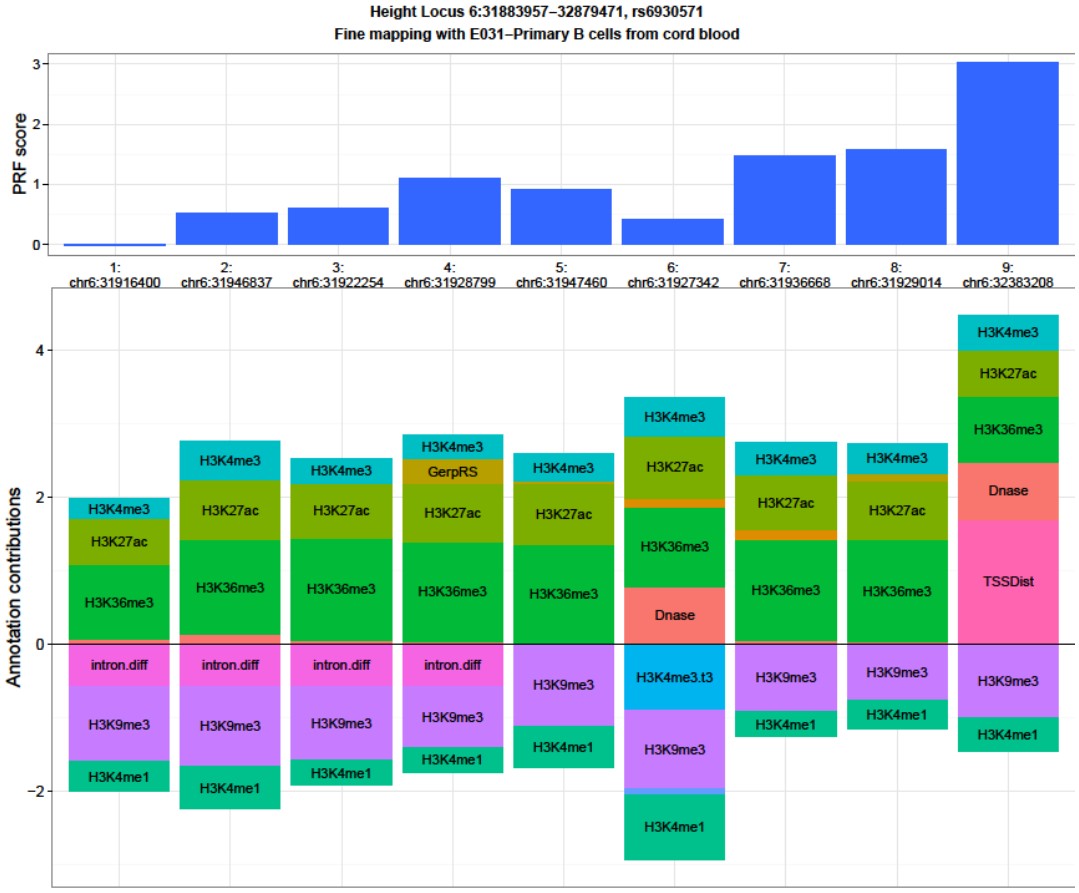
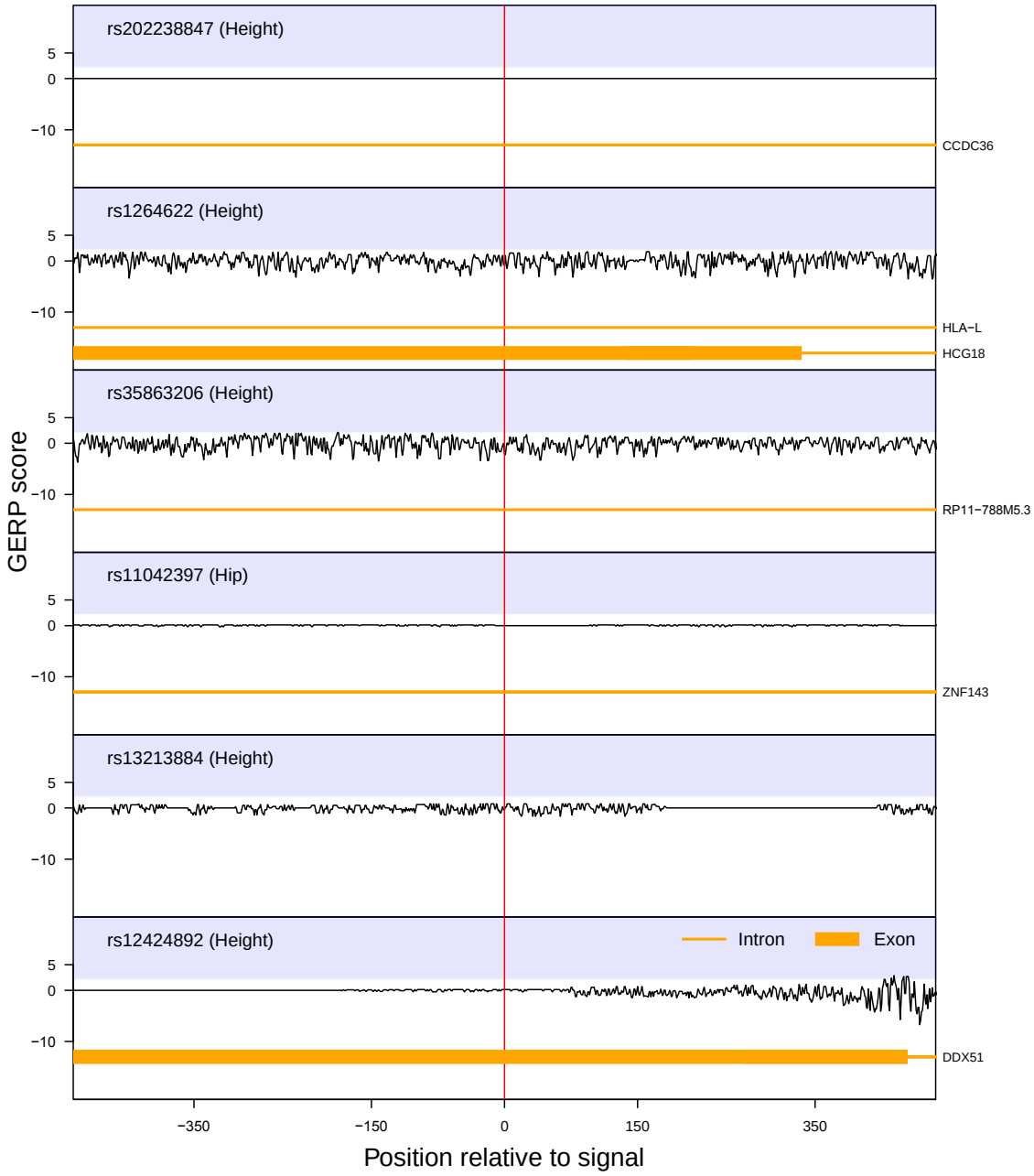
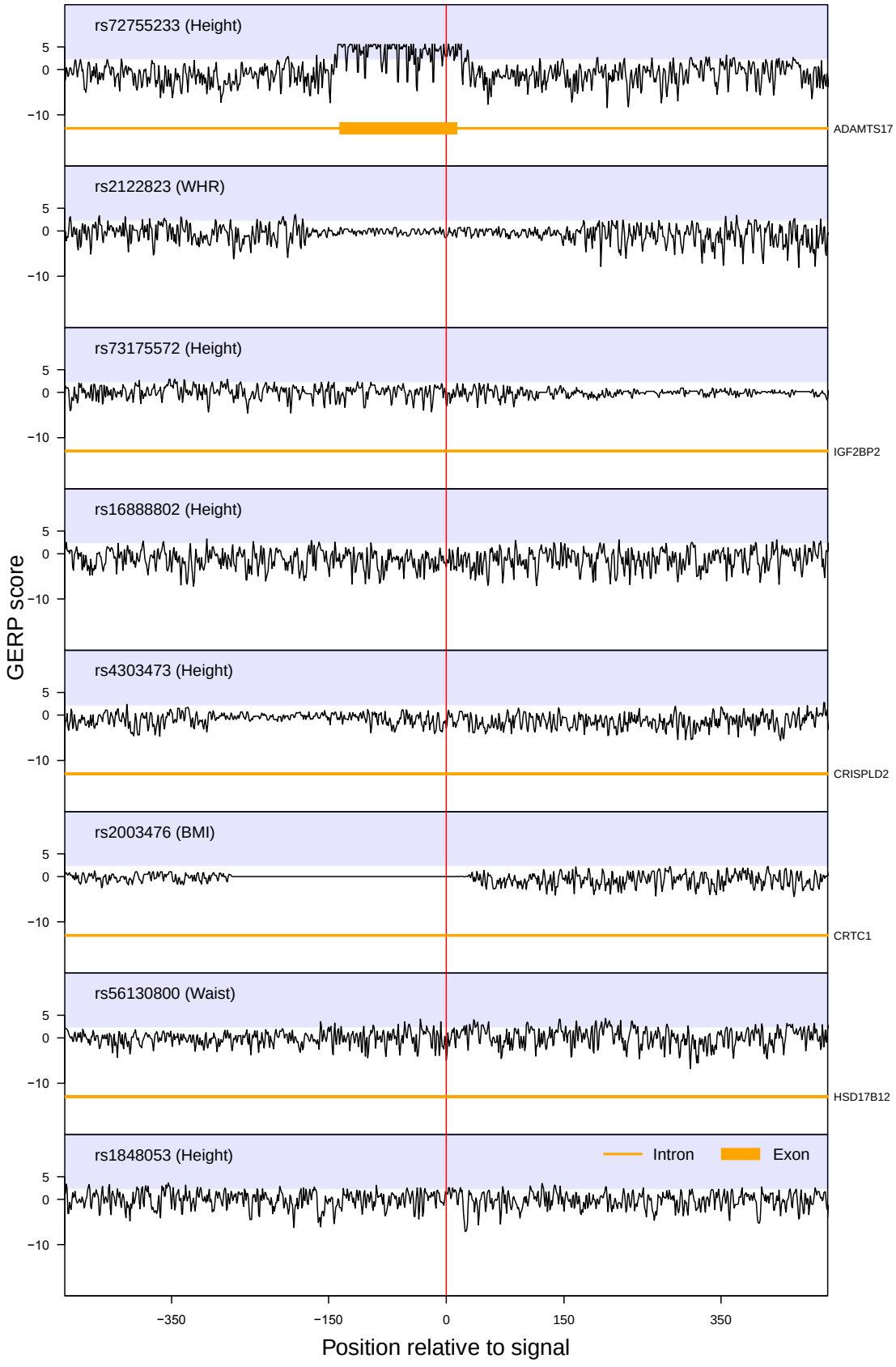


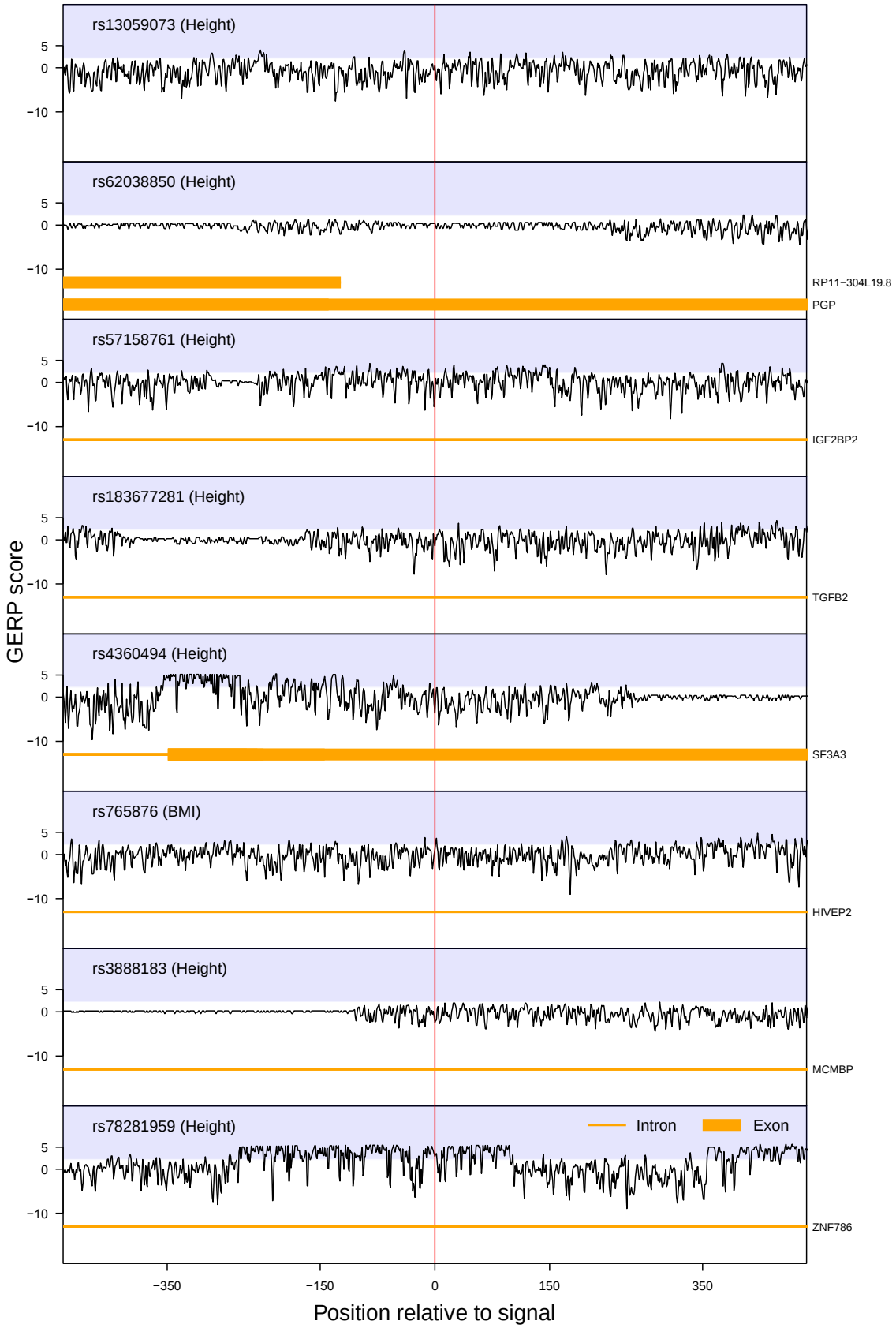
Figure S15: Probability of regulatory function (PRF) plots for the newly identified loci.
For each of the newly identified loci, we attempted to fine-map the association signal using epigenomic annotations (Methods). At each of the regions around the loci, the plots show the PRF scores for variants with high posterior probability of association, after combining association statistics with the PRF scores. Each variant is labeled with its association statistic rank, followed by the variant position (e.g. 1: chr2:407713). The height of the blue bar represents the PRF score itself, which is the sum of the contributions from individual annotations shown below. Annotations with negative enrichments (depletion of causal variants, e.g. H3K9me3) appear below zero in the PRF score breakdown. Regions with high confidence in fine-mapping are shown below (posterior probability of causality for the best SNP > 0.5).

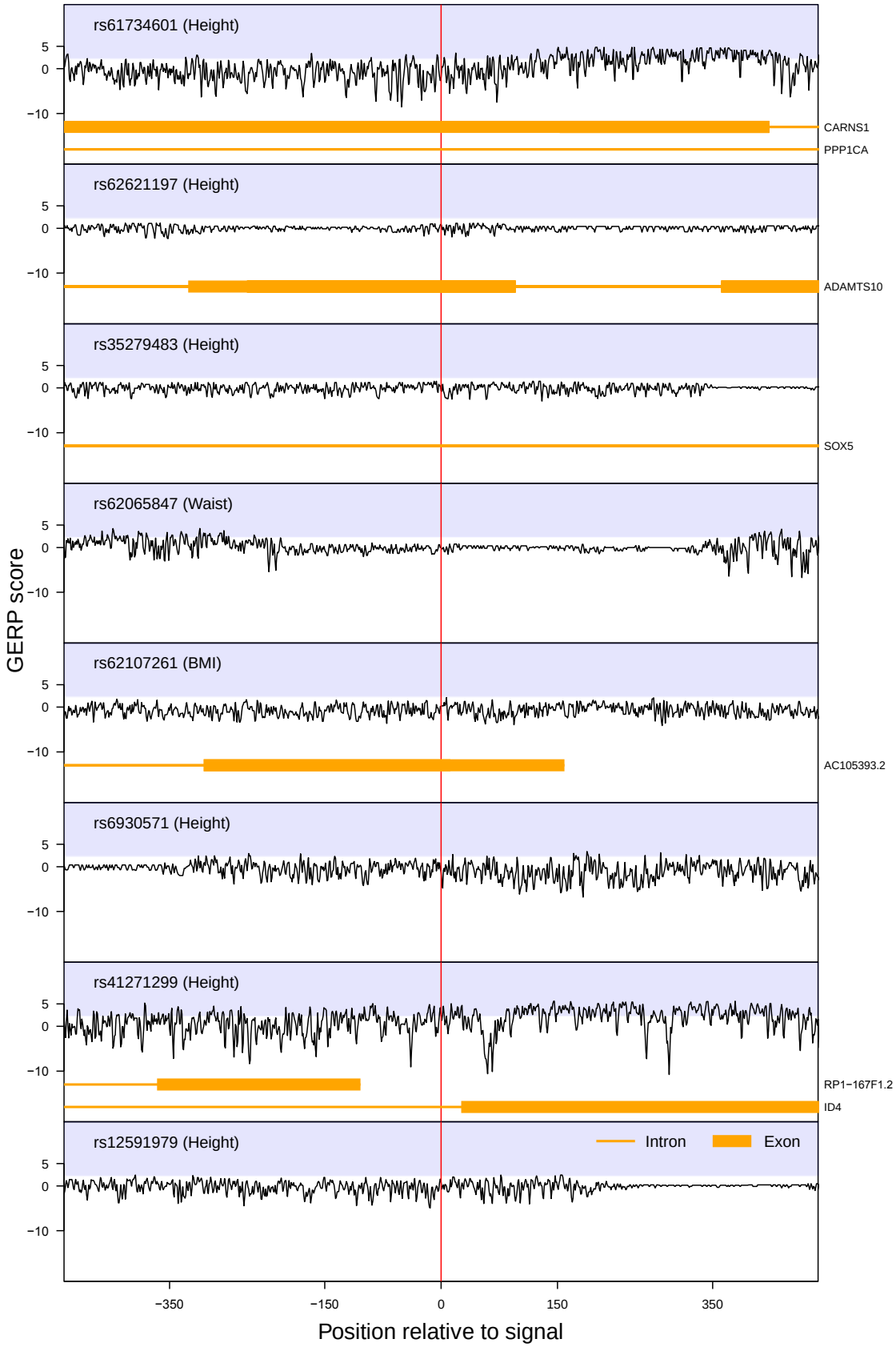
A)


rs202238847 (Height)
rs1264622 (Height)
rs35863206 (Height)
rs11042397 (Hip)
rs13213884 (Height)
rs12424892 (Height)
5
0
−10
CCDC36
HLA−L
HCG18
RP11−788M5.3
ZNF143
DDX51
Intron
Exon
GERP score
−350
−150
0
150
350
Position relative to signal

B)


rs72755233 (Height)
rs2122823 (WHR)
rs73175572 (Height)
rs16888802 (Height)
rs4303473 (Height)
rs2003476 (BMI)
rs56130800 (Waist)
rs1848053 (Height)
ADAMTS17
IGF2BP2
CRISPLD2
CRTC1
HSD17B12
Intron
Exon
GERP score
5
0
−10
−350
−150
0
150
350
Position relative to signal


rs13059073 (Height)
rs62038850 (Height)
RP11−304L19.8
PGP
rs57158761 (Height)
IGF2BP2
rs183677281 (Height)
TGFB2
rs4360494 (Height)
SF3A3
rs765876 (BMI)
HIVEP2
rs3888183 (Height)
MCMBP
rs78281959 (Height)
ZNF786
Intron
Exon
GERP score
5
0
−10
−350
−150
0
150
350
Position relative to signal


rs61734601 (Height)
rs62621197 (Height)
rs35279483 (Height)
rs62065847 (Waist)
rs62107261 (BMI)
rs6930571 (Height)
rs41271299 (Height)
rs12591979 (Height)
5
0
−10
CARNS1
PPP1CA
ADAMTS10
SOX5
AC105393.2
RP1−167F1.2
ID4
Intron
Exon
GERP score
−350
−150
0
150
350
Position relative to signal

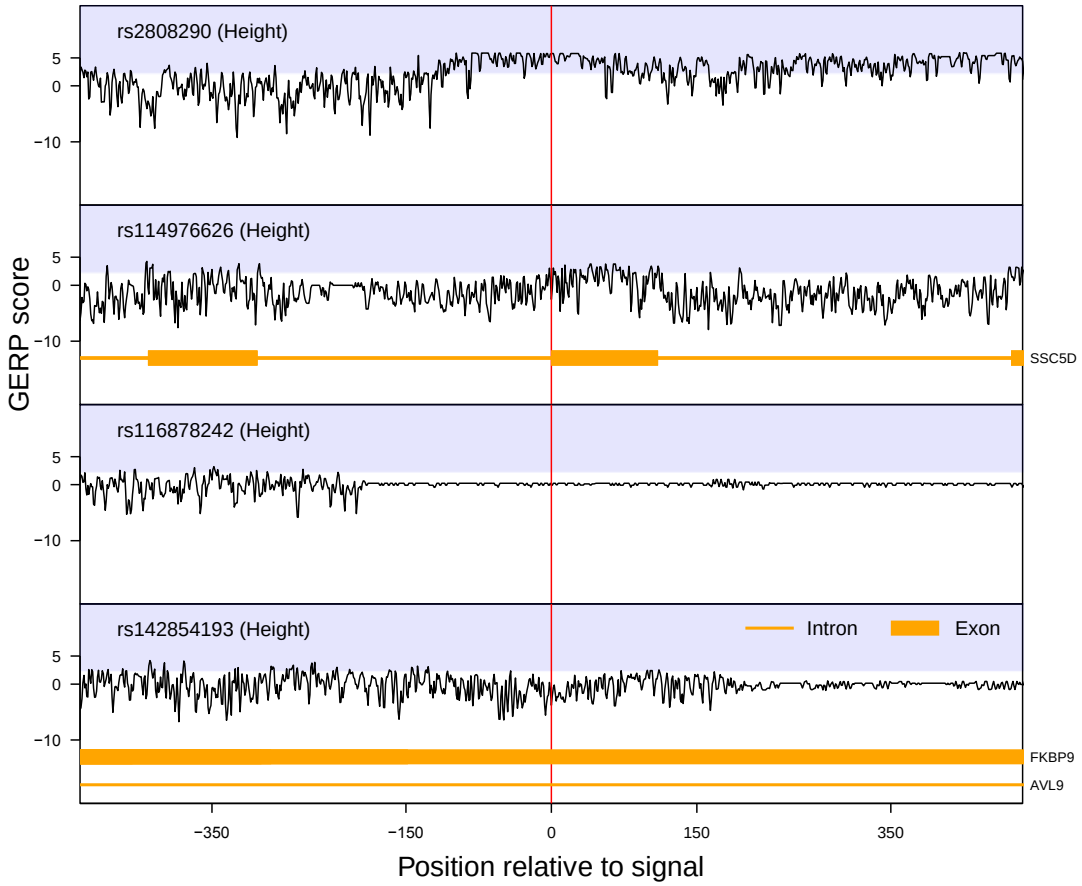


Figure S16: Genomic Evolutionary Rate Profiling (GERP) score as a measure of cross-species conservation of the sequences around each newly identified association.
A – variants listed in Table 1; B – variants listed in Table 2. The GERP score is based on the analysis of the alignment of sequences from 29 mammalian species and captures substitution deficits indicating sequence conservation. A score above zero indicates substitution deficit and thus indicates that a site may be under evolutionary constraint. Negative scores indicate substitution surplus. Stretches of scores close to zero indicate regions where the alignment is too shallow to get a meaningful estimate of the constraint. In practice, a position with GERP score above two is considered to be conserved (this threshold is indicated by the light blue background on the plots). To put the conservation pattern in a genic context, the transcripts of genes located within 500bp of the signals are also shown (annotation from GENCODE release 19). To make the trends in conservation more visible in the plots, GERP scores were averaged in two base pairs long sliding window. The red line indicates the position of the variant.

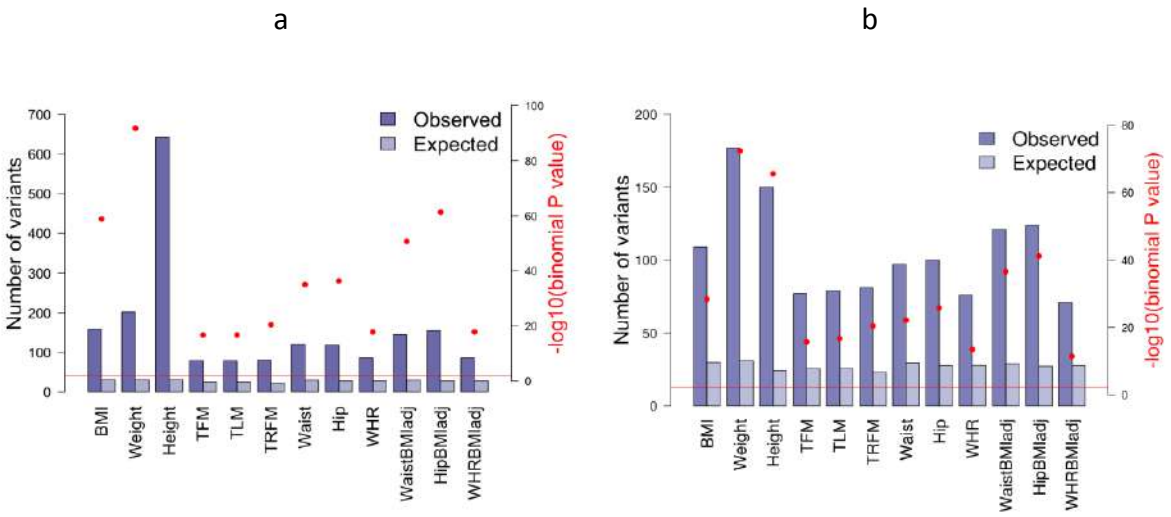
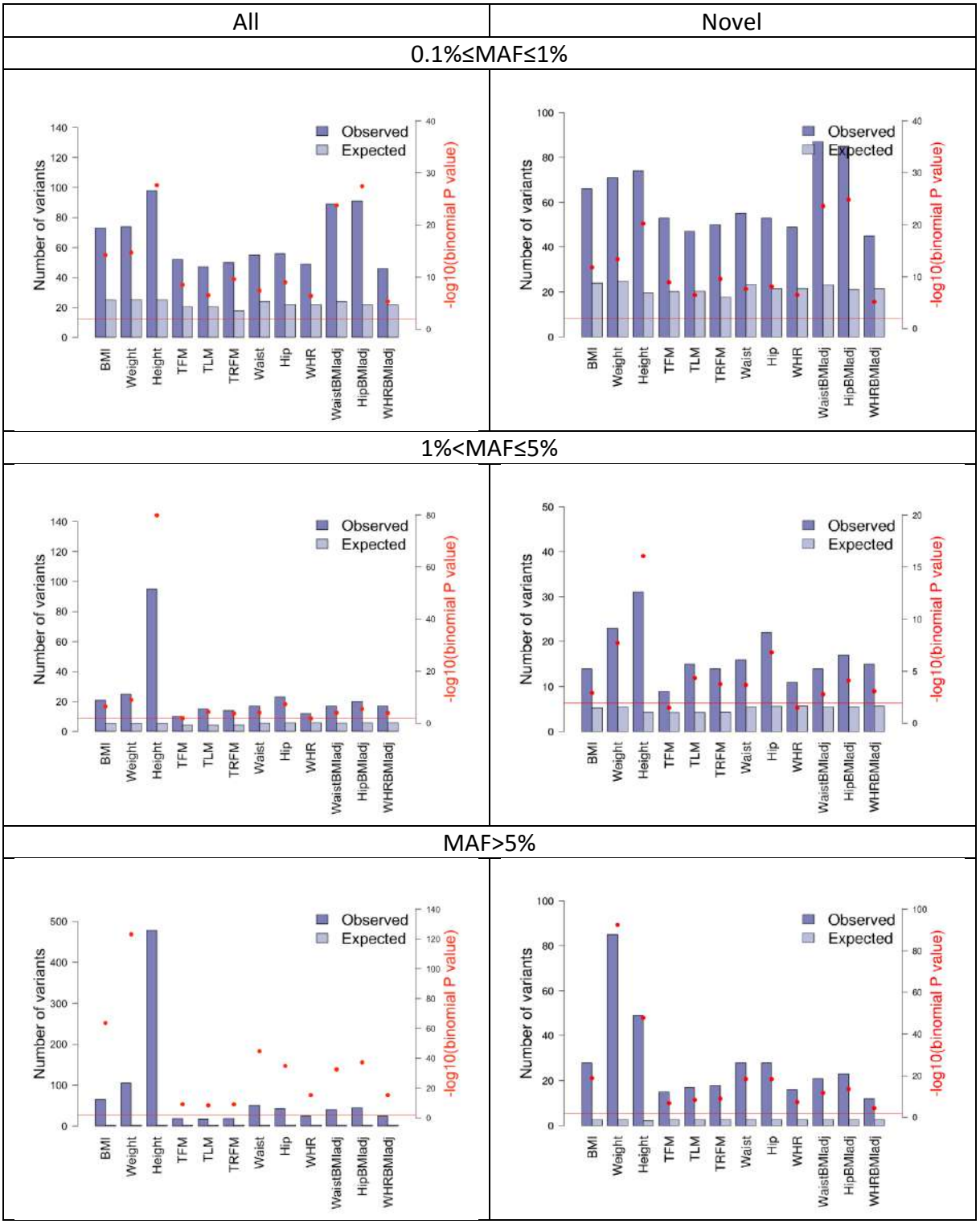


Figure S17: Enrichment in discovery meta-analysis using independent variants (r^2<0.2) with MAF ≥ 0.1% (a) and after excluding previously known loci (±500kb) (b).

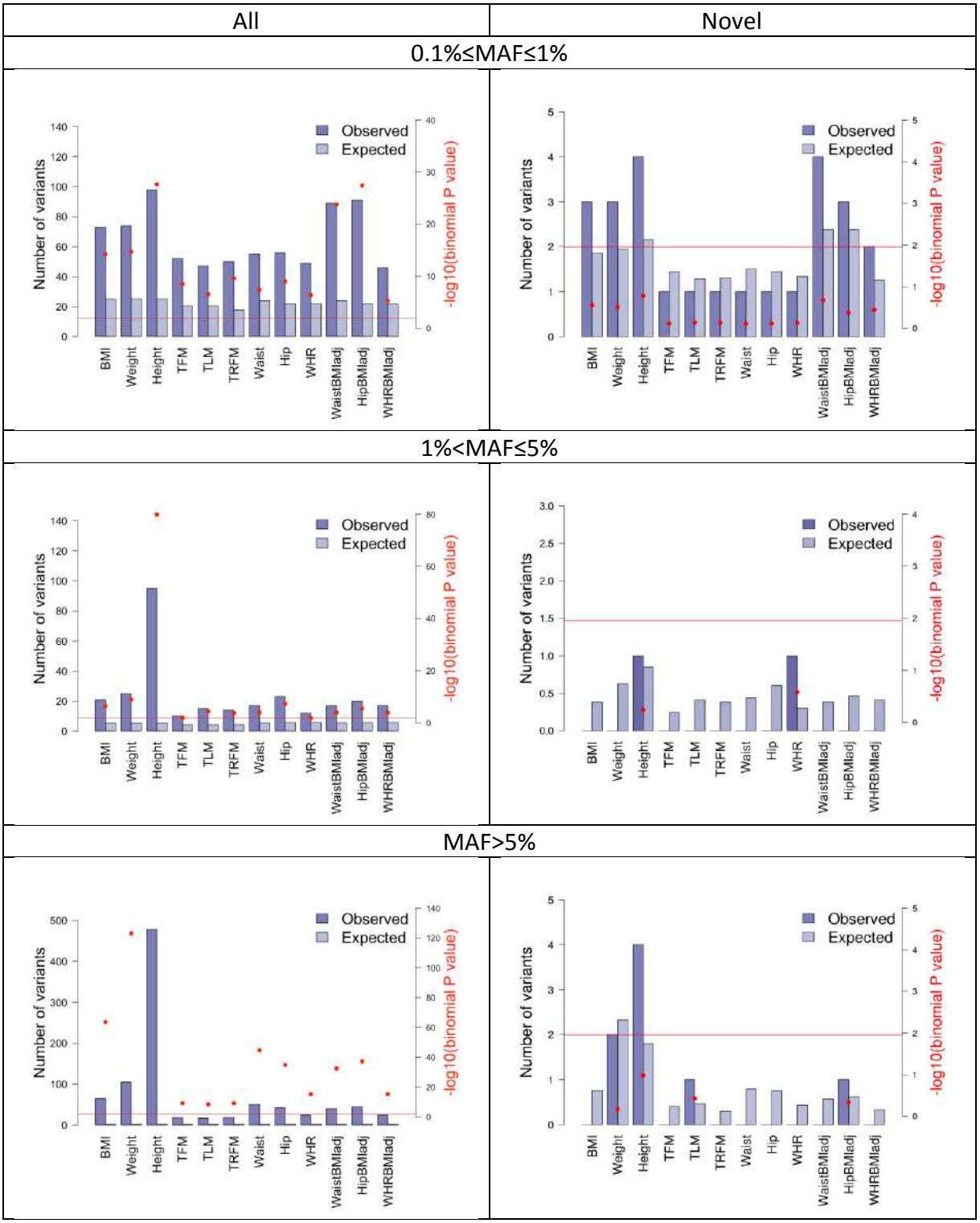
Enrichment of signal is observed if the *P-value* (one-sided, denoted by the red dot) from the binomial test of observed versus expected number of variants with $P \leq 10^{-5}$ is less than 0.05/4.482 (5% significance level Bonferroni corrected for the effective number of independent traits; horizontal red line). The enrichment in height using all variants in (a) is too significant to be calculated with precision (~3M independent variants with MAF≥0.1%, 642 of which have $P \leq 10^{-5}$, 31 expected). Observed and expected counts, Bonferroni corrected *P-values* and FDR *q-values* are given in Table S11.

WaistBMIadj: waist circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass.



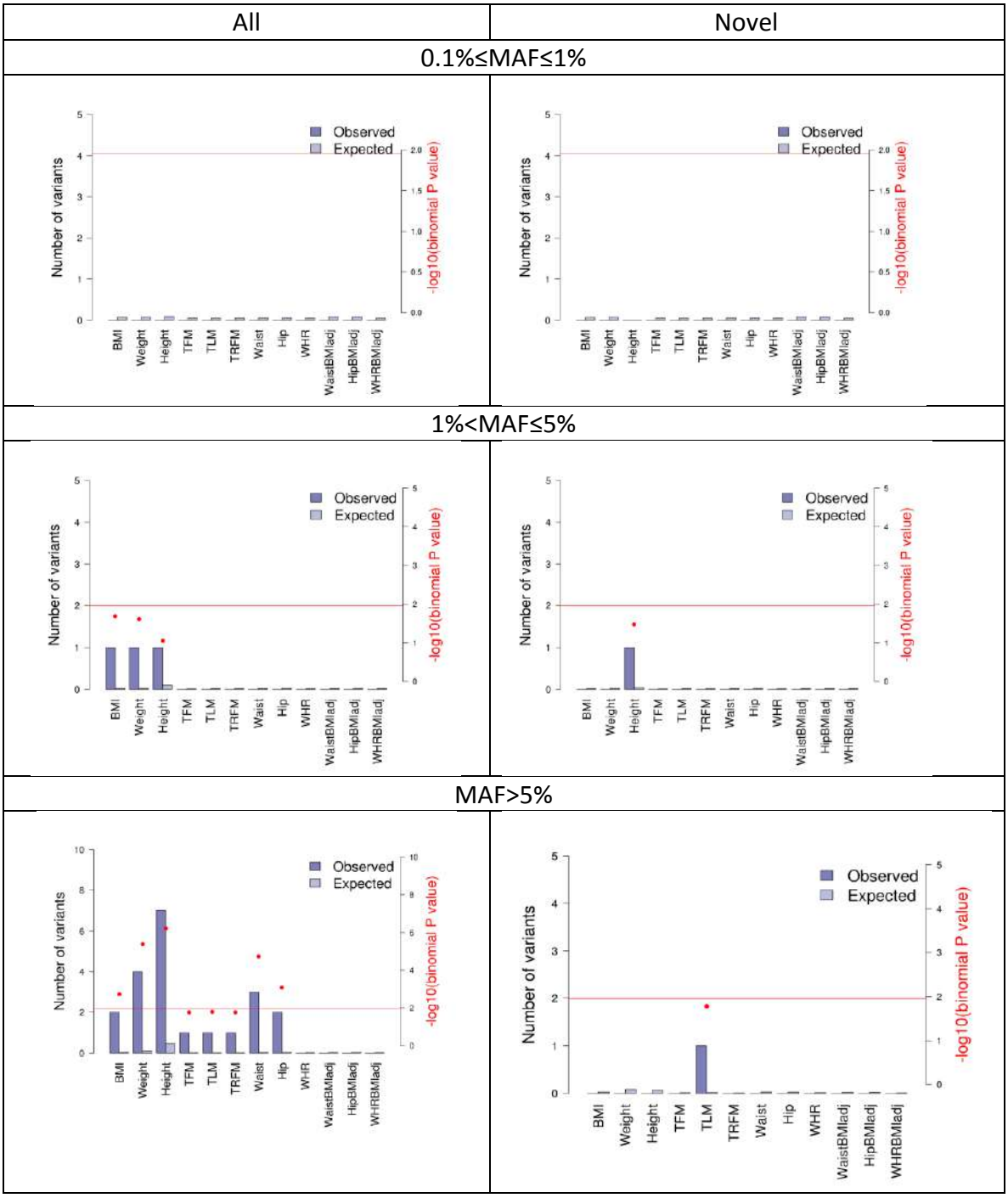
BMI: body mass index; WHR: waist to hip ratio; WaistBMIadj: waist circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass

Figure S18: Enrichment in discovery meta-analysis results. Using independent variants (r^2<0.2) within different Minor Allele Frequency (MAF) bins (left) and after excluding previously known loci (±500 kb) (right). Enrichment of signal is observed if the *P-value* from the binomial test of observed versus expected number of variants with P≤10^{-5} is less than 0.05/4.482 (5% significance level Bonferroni corrected for the effective number of independent traits (horizontal red line).



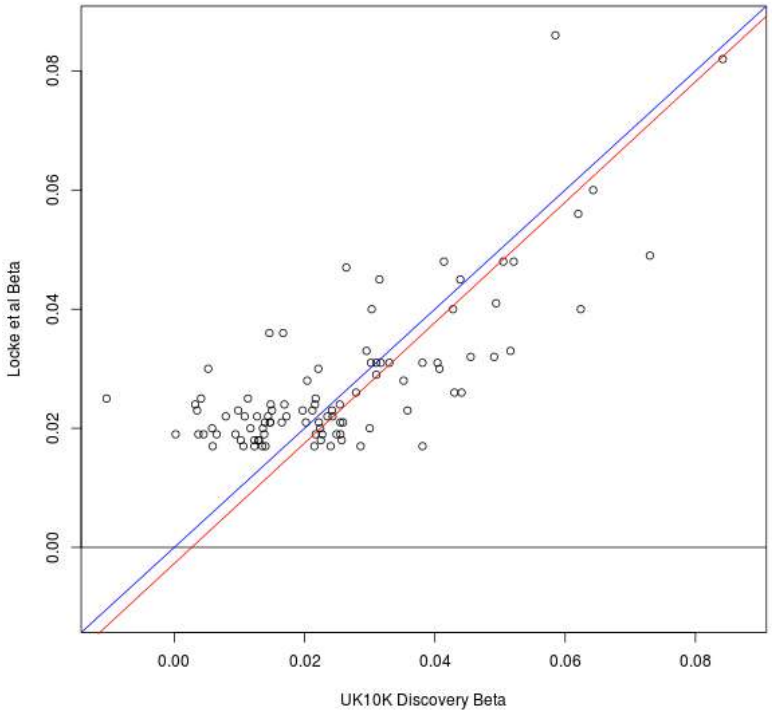
BMI: body mass index; WHR: waist to hip ratio; WaistBMIadj: waist circumference circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass

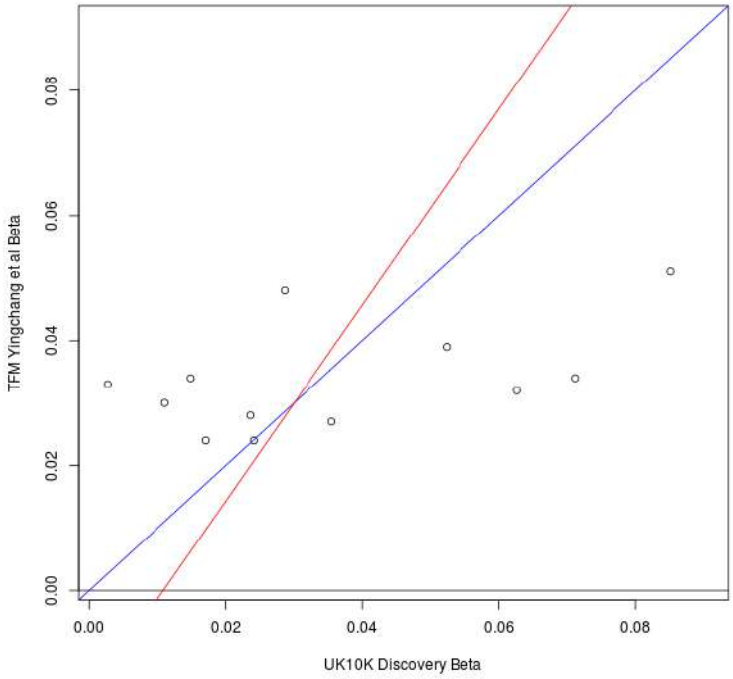
Figure S19: Enrichment of discovery meta-analysis results in Mendelian genes for height.
We used independent variants (r^2<0.2) within different Minor Allele Frequency (MAF) bins (left) and after excluding previously known loci (±500 kb) (right). Enrichment of signal is observed if the *P-value* from the binomial test of observed versus expected number of variants with $P \leq 10^{-5}$ in Mendelian genes for height (as calculated by GREAT) is less than 0.05/4.482 (5% significance level Bonferroni corrected for the effective number of independent traits (horizontal red line).

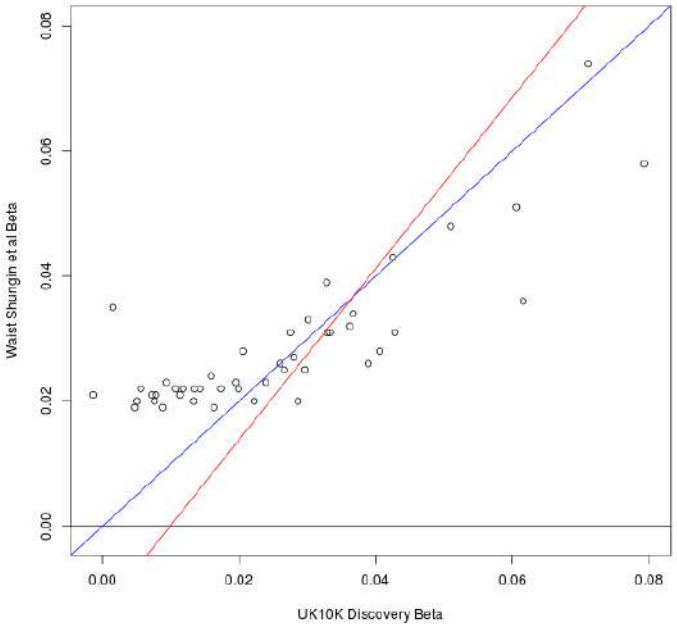


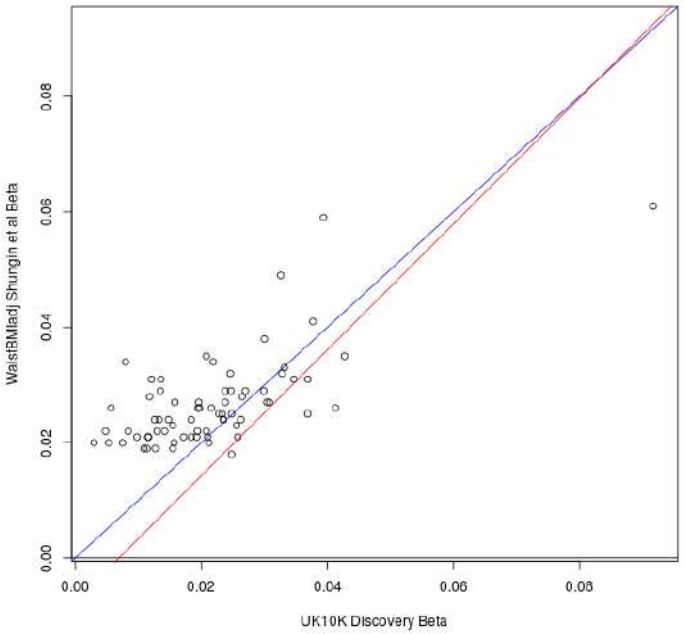
BMI: body mass index; WHR: waist to hip ratio; WaistBMIadj: waist circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass

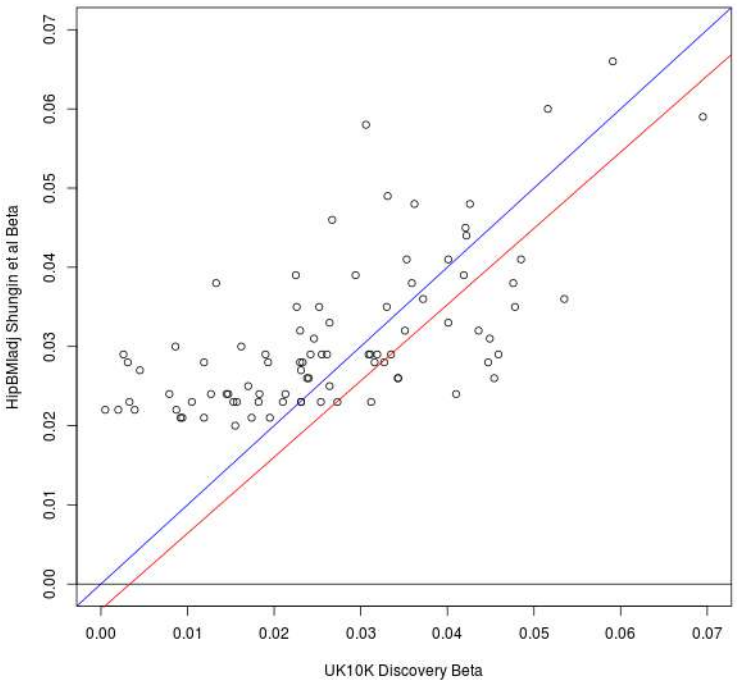
Figure S20: Enrichment of discovery meta-analysis results in monogenic obesity genes.
We used independent variants (r^2<0.2) within different Minor Allele Frequency (MAF) bins (left) and after excluding previously known loci (±500 kb) (right). Enrichment of signal is observed if the *P-value* from the binomial test of observed versus expected number of variants with $P \leq 10^{-5}$ in Mendelian genes for obesity (as calculated by GREAT) is less than 0.05/4.482 (5% significance level Bonferroni corrected for the effective number of independent traits (horizontal red line).

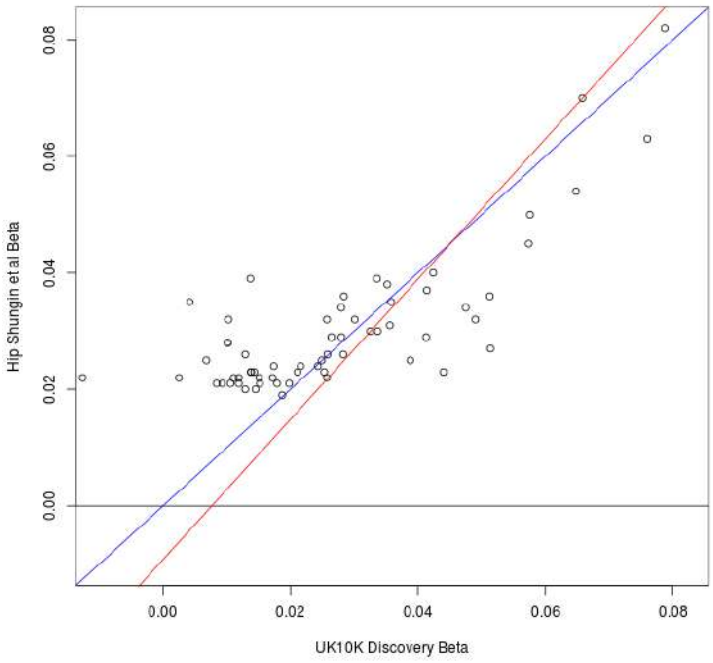

Locke et al Beta
0.00
0.02
0.04
0.06
0.08
UK10K Discovery Beta

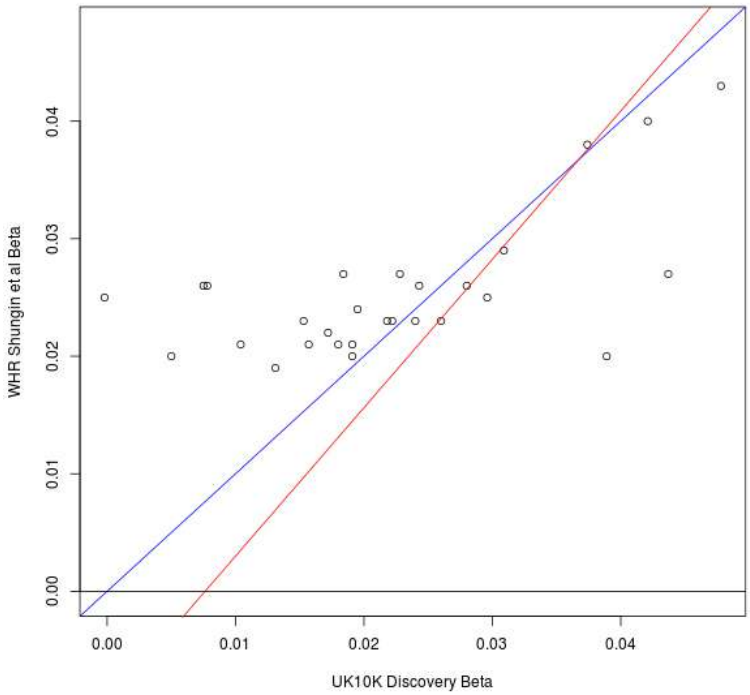

TFM Yingchang et al Beta
0.00
0.02
0.04
0.06
0.08
UK10K Discovery Beta


Waist Shungin et al Beta
UK10K Discovery Beta
0.00
0.02
0.04
0.06
0.08


WaistBMIadj Shungin et al Beta
UK10K Discovery Beta
0.00
0.02
0.04
0.06
0.08


HipBMIadj Shungin et al Beta
0.00
0.01
0.02
0.03
0.04
0.05
0.06
0.07
UK10K Discovery Beta


Hip Shungin et al Beta
0.00
0.02
0.04
0.06
0.08
UK10K Discovery Beta



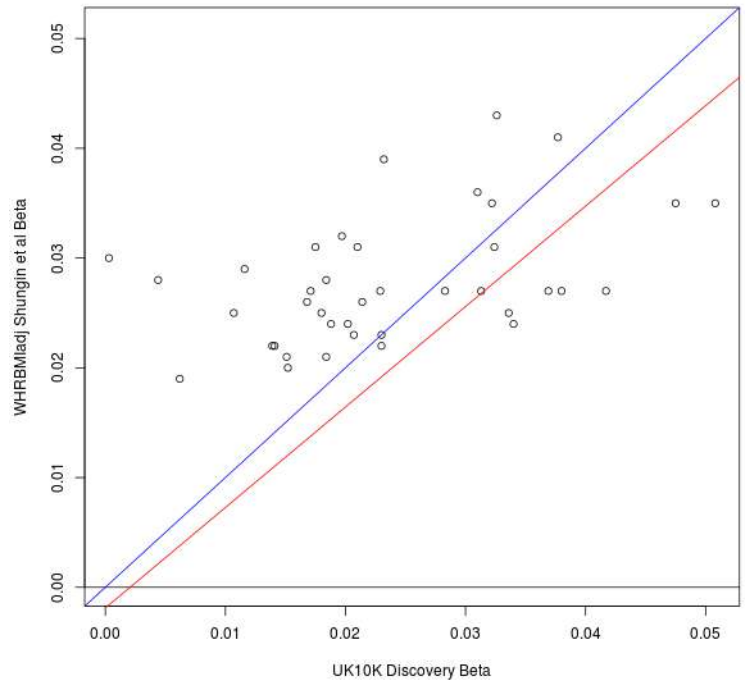
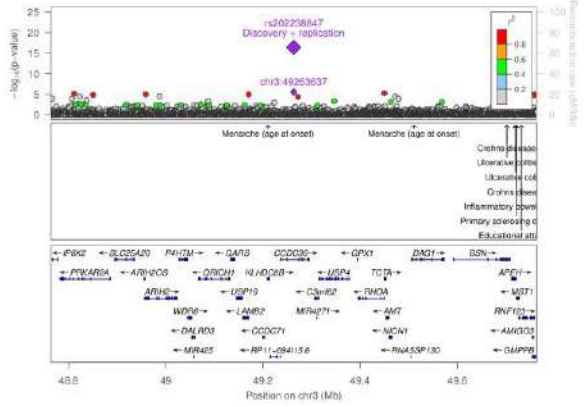
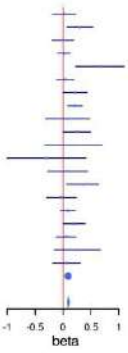
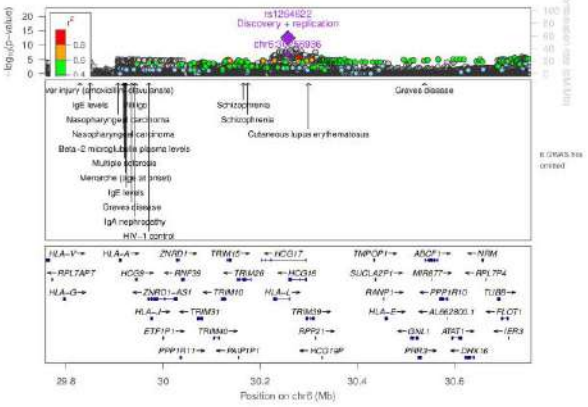


Figure S21: Beta-beta plots.
Effect sizes in our discovery phase (x-axis) versus effect sizes of previously published associations (y-axis) for variants associated with: A. BMI from Locke et al, R-squared: 0.563; B. TFM from Lu et al, R-squared: 0.267; C. waist circumference from Shungin et al, R-squared: 0.701; D. waist circumference adjusted for BMI from Shungin et al, R-squared: 0.489; E. hip circumference from Shungin et al, R-squared: 0.623; F. hip circumference adjusted for BMI from Shungin et al, R-squared: 0.427; G. WHR from Shungin et al, R-squared: 0.397; H. WHR adjusted for BMI from Shungin et al, R-squared: 0.215. The blue line is drawn at y=x. The red line is the observed correlation coefficient of x and y.

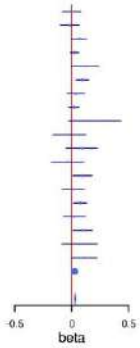


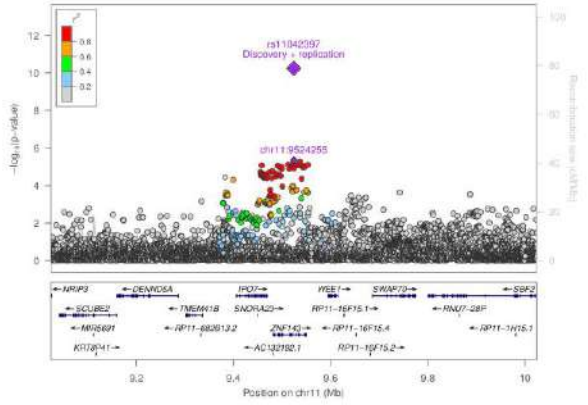
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.004	0.023	8.27e-01	1794	89.59
TwinsUK WGS	0.021	0.299	1.17e-02	1747	71.15
arcOGEN	0.02	-0.006	9.54e-01	2748	102.09
UKHLS	0.021	0.014	7.55e-01	8700	330.98
FINRISK	0.008	0.658	2.95e-03	1249	20.68
ALSPAC GWA	0.022	0.039	6.17e-01	4103	165.71
TwinsUK GWA	0.021	0.215	5.82e-02	3540	77.89
1958 Birth Cohort	0.021	0.214	1.44e-03	5721	221.97
INGI Carlantino	0.036	0.083	6.83e-01	471	25.41
INGI Friuli Venezia Giulia	0.03	0.246	5.55e-02	1197	80.95
HELIC MANOLIS	0.009	0.186	4.77e-01	1058	14.54
HELIC Pomak	0.004	-0.295	4.11e-01	949	7.76
INCIPE 1	0.017	0.082	6.56e-01	937	26.52
INCIPE 2	0.012	0.35	1.79e-02	2057	45.87
LURIC	0.022	-0.029	8.32e-01	1427	54.11
Rotterdam 1	0.021	0.089	1.86e-01	5961	219.15
Rotterdam 2	0.025	0.195	5.45e-02	2151	97.78
Rotterdam 3	0.022	0.054	5.58e-01	3018	119.3
TEENAGE	0.016	0.257	2.21e-01	703	22.72
INGI Val Barbera	0.021	0.063	6.16e-01	1778	63.64
UK BioBank	0.023	0.091	2.05e-12	134797	5994.75
Overall	**0.022**	**0.095**	**3.76e-17**	**186106**	**7631.47**



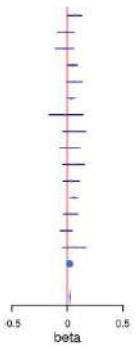


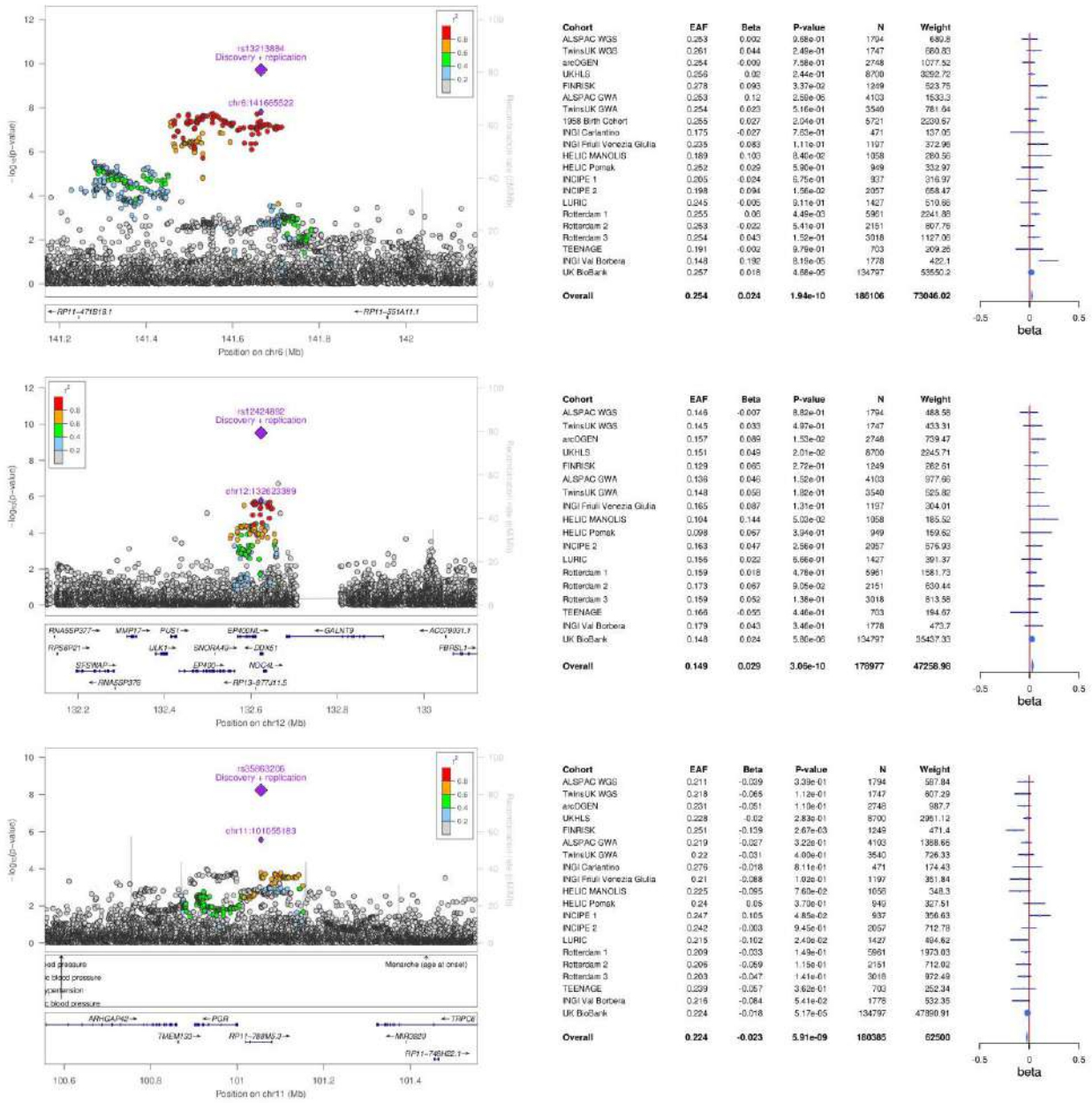
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.198	-0.002	9.51e-01	1794	599.58
TwinsUK WGS	0.211	-0.016	6.97e-01	1747	580.58
arcOGEN	0.194	0.064	5.80e-02	2748	868.62
UKHLS	0.2	0.025	1.91e-01	8700	2787.37
FINRISK	0.138	0.118	5.15e-02	1249	276.17
ALSPAC GWA	0.205	0.093	7.31e-04	4103	1332.66
TwinsUK GWA	0.206	0.035	3.51e-01	3540	695.82
1958 Birth Cohort	0.199	0.02	3.99e-01	5721	1848.02
INGI Carlantino	0.092	0.204	8.29e-02	471	72.8
INGI Friuli Venezia Giulia	0.112	-0.02	7.90e-01	1197	185.26
HELIC MANOLIS	0.13	0.085	2.30e-01	1058	260.8
HELIC Pomak	0.155	0.035	6.19e-01	949	194.02
INCIPE 2	0.167	0.094	2.55e-02	2057	565.44
LURIC	0.177	0.01	8.35e-01	1427	416.03
Rotterdam 1	0.188	0.073	1.50e-02	5961	1118.18
Rotterdam 2	0.198	0.024	6.20e-01	2151	431.94
Rotterdam 3	0.186	0.094	2.55e-02	3018	561.85
TEENAGE	0.127	0.07	3.80e-01	703	155.59
INGI Val Barbera	0.153	0.111	4.92e-02	1778	311.54
UK BioBank	0.201	0.026	4.62e-08	134797	45102.42
Overall	**0.199**	**0.03**	**3.05e-13**	**185169**	**59488.4**





Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.457	0.069	3.66e-02	1808	918.66
TwinsUK WGS	0.455	-0.011	7.76e-01	1266	638.5
FINRISK	0.52	-0.025	5.59e-01	1254	530.94
ALSPAC GWA	0.451	0.047	3.43e-02	4115	2059.74
TwinsUK GWA	0.452	0.065	7.06e-02	2582	765.84
1958 Birth Cohort	0.445	0.035	6.40e-02	5700	2763.97
INGI Carlantino	0.576	-0.01	9.00e-01	400	164.39
INGI Friuli Venezia Giulia	0.548	0.062	2.58e-01	701	335.98
HELIC MANOLIS	0.557	0.024	6.06e-01	1065	474.96
HELIC Pomak	0.514	0.054	2.83e-01	899	389.44
LURIC	0.461	0.037	3.31e-01	1404	699.91
Rotterdam 1	0.445	0.059	1.97e-03	5660	2797.4
Rotterdam 2	0.446	0.052	3.24e-01	1937	953.13
Rotterdam 3	0.452	-0.009	7.34e-01	2931	1378.68
TEENAGE	0.549	0.063	2.56e-01	701	329.16
UK BioBank	0.444	0.02	4.11e-07	134650	66203.42
Overall	**0.446**	**0.023**	**5.74e-11**	**167073**	**81632.65**



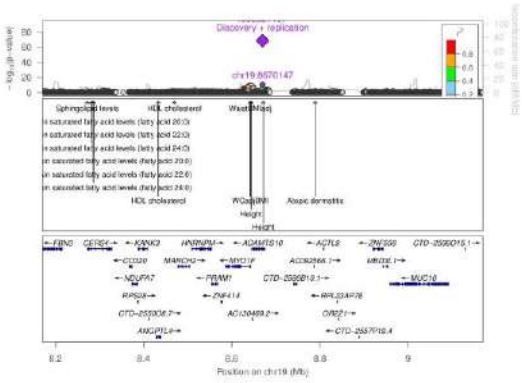


Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.253	0.002	9.68e-01	1794	680.8
TwinsUK WGS	0.261	0.044	2.46e-01	1747	660.83
ascOGEN	0.254	-0.009	7.58e-01	2748	1077.52
UKHLS	0.256	0.02	2.44e-01	8700	3292.72
FINRISK	0.278	0.093	3.37e-02	1249	523.75
ALSPAC GWA	0.253	0.12	2.59e-06	4103	1533.3
TwinsUK GWA	0.254	0.023	5.16e-01	3540	781.64
1958 Birth Cohort	0.255	0.027	2.04e-01	5721	2230.67
INGI Carlantino	0.175	-0.027	7.65e-01	471	137.05
INGI Friuli Venezia Giulia	0.235	0.083	1.11e-01	1197	372.96
HELIC MANOLIS	0.189	0.103	8.40e-02	1058	280.56
HELIC Pomak	0.252	0.029	5.90e-01	949	332.97
INCIPE 1	0.265	-0.024	6.75e-01	937	316.97
INCIPE 2	0.198	0.094	1.56e-02	2057	658.47
LURIC	0.245	0.005	9.11e-01	1427	519.66
Rotterdam 1	0.255	0.06	4.49e-03	5961	2241.89
Rotterdam 2	0.253	-0.022	5.41e-01	2151	807.76
Rotterdam 3	0.254	0.043	1.52e-01	3018	1127.06
TEENAGE	0.191	-0.002	9.79e-01	703	209.26
INGI Val Borbera	0.148	0.192	8.19e-05	1778	422.1
UK BioBank	0.257	0.018	4.66e-05	134797	53550.2
Overall	**0.254**	**0.024**	**1.94e-10**	**186106**	**73046.02**

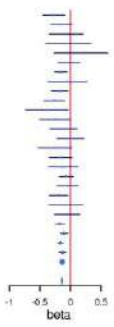
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.146	-0.007	8.82e-01	1794	488.58
TwinsUK WGS	0.145	0.033	4.97e-01	1747	433.31
ascOGEN	0.157	0.089	1.53e-02	2748	759.47
UKHLS	0.151	0.049	2.01e-02	8700	2245.71
FINRISK	0.129	0.065	2.72e-01	1249	282.61
ALSPAC GWA	0.138	0.046	1.52e-01	4103	977.66
TwinsUK GWA	0.148	0.058	1.82e-01	3540	925.82
INGI Friuli Venezia Giulia	0.165	0.087	1.31e-01	1197	304.01
HELIC MANOLIS	0.104	0.144	5.02e-02	1058	185.52
HELIC Pomak	0.098	0.057	3.94e-01	949	159.62
INCIPE 2	0.163	0.047	2.56e-01	2057	575.93
LURIC	0.156	0.022	6.66e-01	1427	391.37
Rotterdam 1	0.159	0.018	4.78e-01	5961	1581.73
Rotterdam 2	0.173	0.067	9.05e-02	2151	630.44
Rotterdam 3	0.159	0.052	1.38e-01	3018	813.58
TEENAGE	0.166	-0.055	4.46e-01	703	194.67
INGI Val Borbera	0.179	0.043	3.46e-01	1778	473.7
UK BioBank	0.148	0.024	5.80e-06	134797	35437.33
Overall	**0.149**	**0.029**	**3.06e-10**	**176977**	**47258.96**

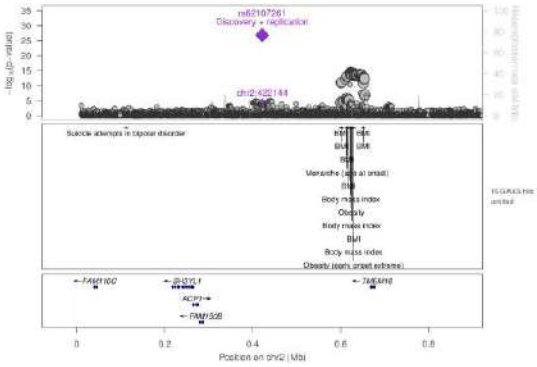
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.211	-0.039	3.39e-01	1794	587.84
TwinsUK WGS	0.218	-0.065	1.12e-01	1747	607.29
ascOGEN	0.231	-0.051	1.10e-01	2748	987.7
UKHLS	0.228	-0.02	2.83e-01	8700	2951.12
FINRISK	0.251	-0.139	2.67e-03	1249	471.4
ALSPAC GWA	0.219	-0.027	3.22e-01	4103	1388.65
TwinsUK GWA	0.22	-0.031	4.00e-01	3540	726.33
INGI Carlantino	0.276	-0.018	8.11e-01	471	174.43
INGI Friuli Venezia Giulia	0.21	-0.088	1.02e-01	1197	351.84
HELIC MANOLIS	0.225	-0.095	7.60e-02	1058	348.3
HELIC Pomak	0.24	0.05	3.70e-01	949	327.51
INCIPE 1	0.247	0.105	4.85e-02	937	356.63
INCIPE 2	0.242	-0.003	9.45e-01	2057	712.78
LURIC	0.215	-0.102	2.40e-02	1427	494.62
Rotterdam 1	0.209	-0.033	1.49e-01	5961	1973.03
Rotterdam 2	0.206	-0.059	1.15e-01	2151	712.02
Rotterdam 3	0.203	-0.047	1.41e-01	3018	972.49
TEENAGE	0.239	-0.057	3.62e-01	703	252.34
INGI Val Borbera	0.216	-0.084	5.41e-02	1778	532.35
UK BioBank	0.224	-0.018	5.17e-05	134797	47890.91
Overall	**0.224**	**-0.023**	**5.91e-09**	**180385**	**62500**

Figure S22: Locus zoom and forest plots for the novel loci reported in Table 1.
Plots display 500kb each side of the top variant, where the smaller diamond represents the discovery *P-value* and the bigger diamond the overall *P-value* (meta-analysis across discovery and follow-up cohorts). LD is calculated from the combined WGS UK10K cohorts (ALSPAC and TwinsUK). Previously reported variants are denoted by large circles.

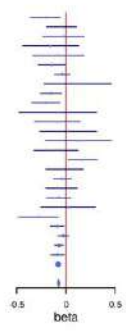


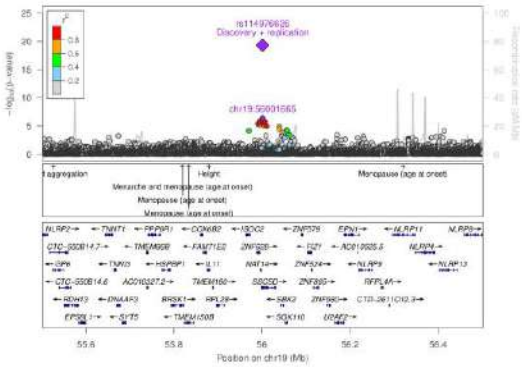
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.934	-0.271	2.93e-03	1794	120.42
TwinsUK WGS	0.936	-0.143	1.06e-01	1747	128.15
LOLIPOP_EWS10	0.937	-0.074	6.98e-01	927	50.77
LOLIPOP_EW_A	0.936	-0.033	8.56e-01	580	28.68
LOLIPOP_EW_P	0.933	0.175	4.36e-01	642	19.97
arcOGEN	0.931	-0.024	7.92e-01	2748	124.46
UKHLS	0.931	-0.156	2.05e-03	8700	389.28
FINRISK	0.915	-0.052	7.47e-01	1249	37.39
ALSPAC GWA	0.935	-0.177	1.01e-02	4103	211.93
TwinsUK GWA	0.936	0.263	2.86e-03	3540	129.11
INGI Carlantino	0.954	-0.386	3.14e-02	471	31.42
INGI Friuli Venezia Giulia	0.946	-0.252	5.11e-02	1197	69.37
HELIC MANOLIS	0.952	-0.112	3.25e-01	1058	75.33
HELIC Pomak	0.957	-0.091	9.97e-01	949	76.96
INCIPE 1	0.942	-0.258	6.57e-02	937	51.14
INCIPE 2	0.945	-0.163	8.75e-02	2057	119.25
LURIC	0.937	-0.119	3.54e-01	1427	65.5
Rotterdam 1	0.934	-0.067	2.47e-01	5961	298.45
Rotterdam 2	0.941	-0.051	5.70e-01	2151	105.82
Rotterdam 3	0.935	-0.199	1.31e-02	3018	162.27
TEENAGE	0.956	-0.079	5.74e-01	703	50.73
INGI Val Borbera	0.942	-0.051	6.29e-01	1778	99.77
Fenland	0.939	-0.171	8.00e-06	8942	680.63
GoT2D	0.939	-0.106	6.99e-04	25790	1633.9
Copenhagen	0.932	-0.164	2.21e-12	28486	1825.62
SardiNIA	0.11	-0.129	3.90e-05	6477	1275.51
UK BioBank	0.936	-0.138	7.26e-38	134797	8710.44
Overall	**0.942**	**-0.129**	**3.22e-69**	**252290**	**16923.07**



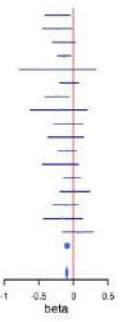


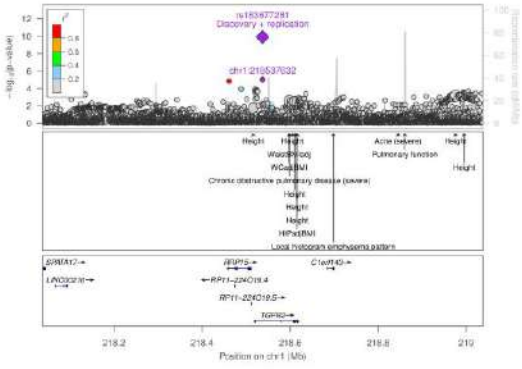
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.05	0.21	6.54e-03	1791	168.3
TwinsUK WGS	0.049	-0.044	5.71e-01	1747	165.59
LOLIPOP_EWS10	0.058	-0.024	8.22e-01	915	86.31
LOLIPOP_EW_A	0.06	-0.157	2.80e-01	580	47.63
LOLIPOP_EW_P	0.051	0.077	5.66e-01	640	56.62
arcOGEN	0.046	-0.146	3.65e-02	2733	265.55
UKHLS	0.049	-0.037	3.46e-01	8553	824.64
FINRISK	0.014	0.12	4.50e-01	1248	32.89
ALSPAC GWA	0.048	-0.152	6.39e-03	4101	394.45
TwinsUK GWA	0.055	-0.206	2.50e-03	3539	196.53
INGI Carlantino	0.042	-0.083	6.80e-01	472	24.74
INGI Friuli Venezia Giulia	0.044	-0.067	4.61e-01	1170	72.61
HELIC MANOLIS	0.035	0.024	8.73e-01	1033	46.41
HELIC Pomak	0.032	0.128	4.56e-01	948	33.84
INCIPE 1	0.054	-0.163	3.70e-01	934	76.16
INCIPE 2	0.053	0.168	2.71e-02	2052	173.23
LURIC	0.05	-0.016	8.70e-01	1427	107.83
Rotterdam 1	0.048	-0.008	4.05e-01	5954	467.08
Rotterdam 2	0.062	-0.004	5.92e-01	2148	159.51
Rotterdam 3	0.051	0.074	2.28e-01	3017	262.74
TEENAGE	0.053	0.021	8.82e-01	701	49.92
INGI Val Borbera	0.041	-0.279	7.00e-03	1774	93.72
Fenland	0.05	-0.09	9.34e-03	8799	537.92
GoT2D	0.039	-0.027	3.41e-01	25996	1267.48
Copenhagen	0.039	-0.07	1.09e-03	28642	2149.47
SardiNIA	0.074	-0.085	1.00e-02	6481	965.65
UK BioBank	0.045	-0.061	3.56e-19	134509	12234.64
Overall	**0.047**	**-0.075**	**1.27e-27**	**255873**	**21003.99**



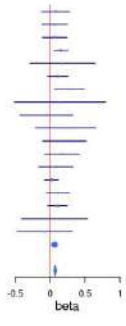


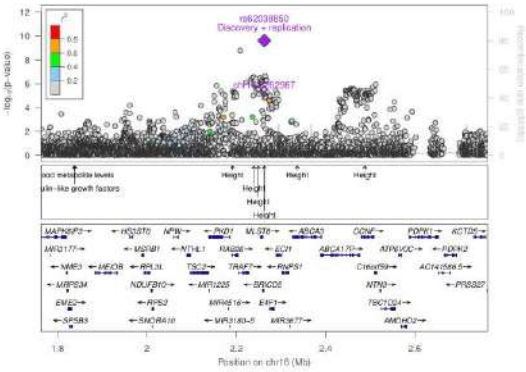
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.03	-0.232	1.26e-02	1794	115.7
TwinsUK WGS	0.035	-0.232	3.14e-02	1747	86.26
arcOGEN	0.027	-0.141	9.90e-02	2748	137.1
UKHLS	0.025	-0.155	5.63e-03	8700	419.81
FINRISK	0.005	-0.227	4.23e-01	1249	12.4
ALSPAC GWA	0.027	-0.064	3.52e-01	4103	216.36
TwinsUK GWA	0.031	0.238	9.12e-03	3540	126.11
INGI Friuli Venezia Giulia	0.011	-0.218	3.05e-01	1197	22.63
HELIC MANOLIS	0.047	-0.072	5.00e-01	1058	87.27
HELIC Pomak	0.033	-0.111	4.18e-01	949	57.87
INCIPE 2	0.048	-0.088	2.10e-01	2057	202.1
LURIC	0.025	-0.189	1.56e-01	1427	56.55
Rotterdam 1	0.032	-0.017	7.87e-01	5961	240.05
Rotterdam 2	0.032	0.019	8.61e-01	2151	83.49
Rotterdam 3	0.021	-0.116	2.10e-01	3018	117.16
TEENAGE	0.039	-0.162	2.88e-01	703	49.16
INGI Val Borbera	0.027	0.065	5.69e-01	1778	76.17
UK BioBank	0.026	-0.092	1.74e-14	134797	7019.26
Overall	**0.027**	**-0.096**	**5.90e-20**	**179977**	**9070.29**



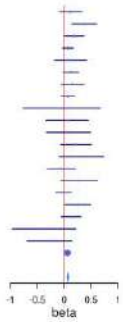


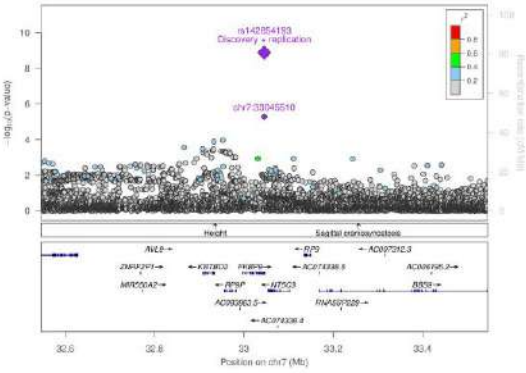
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.935	0.075	4.70e-01	1794	91.61
TwinsUK WGS	0.933	0.061	5.18e-01	1747	113.44
arcOGEN	0.926	0.064	4.74e-01	2748	124.19
UKHLS	0.927	0.151	3.19e-03	8700	382.05
FINRISK	0.907	0.173	4.68e-01	1249	17.62
ALSPAC GWA	0.927	0.11	1.34e-01	4103	187.21
TwinsUK GWA	0.933	0.274	1.15e-02	3540	84.65
INGI Carlantino	0.913	0.139	6.85e-01	471	9.01
INGI Friuli Venezia Giulia	0.916	-0.052	7.84e-01	1197	26.59
HELIC MANOLIS	0.916	0.222	3.09e-01	1058	20.94
INCIPE 1	0.939	0.203	2.02e-01	937	39.68
INCIPE 2	0.923	0.167	1.84e-01	2057	63.63
LURIC	0.935	0.083	5.12e-01	1427	63.65
Rotterdam 1	0.939	0.018	7.20e-01	5961	379.44
Rotterdam 2	0.935	0.113	1.99e-01	2151	131.91
Rotterdam 3	0.941	0.104	1.38e-01	3018	208.11
TEENAGE	0.92	0.059	8.06e-01	703	17.19
INGI Val Borbera	0.914	-0.079	5.94e-01	1778	24.81
UK BioBank	0.926	0.062	9.81e-07	134797	6269.62
Overall	**0.927**	**0.071**	**1.24e-10**	**179436**	**8264.45**



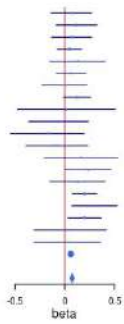


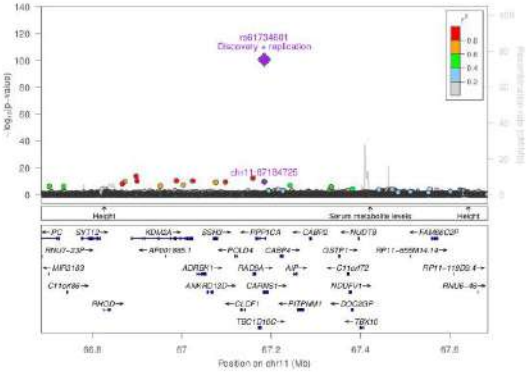
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.025	0.119	2.56e-01	1794	90.46
TwinsUK WGS	0.021	0.372	1.64e-03	1747	71.76
arcOGEN	0.022	0.185	5.32e-02	2748	109.96
UKHLS	0.025	0.071	1.65e-01	8709	385.76
FINRISK	0.016	0.12	4.35e-01	1249	42.71
ALSPAC GWA	0.026	0.124	8.23e-02	4163	183.2
TwinsUK GWA	0.022	0.16	1.45e-01	3540	82.79
1958 Birth Cohort	0.027	0.099	2.63e-01	5721	294.25
INGI Carlantino	0.015	-0.044	9.07e-01	471	7.42
INGI Friuli Venezia Giulia	0.017	0.059	7.66e-01	1197	24.81
HELIC MANOLIS	0.013	0.064	6.87e-01	1058	22.8
HELIC Pomak	0.027	0.222	1.20e-01	949	46.06
INCIPE 1	0.014	0.322	1.30e-01	937	22.37
INCIPE 2	0.016	-0.052	6.95e-01	2057	55.86
LURIC	0.022	0.261	1.01e-01	1427	34.19
Rotterdam 1	0.018	-0.011	8.82e-01	5961	173.37
Rotterdam 2	0.018	0.254	3.77e-02	2151	97.12
Rotterdam 3	0.026	0.131	1.56e-01	3018	116.42
TEENAGE	0.012	-0.372	2.20e-01	703	10.92
INGI Val Borbera	0.009	0.271	2.06e-01	1778	21.91
UK BioBank	0.025	0.061	1.84e-06	122318	6207.24
Overall	**0.024**	**0.071**	**2.44e-10**	**173627**	**7971.94**



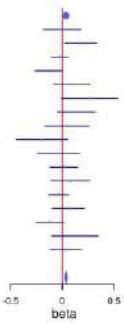


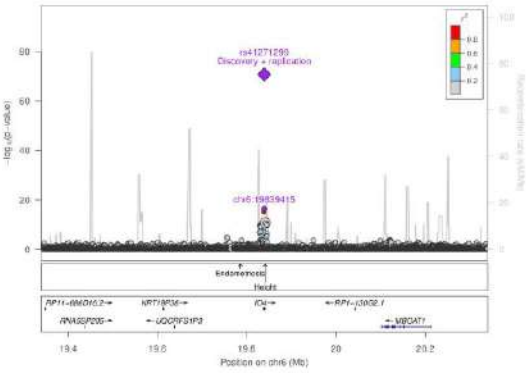
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.027	0.066	5.30e-01	1794	91.63
TwinsUK WGS	0.027	0.116	2.69e-01	1747	91.17
arcOGEN	0.02	0.067	5.15e-01	2748	93.95
UKHLS	0.023	0.046	4.53e-01	8709	263.49
FINRISK	0.019	0.127	3.68e-01	1249	50.48
ALSPAC GWA	0.025	0.061	4.22e-01	4163	174.56
TwinsUK GWA	0.018	-0.001	9.85e-01	3540	70.15
1958 Birth Cohort	0.021	0.12	8.56e-02	5721	293.56
INGI Carlantino	0.03	0.314	8.52e-01	471	15.74
INGI Friuli Venezia Giulia	0.028	-0.065	6.73e-01	1197	42.32
HELIC MANOLIS	0.024	-0.176	3.53e-01	1058	37.95
HELIC Pomak	0.037	0.08	6.23e-01	949	39.26
INCIPE 1	0.025	0.151	3.56e-01	937	37.84
INCIPE 2	0.029	0.234	4.80e-02	2057	71.85
LURIC	0.027	0.128	3.54e-01	1427	50.59
Rotterdam 1	0.026	0.197	1.59e-03	5961	257.82
Rotterdam 2	0.023	0.297	1.00e-02	2151	74.57
Rotterdam 3	0.026	0.196	2.06e-02	3018	130.02
TEENAGE	0.037	0.056	7.62e-01	703	29
INGI Val Borbera	0.018	0.024	8.90e-01	1778	34.53
UK BioBank	0.022	0.06	1.26e-05	134787	5262.74
Overall	**0.022**	**0.072**	**1.31e-09**	**166106**	**7061.65**



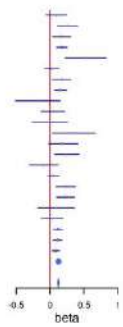


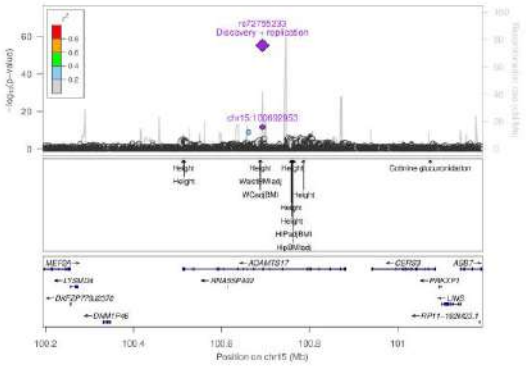
Cohort	EAF	Beta	P-value	N	Weight
Overall	0.066	0.037	6.07e-08	179850	21626.3
TwinsUK WGS	0.039	-0.001	9.89e-01	1747	115.17
arcOGEN	0.033	0.179	2.26e-02	2733	162.06
UKHLS	0.035	-0.024	5.85e-01	8553	538
ALSPAC GWA	0.031	-0.132	4.71e-02	4101	225.31
TwinsUK GWA	0.032	0.091	3.07e-01	3529	185.14
INGI Carlantino	0.069	0.266	5.51e-02	472	52.06
INGI Friuli Venezia Giulia	0.060	0.158	1.42e-01	1170	113.79
HELIC MANOLIS	0.058	0.047	6.66e-01	1039	84.84
HELIC Pomak	0.039	-0.195	1.28e-01	948	52.22
INCIPE 1	0.059	-0.034	7.42e-01	924	94.04
INCIPE 2	0.059	0.016	8.13e-01	2060	221.57
LURIC	0.042	0.079	4.13e-01	1427	106.24
Rotterdam 1	0.039	-0.035	4.74e-01	5954	411.06
Rotterdam 2	0.04	0.059	4.55e-01	2148	196.42
Rotterdam 3	0.037	-0.117	9.08e-02	3017	297.57
TEENAGE	0.061	0.123	2.86e-01	701	75.93
INGI Val Borbera	0.058	0.035	6.50e-01	1774	170.92
Overall	**0.066**	**0.037**	**6.07e-08**	**179850**	**21626.3**



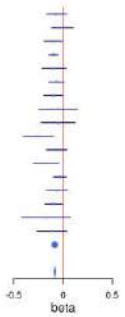


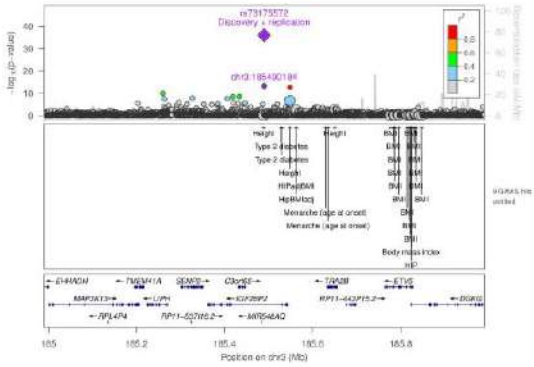
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.047	0.092	2.27e-01	1794	174.21
TwinsUK WGS	0.053	0.259	5.40e-04	1747	178.86
arcOGEN	0.05	0.169	1.20e-02	2748	220.08
UKHLS	0.051	0.174	1.03e-05	8709	668.05
FINRISK	0.017	0.53	6.54e-04	1249	41.85
ALSPAC GWA	0.054	0.021	6.97e-01	4163	349.6
TwinsUK GWA	0.053	0.167	1.59e-02	3540	207.49
1958 Birth Cohort	0.057	0.154	4.24e-04	5721	526.41
INGI Carlantino	0.064	-0.179	2.95e-01	471	36.21
INGI Friuli Venezia Giulia	0.077	0.043	6.30e-01	1197	134.43
HELIC MANOLIS	0.041	-0.004	9.76e-01	1058	55.91
HELIC Pomak	0.034	0.352	3.08e-02	949	37.69
INCIPE 1	0.058	0.194	7.51e-02	937	84.7
INCIPE 2	0.049	0.249	7.01e-03	2057	117.35
LURIC	0.043	-0.092	3.50e-01	1427	66.06
Rotterdam 1	0.057	0.049	2.57e-01	5961	546.26
Rotterdam 2	0.053	0.233	2.05e-03	2151	175.17
Rotterdam 3	0.048	0.226	6.72e-04	3018	227.15
TEENAGE	0.061	0.091	5.00e-01	703	54.63
INGI Val Borbera	0.064	0.029	7.16e-01	1778	156.6
Fenland	0.055	0.118	2.87e-04	9359	944.08
GeT2D	0.026	0.112	4.67e-04	25759	982.69
SardiNIA	0.12	0.063	2.00e-03	8477	1371.74
UK BioBank	0.051	0.126	5.25e-49	134627	13750
Overall	**0.055**	**0.123**	**1.90e-71**	**227153**	**21003.99**



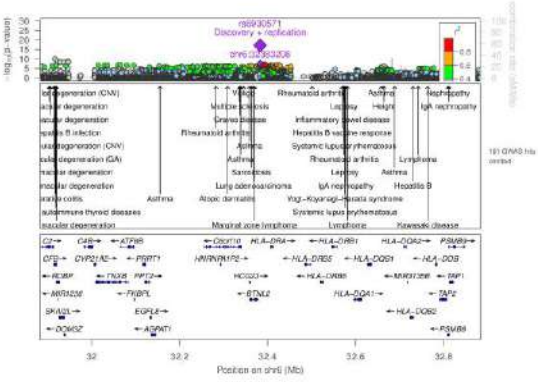


Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.115	-0.095	2.09e-01	1794	373.01
TwinsUK WGS	0.107	-0.007	9.05e-01	1747	328.77
arcOGEN	0.116	-0.101	2.92e-02	2748	456.99
UKHLS	0.117	-0.097	3.70e-05	8709	1800.19
FINRISK	0.112	-0.092	1.42e-01	1249	258.1
ALSPAC GWA	0.116	-0.064	9.99e-02	4103	855.91
TwinsUK GWA	0.121	-0.1	4.08e-02	3540	419.14
INGI Friuli Venezia Giulia	0.085	-0.051	6.03e-01	1197	101.66
HELIC MANOLIS	0.072	-0.047	5.86e-01	1058	129.42
HELIC Pomak	0.095	-0.25	1.34e-03	949	165.24
INCIPE 2	0.088	-0.064	2.28e-01	2657	364.03
LURIC	0.117	-0.171	9.84e-03	1427	228.38
Rotterdam 1	0.11	-0.033	2.99e-01	5961	973.27
Rotterdam 2	0.115	-0.092	2.57e-01	2151	306.08
Rotterdam 3	0.116	-0.094	3.40e-02	3018	512.23
TEENAGE	0.089	-0.172	1.68e-01	763	64.41
INGI Val Borbera	0.095	-0.111	1.51e-01	1778	168.03
UK BioBank	0.112	-0.084	3.40e-45	134655	28105.66
Overall	**0.112**	**-0.084**	**5.42e-50**	**178815**	**35599.86**

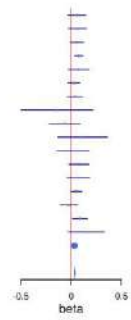


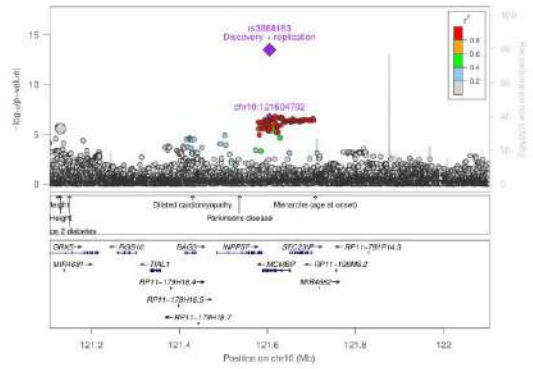


Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.114	-0.009	8.56e-01	1794	376.66
TwinsUK WGS	0.113	0.096	7.21e-02	1747	354.96
arcOGEN	0.111	0.07	1.03e-01	2748	547.61
UKHLS	0.112	0.12	8.71e-07	8709	1670.52
FINRISK	0.11	0.055	3.63e-01	1249	254.47
ALSPAC GWA	0.114	-0.003	9.39e-01	4103	785.86
TwinsUK GWA	0.109	0.178	3.00e-04	3540	415.29
INGI Carlantino	0.174	0.186	3.90e-02	471	122.33
INGI Friuli Venezia Giulia	0.133	0.071	2.70e-01	1197	230.19
HELIC MANOLIS	0.173	0.033	5.96e-01	1058	261.76
HELIC Pomak	0.158	0.031	6.45e-01	949	238.84
INCIPE 1	0.137	0.164	1.63e-02	937	215.02
INCIPE 2	0.146	0.043	3.29e-01	2657	510.62
LURIC	0.133	0.055	3.38e-01	1427	304.36
Rotterdam 1	0.125	0.128	4.78e-06	5961	1274.14
Rotterdam 2	0.126	0.033	5.63e-01	2151	426.51
Rotterdam 3	0.126	0.05	2.07e-01	3018	648.35
TEENAGE	0.144	0.104	1.67e-01	763	176.81
INGI Val Borbera	0.145	0.022	6.68e-01	1778	403.44
UK BioBank	0.112	0.063	8.26e-25	134797	27080.47
Overall	**0.115**	**0.067**	**8.27e-37**	**180365**	**35599.86**

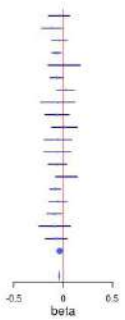


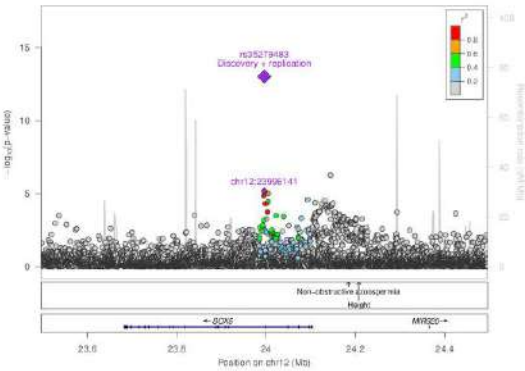
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.155	0.06	1.79e-01	1794	507.15
TwinsUK WGS	0.15	0.065	1.58e-01	1747	467.9
arcOGEN	0.196	0.068	9.26e-02	2748	845.94
UKHLS	0.16	0.078	3.28e-04	8709	2117.58
FINRISK	0.174	0.075	1.46e-01	1249	375
ALSPAC GWA	0.178	0.03	2.95e-01	4103	1189.8
TwinsUK GWA	0.198	0.039	3.12e-01	3540	670.96
INGI Carlantino	0.043	-0.142	4.36e-01	471	30.1
INGI Friuli Venezia Giulia	0.116	0.061	4.02e-01	1197	195.44
HELIC MANOLIS	0.035	0.114	3.64e-01	1058	83.55
HELIC Pomak	0.122	0.02	8.12e-01	949	150.07
INCIPE 2	0.111	0.077	1.18e-01	2657	497.96
LURIC	0.132	0.073	2.69e-01	1427	294.91
Rotterdam 1	0.184	0.095	4.69e-02	5961	1378.17
Rotterdam 2	0.191	-0.021	6.27e-01	2151	517.3
Rotterdam 3	0.179	0.09	1.77e-02	3018	780.76
TEENAGE	0.094	0.152	9.37e-02	763	121.84
UK BioBank	0.182	0.034	6.63e-12	134462	41846.7
Overall	**0.170**	**0.038**	**6.01e-18**	**177335**	**51652.89**



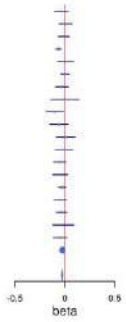


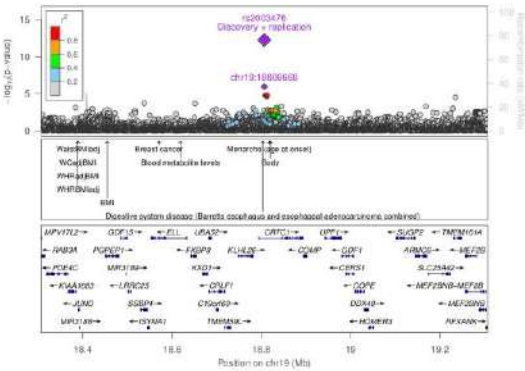
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.104	-0.041	4.49e-01	1794	330.19
TwinsUK WGS	0.119	-0.113	3.19e-02	1747	362.06
arcOGEN	0.127	-0.034	3.92e-01	2748	622.76
UKHLS	0.122	-0.095	4.54e-03	8709	1943.26
FINRISK	0.059	0.011	8.97e-01	1249	143.38
ALSPAC GWA	0.117	-0.066	5.91e-02	4103	882.18
TwinsUK GWA	0.128	0.027	5.61e-01	3540	473.04
INGI Carlantino	0.18	-0.052	5.72e-01	471	125.13
INGI Friuli Venezia Giulia	0.139	-0.061	3.24e-01	1197	263.83
HELIC MANOLIS	0.138	0.014	8.39e-01	1058	229.44
HELIC Pomak	0.119	-0.052	4.66e-01	949	191.25
INCIPE 1	0.117	-0.059	4.33e-01	937	197.22
INCIPE 2	0.119	-0.095	2.43e-01	2657	431.4
LURIC	0.126	0.034	5.40e-01	1427	319.96
Rotterdam 1	0.118	-0.079	5.32e-03	5961	1240.86
Rotterdam 2	0.116	-0.05	2.91e-01	2151	445.03
Rotterdam 3	0.12	-0.085	2.49e-02	3018	645.1
TEENAGE	0.123	-0.086	2.93e-01	763	150.96
INGI Val Borbera	0.102	-0.066	2.42e-01	1778	308.52
UK BioBank	0.118	-0.034	8.88e-09	134797	29004.26
Overall	**0.118**	**-0.039**	**3.25e-14**	**180365**	**30440.75**



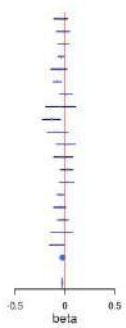


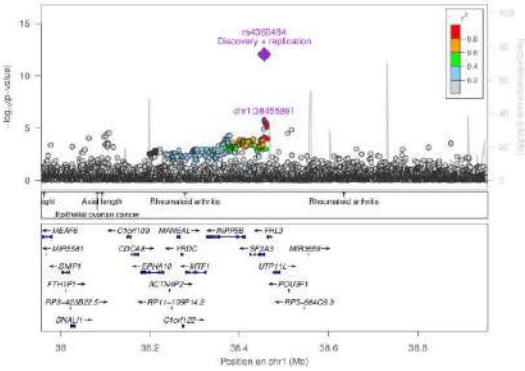
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.402	-0.031	3.61e-01	1794	868.98
TwinsUK WGS	0.403	0.009	7.80e-01	1747	897.85
arcOGEN	0.39	-0.007	7.95e-01	2748	1314.75
UKHLS	0.405	-0.061	1.05e-04	8700	4011.86
FINRISK	0.395	0.01	8.02e-01	1249	574.8
ALSPAC GWA	0.395	0.003	9.09e-01	4103	1888.55
TwinsUK GWA	0.396	-0.027	4.00e-01	3540	953.56
INGI Carlantino	0.451	0.001	9.85e-01	471	194.8
INGI Friuli Venezia Giulia	0.421	-0.101	2.30e-02	1197	512.56
HELIC MANOLIS	0.477	-0.059	2.03e-01	1058	472.25
HELIC Pomak	0.469	0.007	8.82e-01	949	447.24
INCIPE 1	0.395	0.009	9.00e-01	937	486.9
INCIPE 2	0.405	-0.049	1.25e-01	2057	964.11
LURIC	0.407	-0.047	2.20e-01	1427	690.7
Rotterdam 1	0.393	-0.023	2.13e-01	5961	2812.95
Rotterdam 2	0.391	0.044	1.67e-01	2151	1003.13
Rotterdam 3	0.385	-0.033	2.15e-01	3018	1387.94
TEENAGE	0.429	-0.015	7.79e-01	703	339.58
INGI Val Borbera	0.412	0.048	1.72e-01	1778	822.81
UK BioBank	0.402	-0.023	1.83e-08	134797	67445.93
Overall	**0.402**	**-0.025**	**1.00e-13**	**180385**	**86505.19**



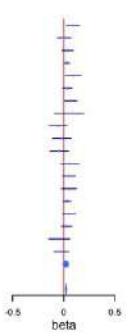


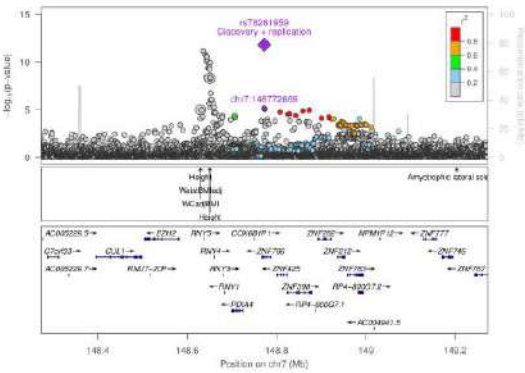
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.393	-0.04	2.35e-01	1791	880.42
TwinsUK WGS	0.399	-0.018	6.09e-01	1747	844.66
arcOGEN	0.399	-0.01	7.38e-01	2733	1235.95
UKHLS	0.399	-0.034	2.75e-02	8553	4089.72
FINRISK	0.5	-0.058	1.43e-01	1249	629.13
ALSPAC GWA	0.409	-0.074	9.83e-04	4101	1983.76
TwinsUK GWA	0.406	0.012	7.09e-01	3539	912.06
INGI Carlantino	0.393	-0.043	5.79e-01	472	169.22
INGI Friuli Venezia Giulia	0.375	-0.133	3.21e-03	1170	497.89
HELIC MANOLIS	0.393	-0.071	1.73e-01	1033	371.59
HELIC Pomak	0.406	0.009	8.50e-01	946	425.03
INCIPE 1	0.395	-0.013	7.91e-01	934	418.54
INCIPE 2	0.35	0.019	5.68e-01	2050	905.01
LURIC	0.398	0.02	5.98e-01	1427	693.1
Rotterdam 1	0.419	-0.04	3.55e-02	5954	2833.85
Rotterdam 2	0.436	-0.049	1.12e-01	2148	1067.55
Rotterdam 3	0.414	-0.017	5.22e-01	3017	1382.47
TEENAGE	0.344	-0.028	6.15e-01	701	320.6
INGI Val Borbera	0.355	-0.077	4.45e-02	1774	685.96
UK BioBank	0.406	-0.022	3.32e-08	134509	64144.57
Overall	**0.404**	**-0.025**	**5.89e-13**	**179650**	**86505.19**



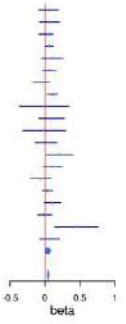


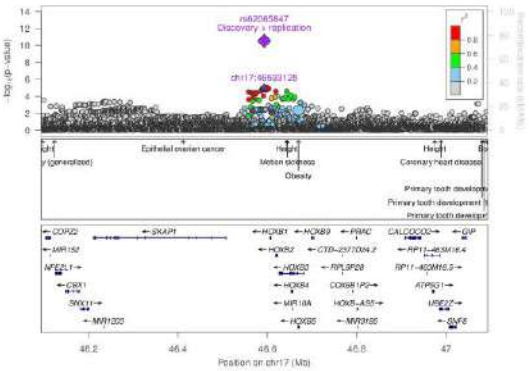
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.448	0.091	5.31e-03	1754	946.84
TwinsUK WGS	0.401	0.005	8.66e-01	1747	866.3
arcOGEN	0.448	0.041	1.43e-01	2748	1310.75
UKHLS	0.452	0.031	4.76e-02	8709	4156.36
FINRISK	0.398	0.094	1.85e-02	1249	632.74
ALSPAC GWA	0.443	0.036	1.13e-01	4103	1936.54
TwinsUK GWA	0.449	0.071	2.53e-02	3540	1004.56
INGI Carlantino	0.526	0.055	4.57e-01	471	192.59
INGI Friuli Venezia Giulia	0.465	-0.056	2.16e-01	1197	487.1
HELIC MANOLIS	0.513	-0.021	6.56e-01	1058	466.72
HELIC Pomak	0.467	-0.042	3.58e-01	949	456.86
INCIPE 1	0.492	0.058	2.06e-01	937	467.33
INCIPE 2	0.451	0.052	9.07e-02	2057	1012.76
LURIC	0.457	0.053	1.62e-01	1427	698.91
Rotterdam 1	0.441	0.032	9.85e-02	5961	2780.32
Rotterdam 2	0.429	0.053	9.25e-02	2151	998.88
Rotterdam 3	0.442	0.026	2.85e-01	3018	1407.36
TEENAGE	0.5	-0.043	4.14e-01	703	353.17
INGI Val Borbera	0.485	-0.092	5.56e-01	1778	739.68
UK BioBank	0.445	0.021	3.24e-08	134797	69002.77
Overall	**0.447**	**0.024**	**8.98e-13**	**180385**	**91827.36**



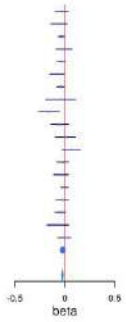


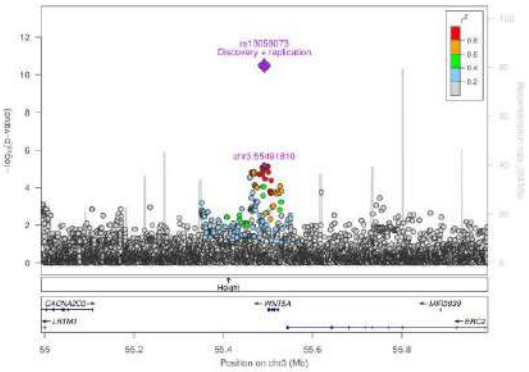
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.065	0.053	4.56e-01	1794	194.93
TwinsUK WGS	0.068	0.066	3.47e-01	1747	201.12
arcOGEN	0.069	0.017	7.40e-01	2748	364.27
UKHLS	0.063	0.065	3.01e-02	8709	1000.3
FINRISK	0.064	0.103	1.52e-01	1249	160.81
ALSPAC GWA	0.065	0.063	1.74e-01	4103	471.93
TwinsUK GWA	0.068	-0.051	4.16e-01	3540	266.25
1958 Birth Cohort	0.065	0.111	3.56e-03	5721	679.51
INGI Carlantino	0.036	-0.007	9.73e-01	471	30.61
INGI Friuli Venezia Giulia	0.057	0.068	2.88e-01	1197	117.15
HELIC MANOLIS	0.023	-0.009	9.54e-01	1058	49.83
HELIC Pomak	0.101	0.02	8.17e-01	949	157.82
INCIPE 1	0.058	0.214	2.76e-02	937	165.49
INCIPE 2	0.057	0.115	9.34e-02	2057	214.51
LURIC	0.067	-0.056	4.54e-01	1427	179.43
Rotterdam 1	0.068	0.036	3.27e-01	5961	732
Rotterdam 2	0.072	0.109	6.96e-02	2151	276.08
Rotterdam 3	0.068	-0.004	9.37e-01	3018	361.26
TEENAGE	0.031	0.452	4.16e-03	703	49.49
INGI Val Borbera	0.068	0.089	3.34e-01	1778	197.88
UK BioBank	0.062	0.044	2.77e-08	134797	16021.94
Overall	**0.062**	**0.046**	**1.56e-12**	**186106**	**21026.3**



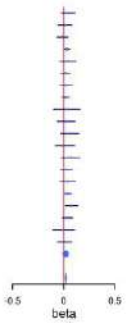


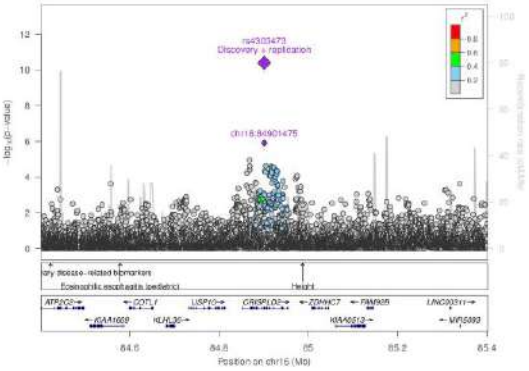
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.476	-0.028	3.85e-01	1807	931.15
TwinsUK WGS	0.482	-0.057	1.55e-01	1205	622.86
UKHLS	0.492	-0.031	4.28e-02	8727	4333.38
FINRISK	0.491	-0.008	8.49e-01	1254	697.14
ALSPAC GWA	0.473	-0.035	1.13e-01	4121	2165.75
TwinsUK GWA	0.494	-0.075	3.77e-02	2585	753.41
1958 Birth Cohort	0.482	-0.04	3.09e-02	5713	2845.96
INGI Carlantino	0.502	-0.042	5.85e-01	397	170.9
INGI Friuli Venezia Giulia	0.54	-0.157	2.92e-03	791	380.2
HELIC MANOLIS	0.476	-0.048	2.92e-01	1075	487.95
HELIC Pomak	0.542	0.009	9.20e-01	903	402.58
INCIPE 1	0.496	0.066	1.57e-01	934	455.13
INCIPE 2	0.483	-0.02	5.68e-01	2050	1042.67
LURIC	0.457	-0.037	3.30e-01	1403	707.86
Rotterdam 1	0.505	-0.002	9.91e-01	5665	2812.85
Rotterdam 2	0.511	-0.024	4.61e-01	1935	922.93
Rotterdam 3	0.504	-0.043	1.00e-01	2930	1485.5
TEENAGE	0.451	-0.068	2.27e-01	698	333.79
INGI Val Borbera	0.438	0.005	8.77e-01	1740	929.46
UK BioBank	0.485	-0.02	3.23e-07	134798	67319.79
Overall	**0.486**	**-0.022**	**2.86e-11**	**180795**	**91827.38**



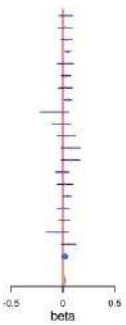


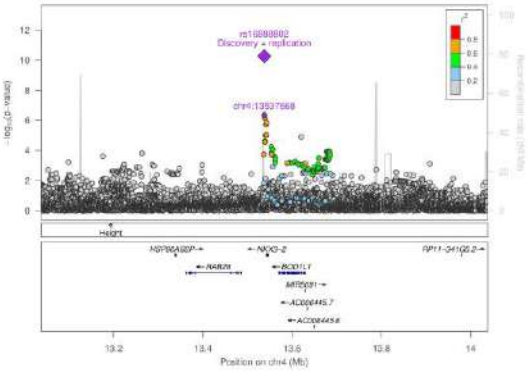
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.457	0.045	1.76e-01	1794	917.72
TwinsUK WGS	0.443	0.013	6.97e-01	1747	884.66
arcOGEN	0.455	-0.013	6.23e-01	2748	1326.78
UKHLS	0.451	0.031	4.66e-02	8709	4240.76
FINRISK	0.408	0.042	2.06e-01	1249	625.24
ALSPAC GWA	0.456	0.017	4.26e-01	4103	1979
TwinsUK GWA	0.448	0.033	4.46e-01	3548	1044.77
1958 Birth Cohort	0.451	0.02	2.57e-01	5721	2863.96
INGI Carlantino	0.419	0.031	6.41e-01	471	223.23
INGI Friuli Venezia Giulia	0.488	0.022	6.17e-01	1197	521.96
HELIC MANOLIS	0.471	0.057	2.10e-01	1058	484.92
HELIC Pomak	0.425	0.012	8.17e-01	949	426.76
INCIPE 1	0.44	0.066	1.51e-01	937	470.05
INCIPE 2	0.455	0.026	3.98e-01	2057	1078.23
LURIC	0.441	0.036	3.21e-01	1427	667.23
Rotterdam 1	0.454	0.036	3.97e-02	5961	2909.98
Rotterdam 2	0.438	0.078	1.08e-02	2151	1063.86
Rotterdam 3	0.46	0.04	1.26e-01	3018	1473.39
TEENAGE	0.466	-0.003	9.61e-01	703	334.62
INGI Val Borbera	0.494	0.009	7.86e-01	1778	879.4
UK BioBank	0.456	0.019	4.62e-07	134767	69366.92
Overall	**0.455**	**0.022**	**3.23e-11**	**186106**	**91827.36**



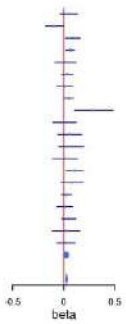


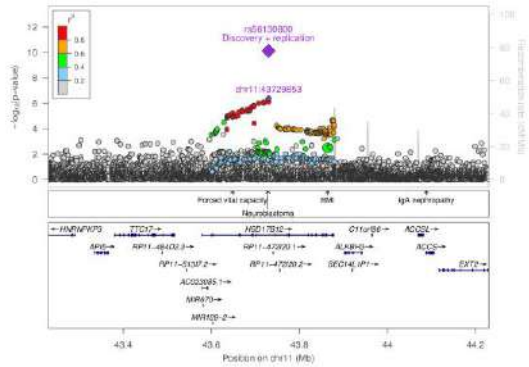
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.377	0.03	3.71e-01	1794	872.91
TwinsUK WGS	0.382	0.024	4.81e-01	1747	843.39
arcOGEN	0.387	0.034	2.39e-01	2748	1225.58
UKHLS	0.374	0.048	3.77e-03	8700	3981.04
FINRISK	0.362	0.025	5.42e-01	1249	610.22
ALSPAC GWA	0.381	0.03	2.02e-01	4103	1858.55
TwinsUK GWA	0.374	0.025	4.37e-01	3540	934.69
1958 Birth Cohort	0.378	0.049	1.99e-02	5721	2674.65
INGI Carlantino	0.437	0.081	2.49e-01	471	203.75
INGI Friuli Venezia Giulia	0.418	0.014	7.54e-01	1197	498.75
HELIC MANOLIS	0.459	0.033	4.65e-01	1058	479.21
HELIC Pomak	0.368	0.075	1.26e-01	949	414.25
INCIPE 1	0.436	0.073	1.12e-01	937	473.35
INCIPE 2	0.41	-0.006	8.50e-01	2057	979.99
LURIC	0.378	0.022	5.68e-01	1427	660.44
Rotterdam 1	0.383	0.043	2.97e-02	5961	2766.86
Rotterdam 2	0.386	0.009	9.18e-01	2151	1012.37
Rotterdam 3	0.389	0.016	5.56e-01	3018	1362.84
TEENAGE	0.444	-0.051	3.50e-01	703	338.13
INGI Val Borbera	0.45	0.055	1.15e-01	1778	778.97
UK BioBank	0.378	0.019	1.60e-06	134797	66252.38
Overall	**0.38**	**0.022**	**4.08e-11**	**186106**	**86505.19**



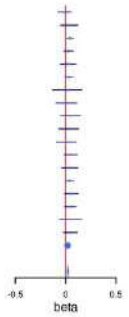


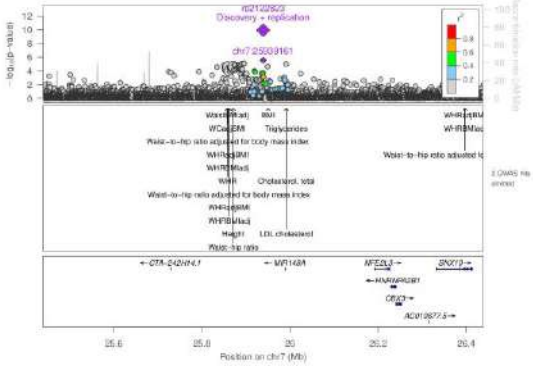
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.172	0.05	2.57e-01	1794	513.35
TwinsUK WGS	0.182	-0.093	3.56e-02	1747	514.14
arcOGEN	0.17	0.061	1.43e-02	2748	720.38
UKHLS	0.177	0.063	2.01e-03	8709	2368.66
FINRISK	0.167	0.019	7.24e-01	1249	362.91
ALSPAC GWA	0.176	0.034	2.56e-01	4103	1116.91
TwinsUK GWA	0.174	0.01	8.10e-01	3548	976.92
1958 Birth Cohort	0.174	0.049	5.21e-02	5721	1567.15
INGI Carlantino	0.184	0.294	2.11e-03	471	109.59
INGI Friuli Venezia Giulia	0.18	0.008	8.94e-01	1197	281.62
HELIC MANOLIS	0.196	0.06	3.07e-01	1058	287.93
HELIC Pomak	0.202	0.074	2.40e-01	949	255.8
INCIPE 1	0.186	0.012	8.51e-01	937	248.81
INCIPE 2	0.18	0.106	1.10e-02	2057	575.66
LURIC	0.17	0.079	1.47e-01	1427	336.08
Rotterdam 1	0.176	0.025	3.12e-01	5961	1506.52
Rotterdam 2	0.181	0.01	8.05e-01	2151	505.47
Rotterdam 3	0.183	0.052	1.32e-01	3018	806.28
TEENAGE	0.196	0.033	7.46e-01	703	206.06
INGI Val Borbera	0.202	0.02	6.58e-01	1778	484.89
UK BioBank	0.175	0.023	3.16e-08	134615	49931.54
Overall	**0.176**	**0.026**	**5.49e-11**	**185924**	**54083.29**



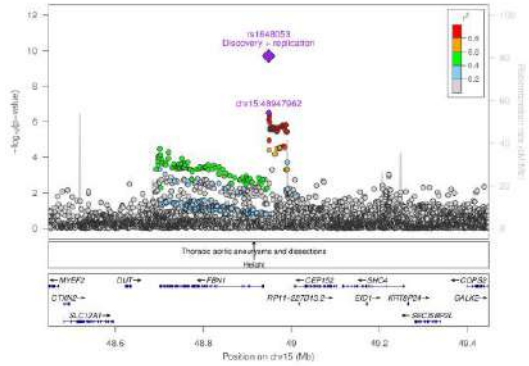


Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.394	-0.009	7.90e-01	1807	657.73
TwinsUK WGS	0.308	0.006	4.02e-01	1265	549.23
UKHLS	0.317	0.043	8.72e-03	8727	3781.86
ALSPAC GWA	0.32	0.03	1.95e-01	4121	1615.1
TwinsUK GWA	0.311	0.026	5.14e-01	2585	650.42
1958 Birth Cohort	0.312	0.034	8.76e-02	5713	2472.73
INGI Carlantino	0.377	0.016	8.25e-01	397	182.35
INGI Friuli Venezia Giulia	0.414	0.009	8.65e-01	791	360.53
HELIC MANOLIS	0.314	0.049	3.15e-01	1075	413.13
HELIC Pomak	0.332	0.032	5.37e-01	903	341.6
INCIPE 1	0.336	0.008	8.65e-01	934	411.62
INCIPE 2	0.334	0.05	1.15e-01	2050	964.83
LURIC	0.309	0.041	3.21e-01	1403	594.3
Rotterdam 1	0.311	0.026	5.06e-02	5665	2370.74
Rotterdam 2	0.306	0.059	6.81e-02	1938	823.61
Rotterdam 3	0.308	0.047	9.84e-02	2930	1250.2
TEENAGE	0.352	0.05	3.79e-01	696	326.12
INGI Val Borbera	0.3	0.067	1.85e-01	1740	807.04
UK BioBank	0.317	0.019	4.03e-06	134798	56319.9
Overall	**0.317**	**0.023**	**7.52e-11**	**179540**	**77160.49**

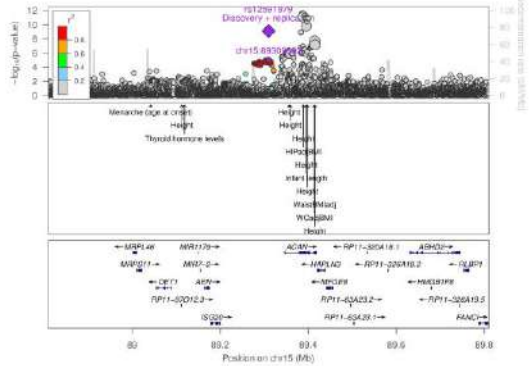




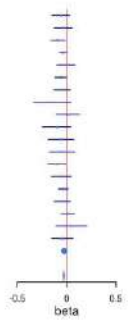
Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.203	0.062	1.35e-01	1806	585.11
TwinsUK WGS	0.212	0.033	4.00e-01	1265	439.4
FINRISK	0.246	0.017	7.19e-01	1254	461.97
ALSPAC GWA	0.21	0.055	4.72e-02	4116	1313.23
TwinsUK GWA	0.217	-0.034	4.42e-01	2582	592.5
1958 Birth Cohort	0.208	0.043	6.05e-02	5720	1890.03
INGI Carlantino	0.224	-0.084	7.82e-01	395	127.95
INGI Friuli Venezia Giulia	0.199	0.018	7.73e-01	791	227.51
HELIC MANOLIS	0.205	0.064	1.43e-01	1068	303.53
HELIC Pomak	0.192	-0.026	7.05e-01	895	226.76
LURIC	0.212	0.115	1.72e-02	1400	427.34
Rotterdam 1	0.198	0.047	4.25e-02	5660	1829.72
Rotterdam 2	0.215	0.065	2.95e-02	1937	664.43
Rotterdam 3	0.203	0.059	6.53e-02	2925	961.66
TEENAGE	0.251	0.037	5.53e-01	697	256.14
UK BioBank	0.211	0.023	9.95e-07	134795	43727.03
Overall	**0.21**	**0.026**	**1.13e-10**	**167302**	**54083.29**



Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.252	-0.015	6.91e-01	1794	707.33
TwinsUK WGS	0.251	-0.023	5.58e-01	1747	863.4
arcOGEN	0.261	-0.053	8.70e-02	2748	1092.24
UKHLS	0.251	-0.029	1.54e-01	8700	3102.95
FINRISK	0.282	-0.057	1.93e-01	1249	525.76
ALSPAC GWA	0.249	0.03	2.37e-01	4103	1525.88
TwinsUK GWA	0.247	-0.086	1.86e-02	3540	750.83
1958 Birth Cohort	0.245	-0.037	9.58e-02	5721	2002.81
INGI Carlantino	0.222	0.065	4.43e-01	471	136.96
INGI Friuli Venezia Giulia	0.262	-0.042	4.17e-01	1197	372.95
HELIC MANOLIS	0.256	0.001	9.79e-01	1058	356.14
HELIC Pomak	0.301	0.019	7.10e-01	949	376.9
INCIPE 1	0.234	-0.106	6.19e-02	937	313.14
INCIPE 2	0.236	-0.045	2.38e-01	2057	678.66
LURIC	0.236	-0.065	2.19e-01	1427	496.96
Rotterdam 1	0.232	-0.049	2.76e-02	5661	2017.23
Rotterdam 2	0.242	-0.055	1.40e-01	2151	733.23
Rotterdam 3	0.238	-0.033	2.97e-01	3018	1025.51
TEENAGE	0.225	-0.123	4.93e-02	703	234.72
INGI Val Borbera	0.258	-0.018	6.62e-01	1778	575.66
UK BioBank	0.248	-0.019	1.24e-05	134797	50617.47
Overall	**0.248**	**-0.024**	**2.06e-10**	**186106**	**69252.06**



Cohort	EAF	Beta	P-value	N	Weight
ALSPAC WGS	0.163	-0.08	1.77e-01	1794	500.77
TwinsUK WGS	0.163	-0.039	4.47e-01	1747	462.14
arcOGEN	0.161	-0.09	1.52e-02	2748	735.86
UKHLS	0.17	-0.033	1.65e-01	8700	2340.5
FINRISK	0.222	-0.004	9.36e-01	1249	455.09
ALSPAC GWA	0.16	-0.059	5.72e-02	4103	1036.44
TwinsUK GWA	0.159	-0.046	2.67e-01	3540	569.6
INGI Carlantino	0.152	-0.143	1.40e-01	471	108.17
INGI Friuli Venezia Giulia	0.17	0.014	8.21e-01	1197	275.36
HELIC MANOLIS	0.112	-0.1	1.79e-01	1058	181.24
HELIC Pomak	0.157	0.066	3.90e-01	949	229.56
INCIPE 1	0.135	0.044	5.09e-01	937	229.42
INCIPE 2	0.144	-0.101	2.88e-02	2057	464.48
LURIC	0.16	-0.052	3.16e-01	1427	370.38
Rotterdam 1	0.155	-0.033	1.92e-01	5661	1527.76
Rotterdam 2	0.157	-0.044	2.66e-01	2151	584.74
Rotterdam 3	0.159	0.013	7.18e-01	3018	813.4
TEENAGE	0.132	0.05	5.37e-01	703	155.13
INGI Val Borbera	0.124	-0.045	4.10e-01	1778	333.32
UK BioBank	0.165	-0.024	4.86e-06	134797	37438.46
Overall	**0.164**	**-0.028**	**8.06e-10**	**180385**	**49382.72**



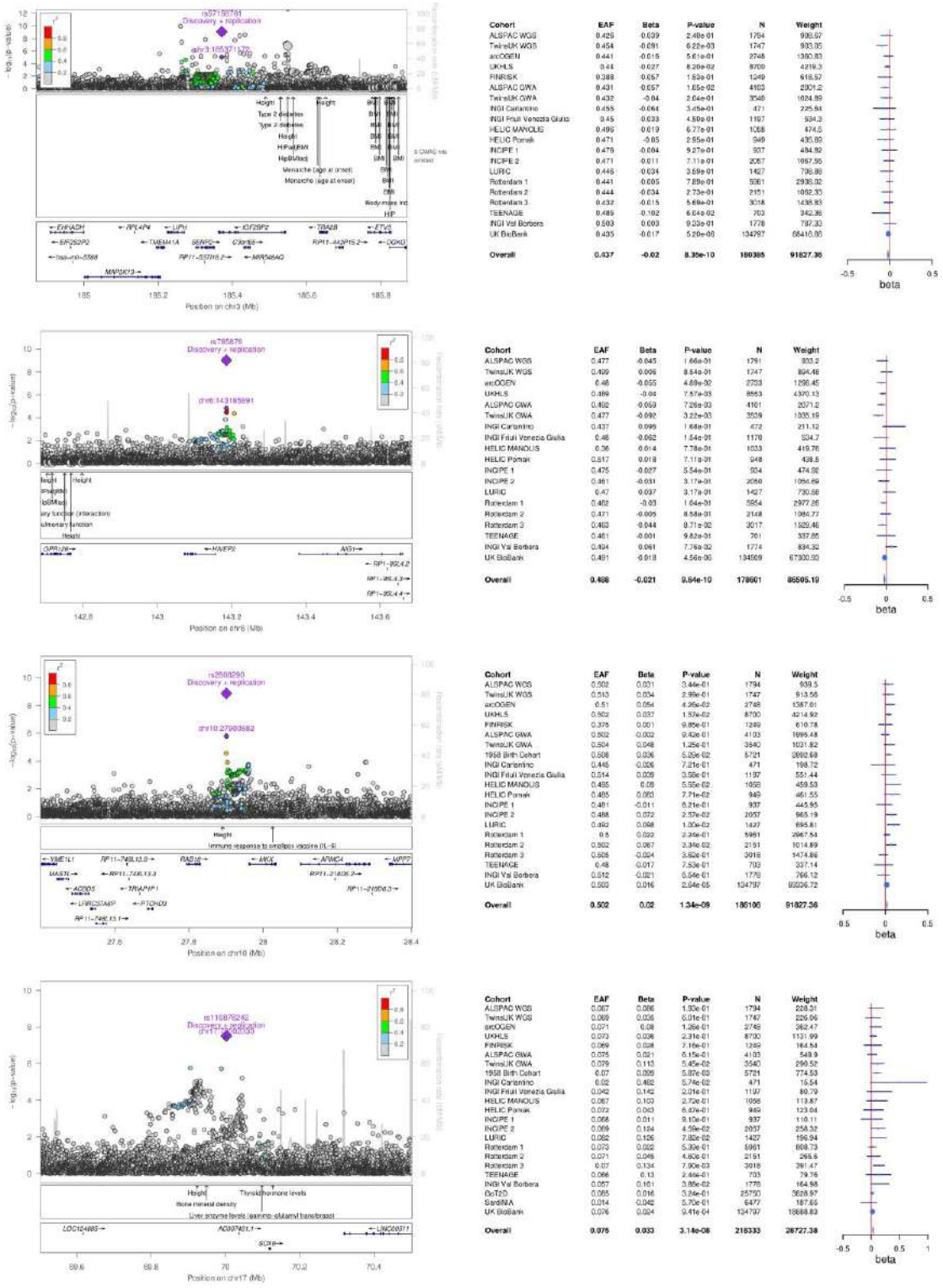


Figure S23: Locus zoom and forest plots for the novel loci reported in Table 2.
Plots display 500kb each side of the top variant, where the smaller diamond represents the discovery *P-value* and the bigger diamond the overall *P-value* (meta-analysis across discovery and follow-up cohorts). LD is calculated from the combined WGS UK10K cohorts (ALSPAC and TwinsUK). Previously reported variants are denoted by large circles.

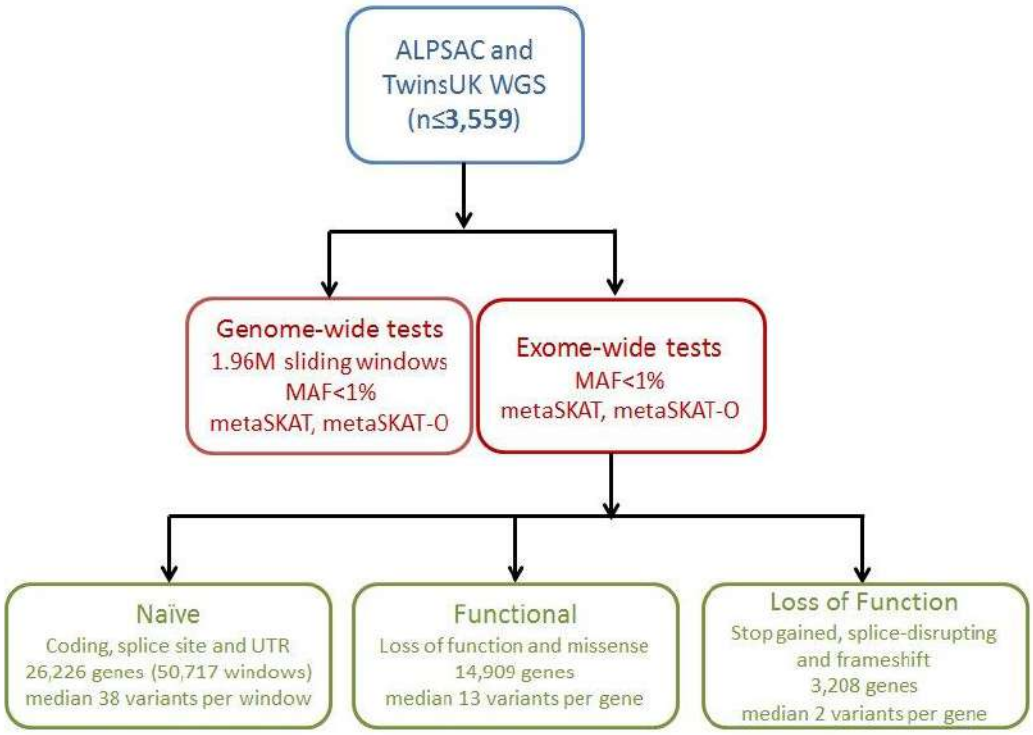
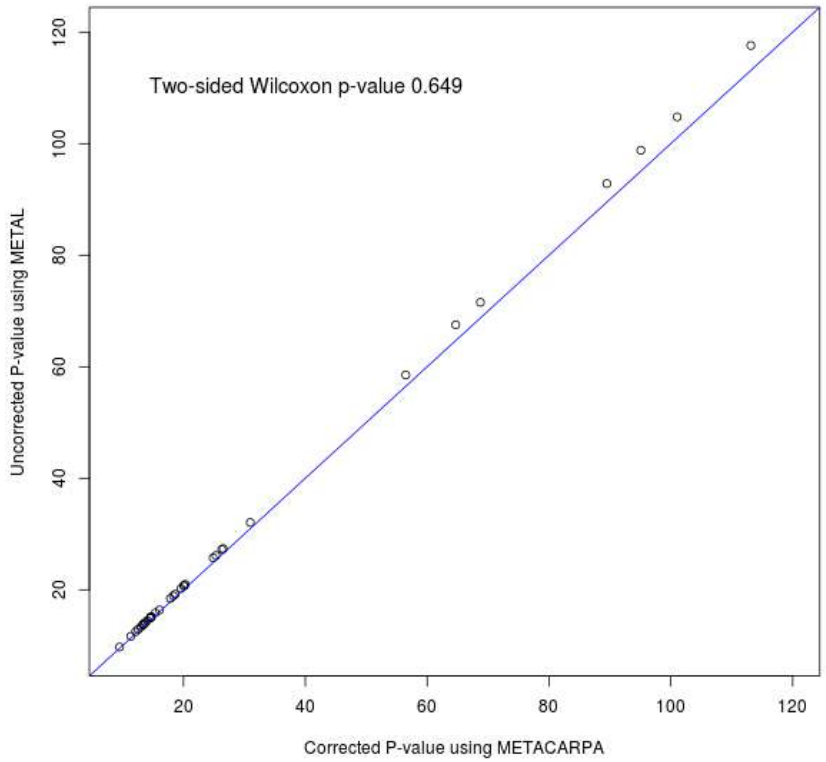


Figure S24: Study design for rare variants tests.



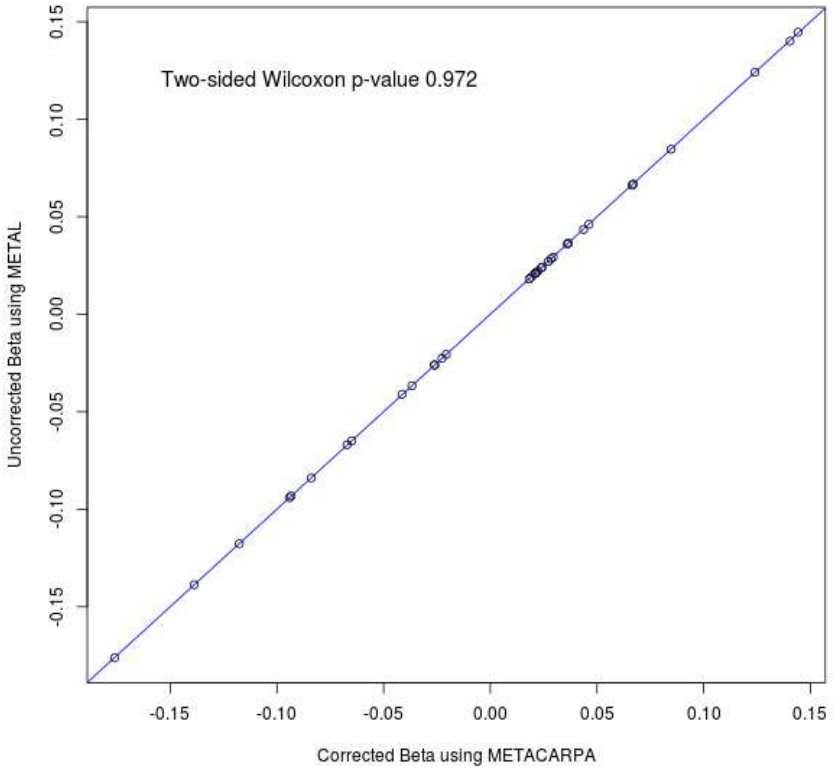
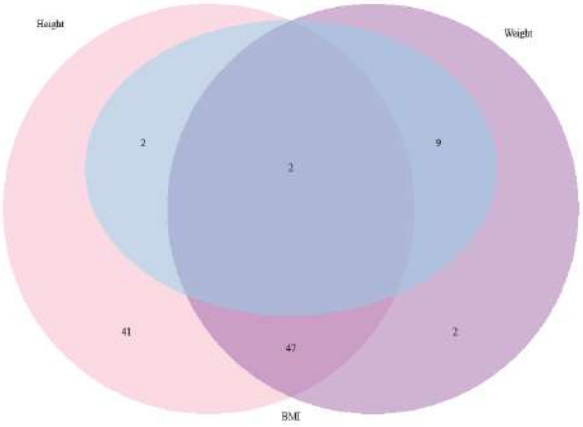
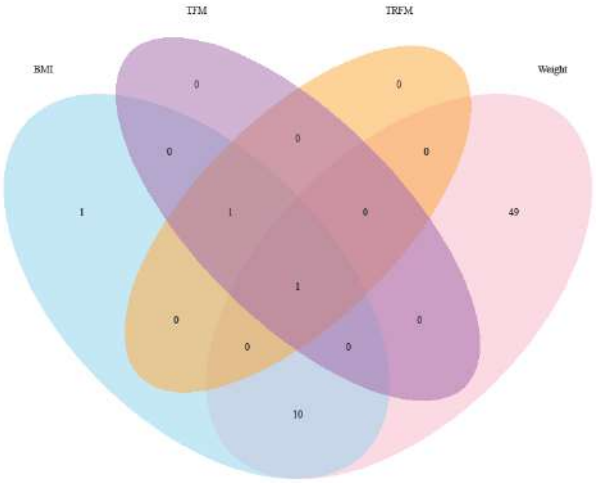


Figure S25: Meta-analysis *P-values* (top) and effect sizes (bottom) of variants associated with height across discovery cohorts and UKBiobank using METACARPA and METAL.

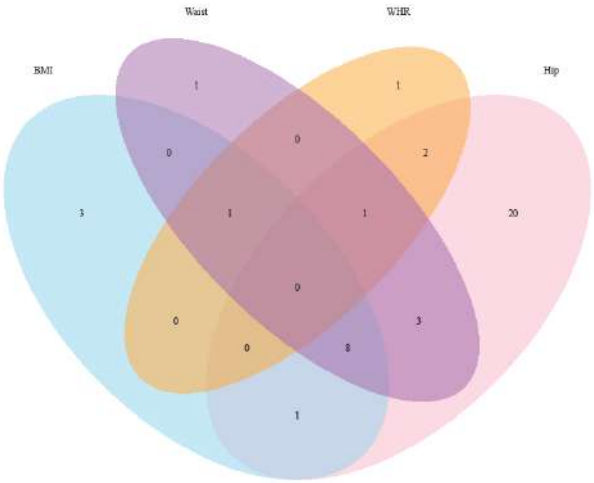
A


Height
Weight
BMI
2
2
9
41
47
2

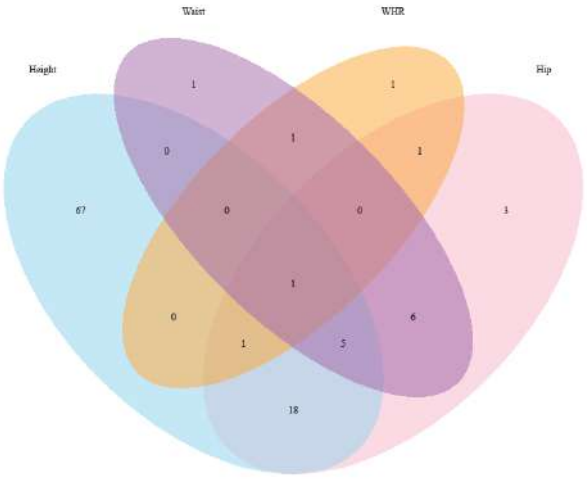
B


TFM
TRFM
BMI
Weight
0
0
0
0
0
1
1
0
49
1
0
0
0
0
10

C


Waist
WHR
BMI
Hip
1
1
0
0
2
3
1
1
20
0
0
3
0
8
1

D


Waist
WHR
Height
Hip
1
1
0
1
1
67
0
0
3
1
0
6
1
5
18

E

F

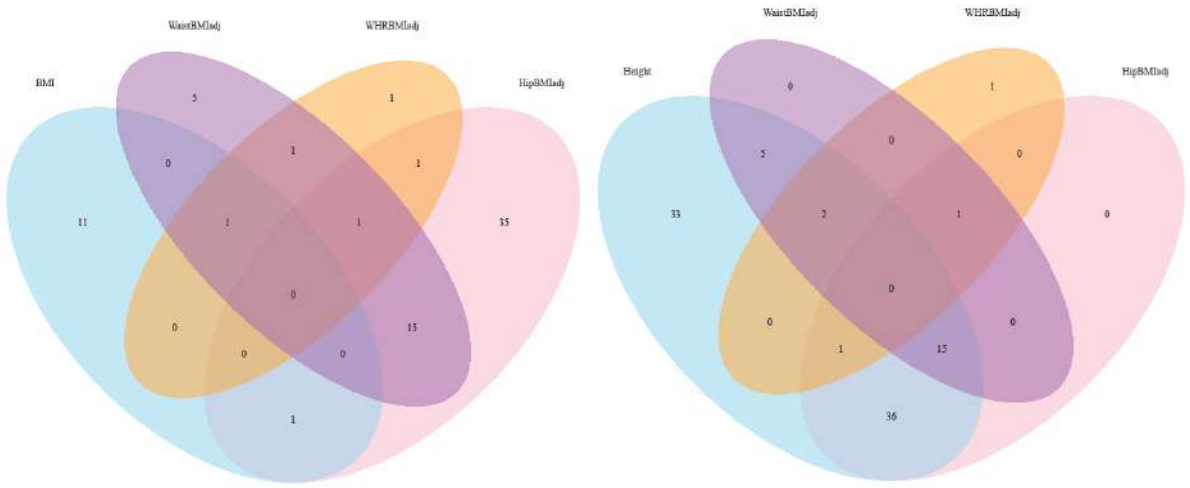
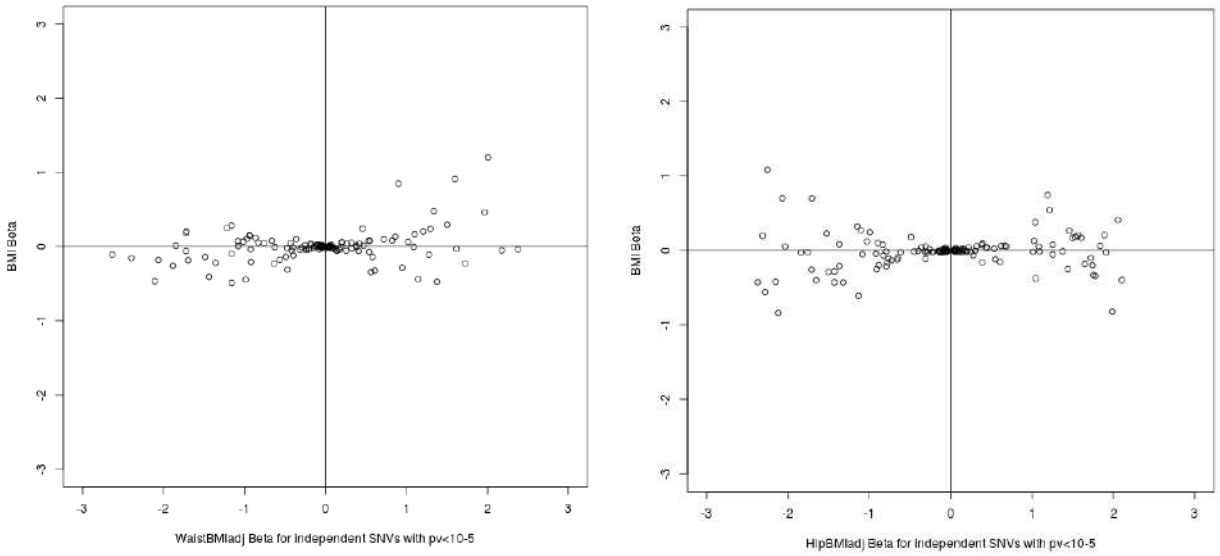


Figure S26: Venn diagrams showing overlap of the 106 signals from Tables 1, 2 and S3 robustly associated with an anthropometric trait at *P-value* ≤ 5x10^{-8} in stage1+stage2 with other anthropometric traits also associated at *P-value* ≤ 5x10^{-8} in stage1+stage2.



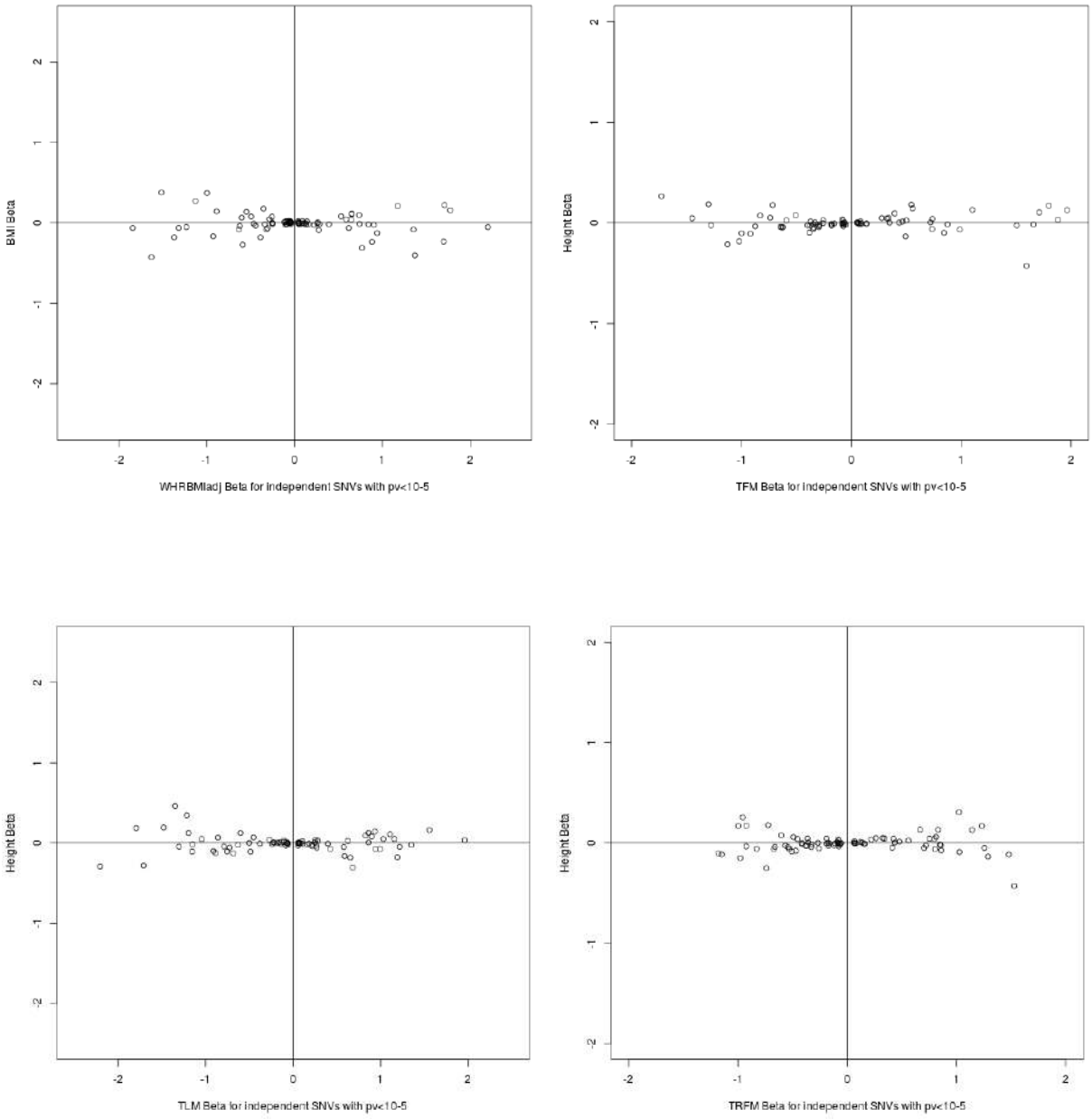
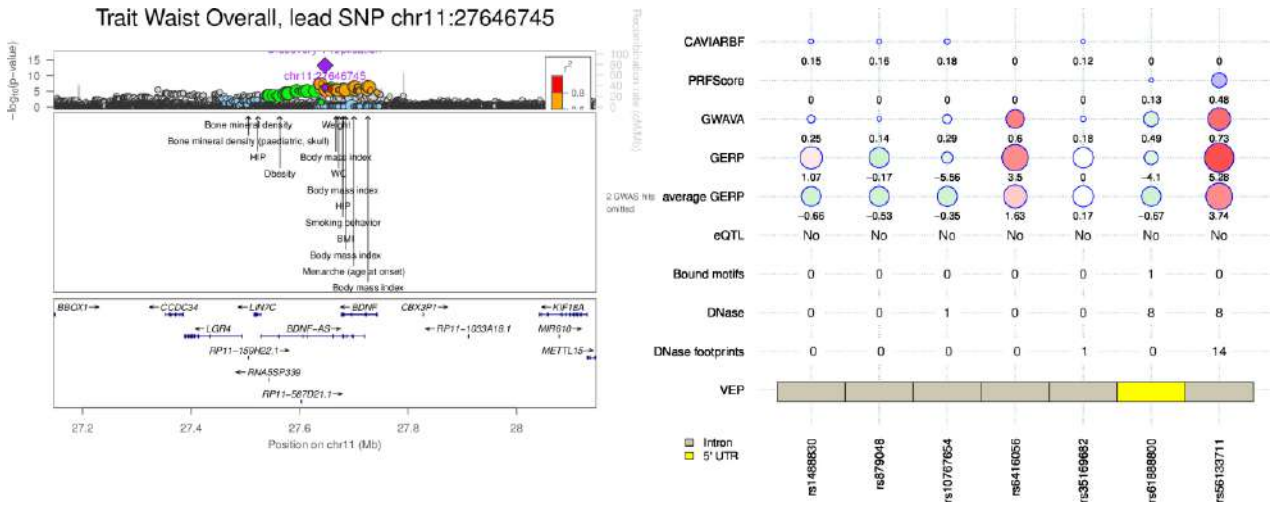
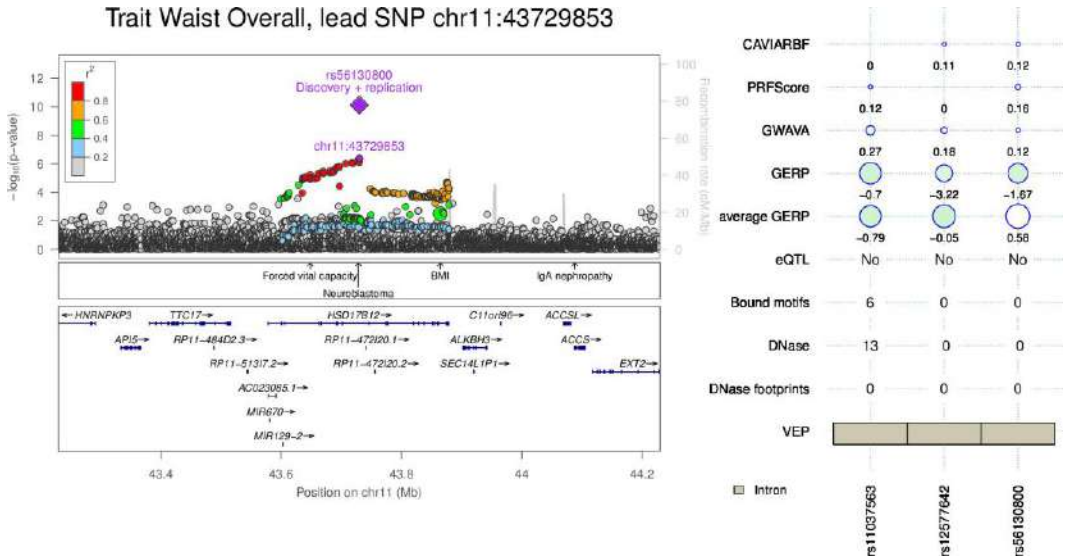
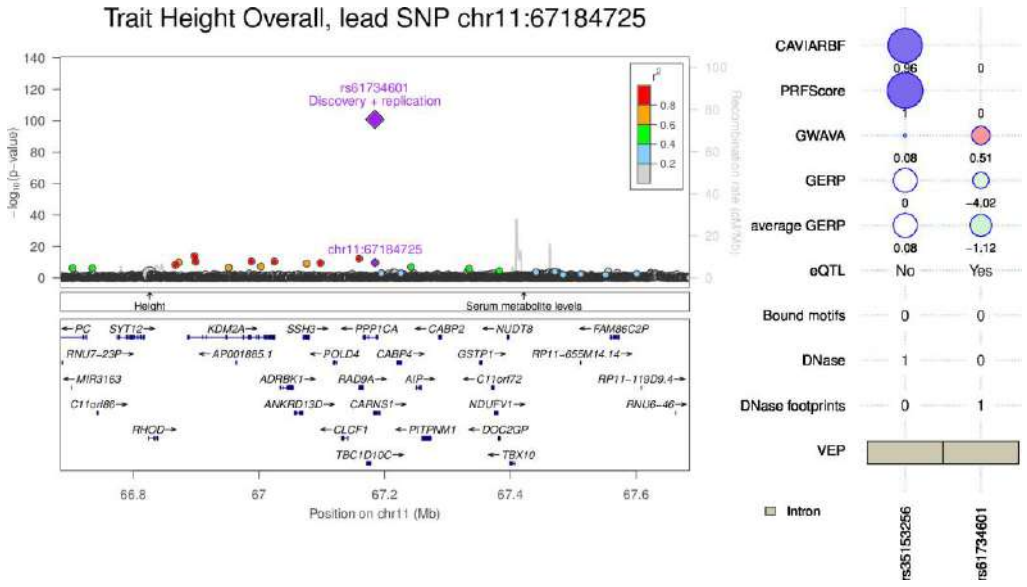


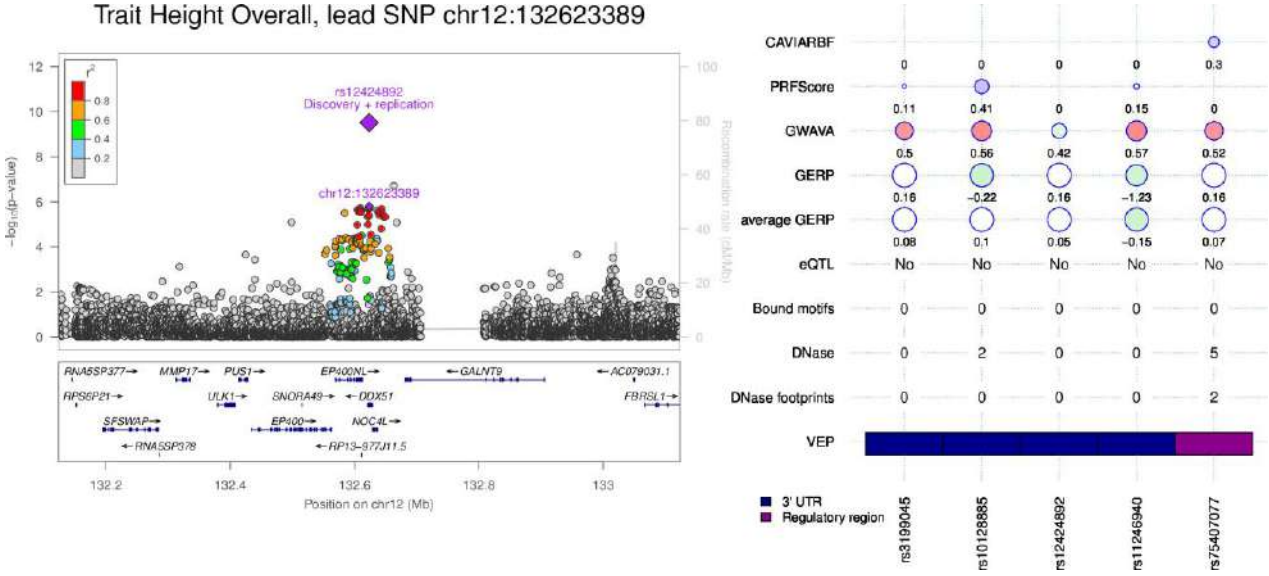
Figure S27: No evidence of collider bias for traits adjusted for BMI or Height.
Effect sizes of independent (pairwise r^2<0.2 and further than 500kb) SNPs suggestive (P<10^{-5}) for waist circumference, hip circumference and waist to hip ratio adjusted for BMI (R-squared 0.11, 0.0051, 0.004 respectively) versus effect sizes for BMI. Similarly, effect sizes of independent SNPs suggestive for total fat mass, total lean mass and trunk fat mass (R-squared 0.0003, 0.0007, 0.0011 respectively) versus effect sizes for height.


Trait Waist Overall, lead SNP chr11:27646745
chr11:27646745
Bone mineral density
Weight
Bone mineral density (paediatric, skull)
HIP
Body mass index
Obesity
WC
Body mass index
HIP
Smoking behavior
BMI
Body mass index
Menarche (age at onset)
Body mass index
Position on chr11 (Mb)
CAVIARBF
PRFScore
GWAVA
GERP
average GERP
2 GWAS hits omitted
eQTL
Bound motifs
DNase
DNase footprints
VEP
Intron
5' UTR
rs11488830
rs879048
rs10767654
rs6416056
rs35169682
rs61888800
rs56133711

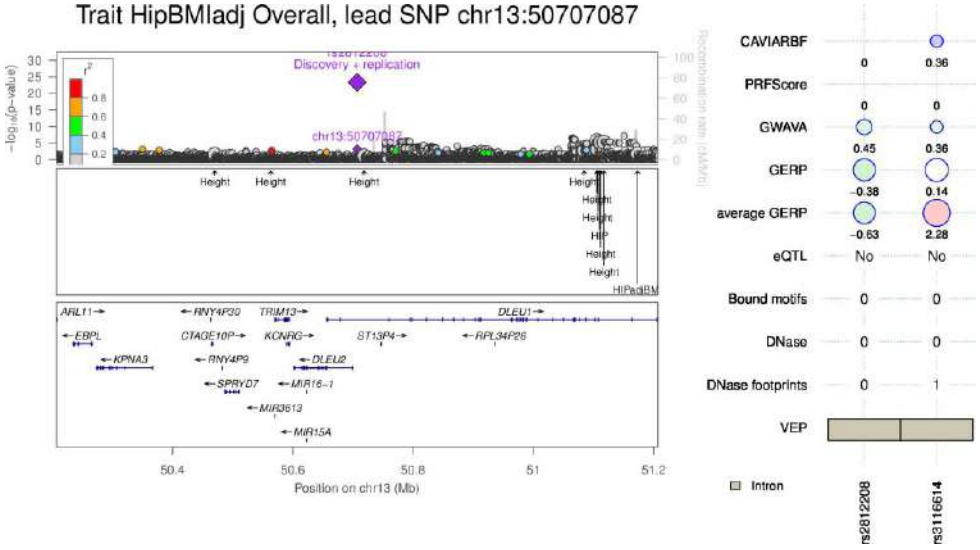

Trait Waist Overall, lead SNP chr11:43729853
rs56130800
Discovery + replication
chr11:43729853
Forced vital capacity
BMI
IgA nephropathy
Neuroblastoma
Position on chr11 (Mb)
CAVIARBF
PRFScore
GWAVA
GERP
average GERP
eQTL
Bound motifs
DNase
DNase footprints
VEP
Intron
rs11037563
rs12577642
rs56130800


Trait Height Overall, lead SNP chr11:67184725
rs61734601
Discovery + replication
chr11:67184725
Height
Serum metabolite levels
Position on chr11 (Mb)
CAVIARBF
PRFScore
GWAVA
GERP
average GERP
eQTL
Bound motifs
DNase
DNase footprints
VEP
Intron
rs35153256
rs61734601

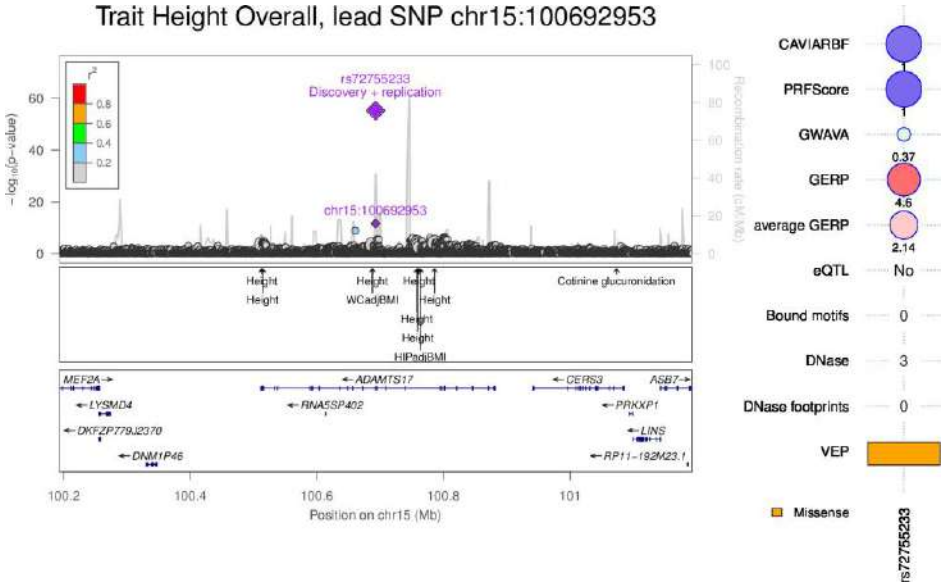
Trait Height Overall, lead SNP chr12:132623389



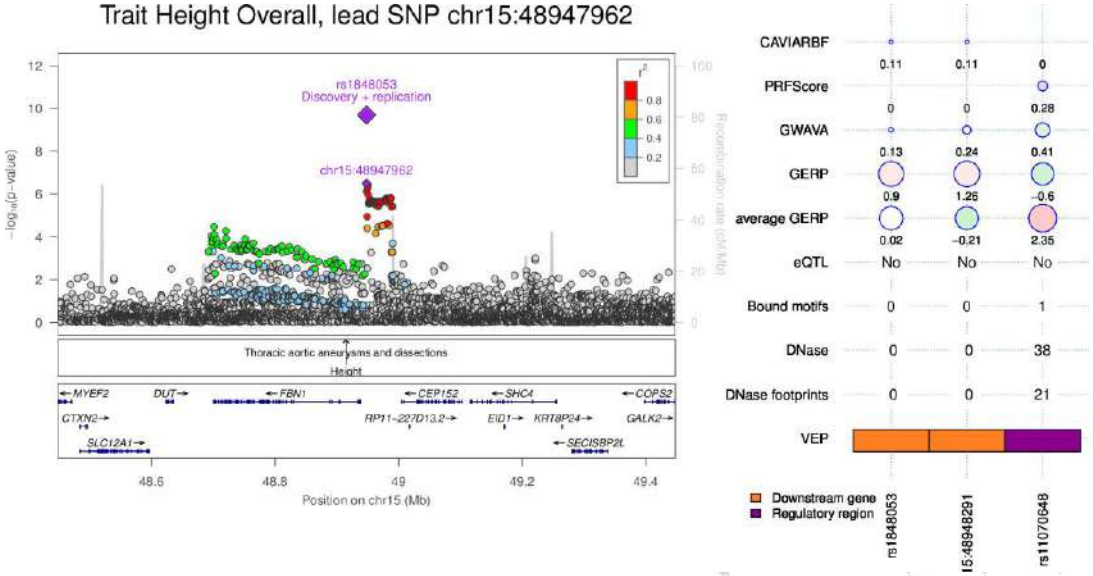
Trait HipBMIadj Overall, lead SNP chr13:50707087



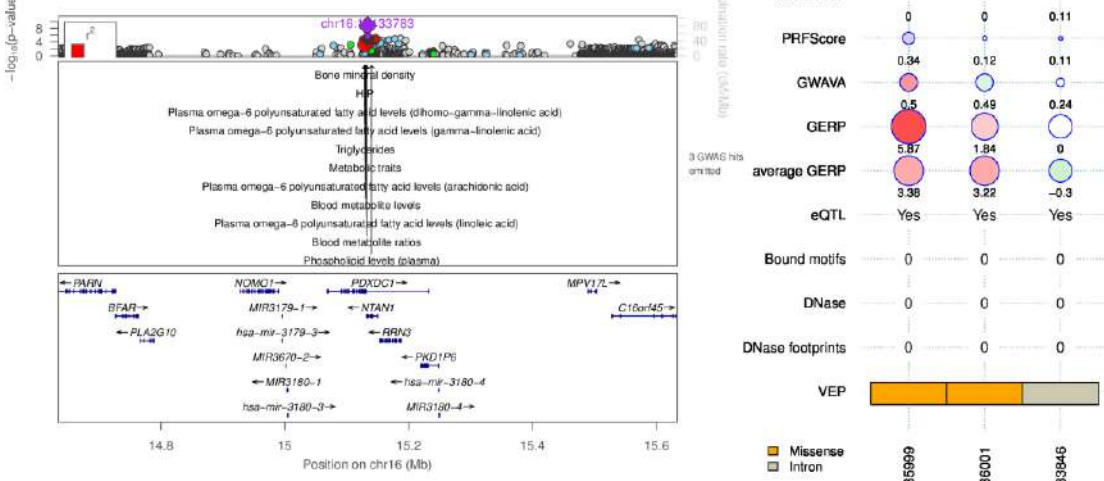
Trait Height Overall, lead SNP chr15:100692953



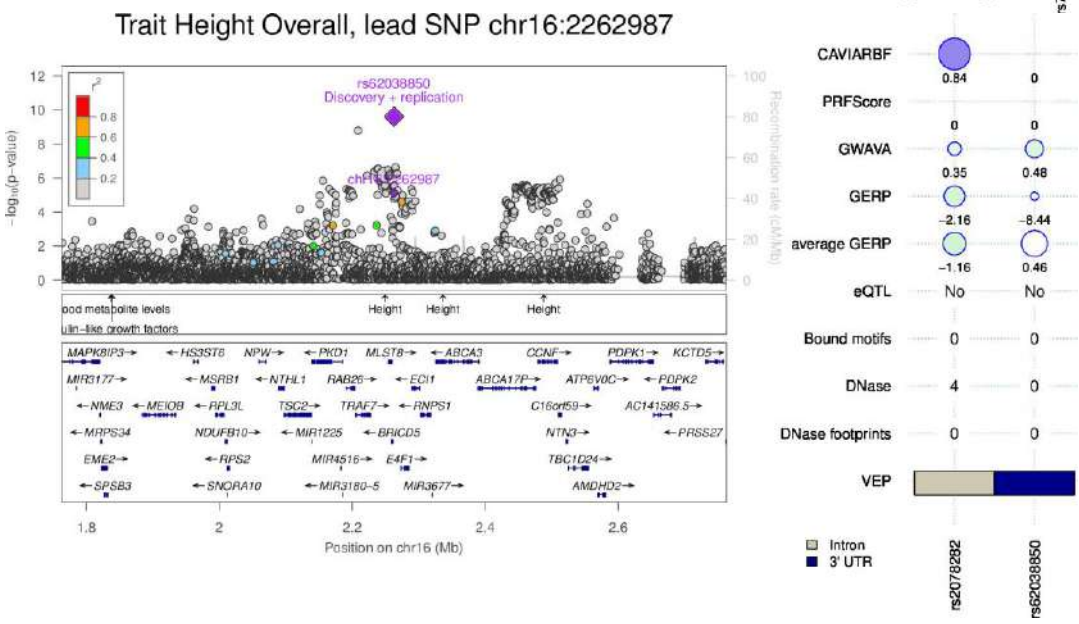
Trait Height Overall, lead SNP chr15:48947962



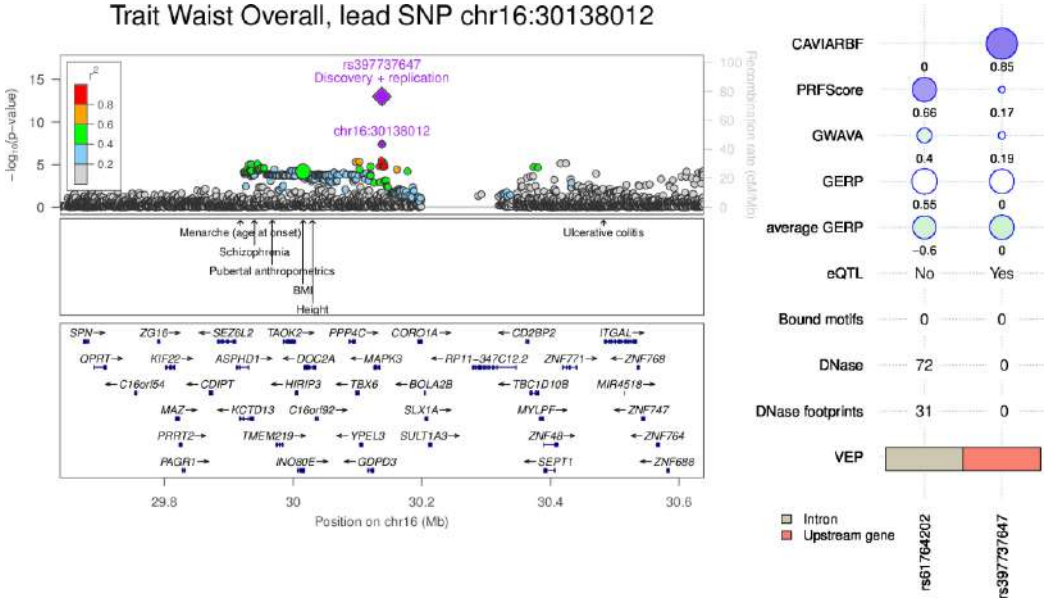
Trait Weight Overall, lead SNP chr16:15133783



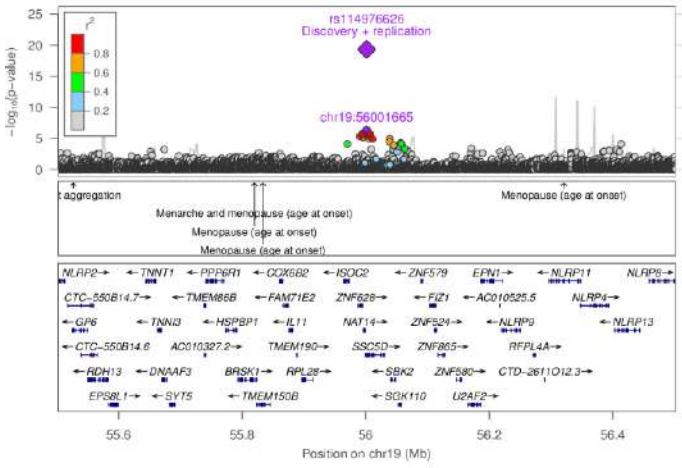
Trait Height Overall, lead SNP chr16:2262987

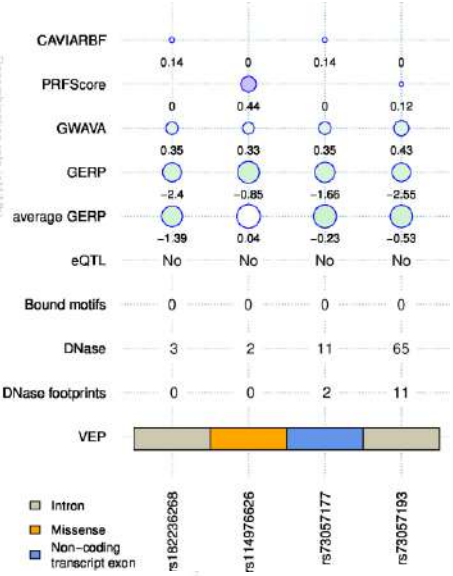


Trait Waist Overall, lead SNP chr16:30138012

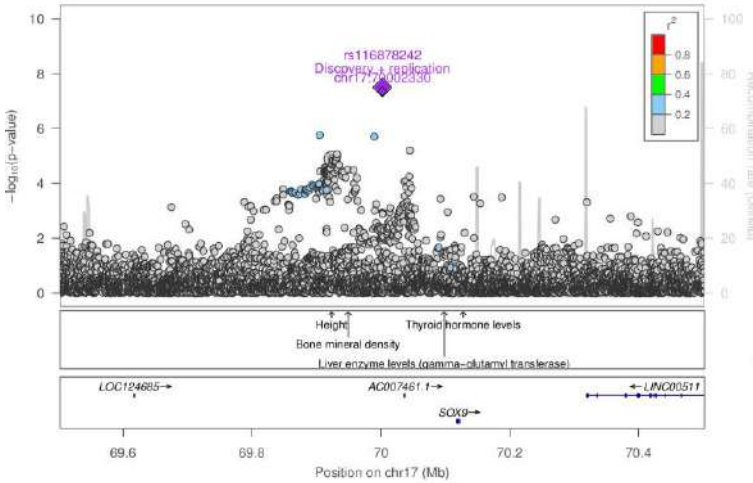


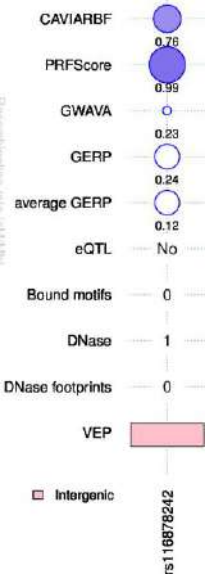
Trait Height Overall, lead SNP chr19:56001665



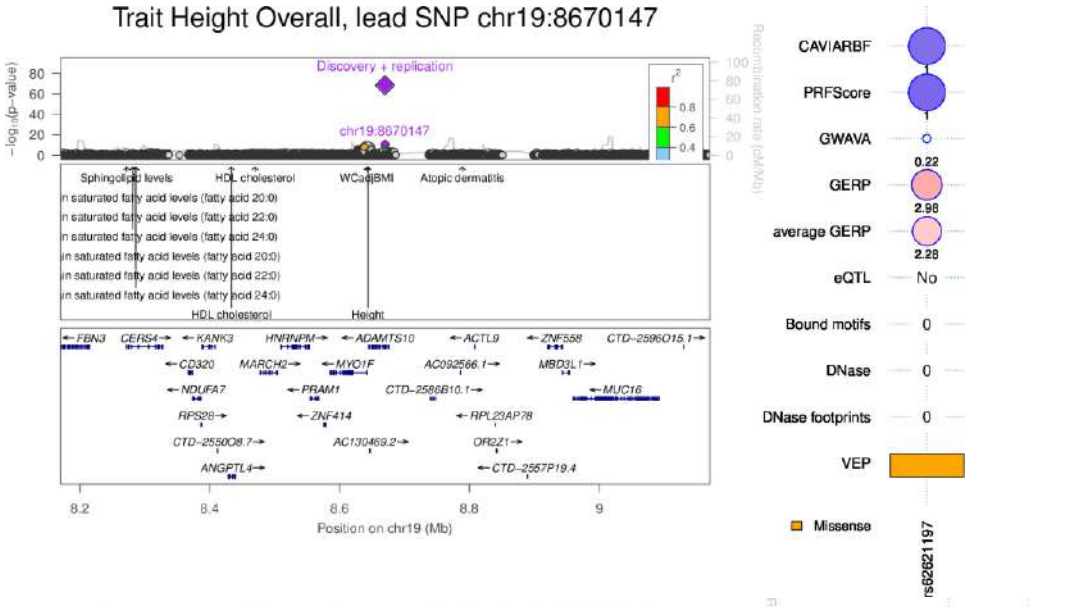


Trait Height Overall, lead SNP chr17:70002330

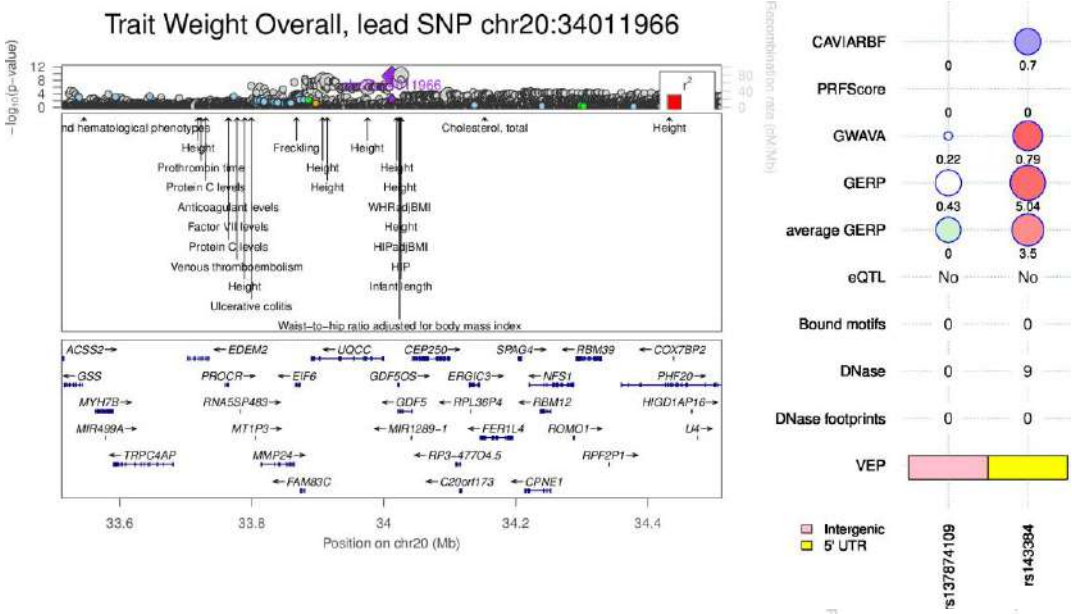




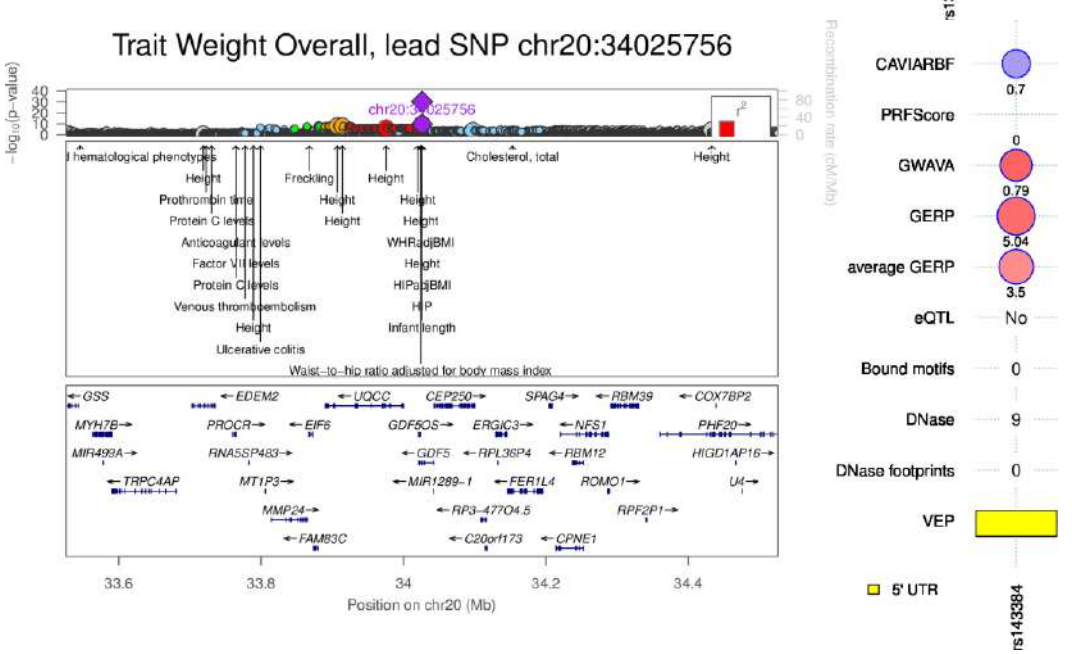
Trait Height Overall, lead SNP chr19:8670147



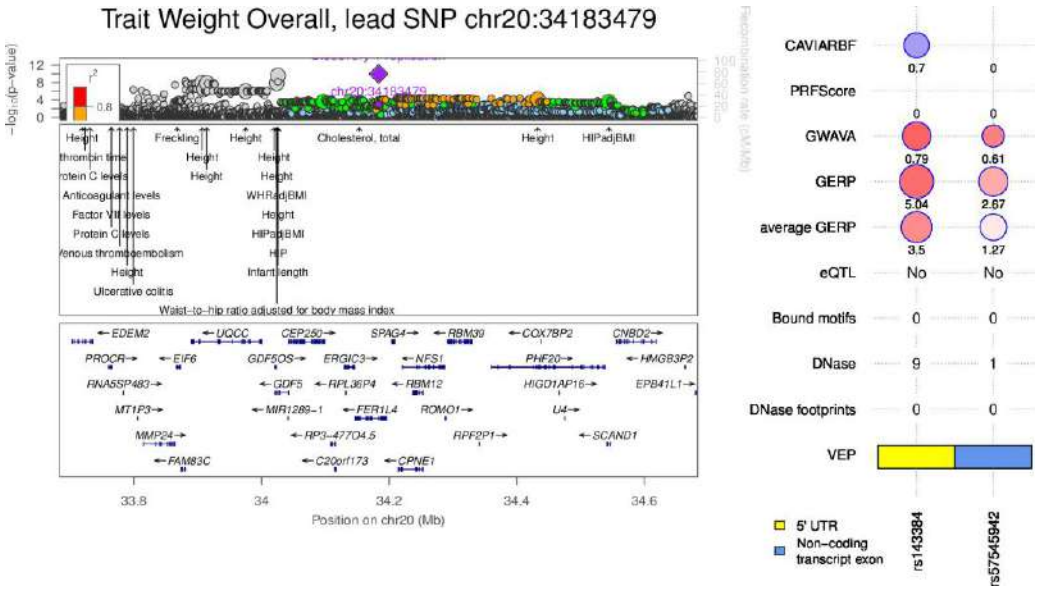
Trait Weight Overall, lead SNP chr20:34011966



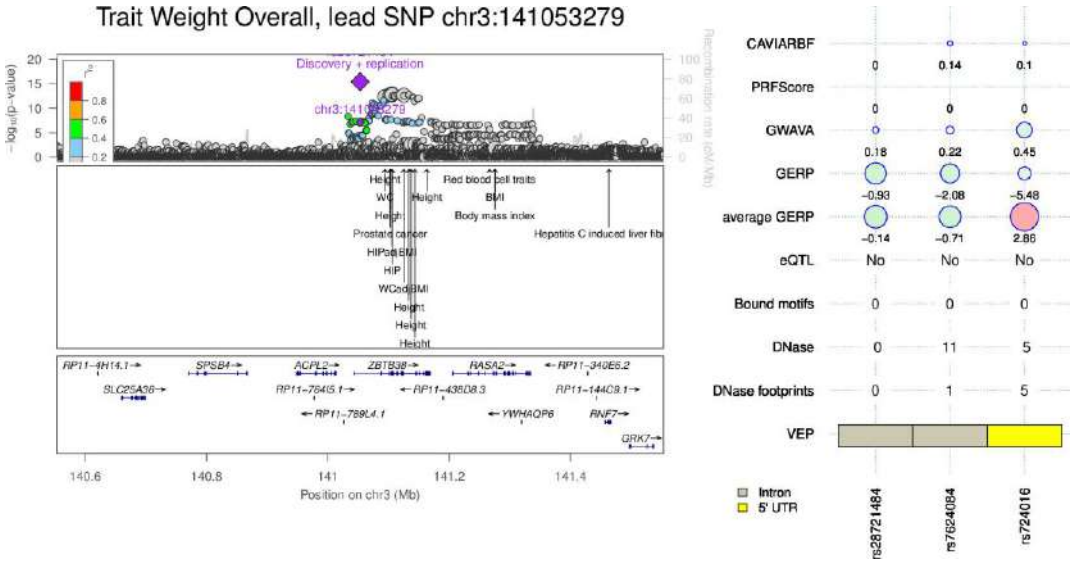
Trait Weight Overall, lead SNP chr20:34025756



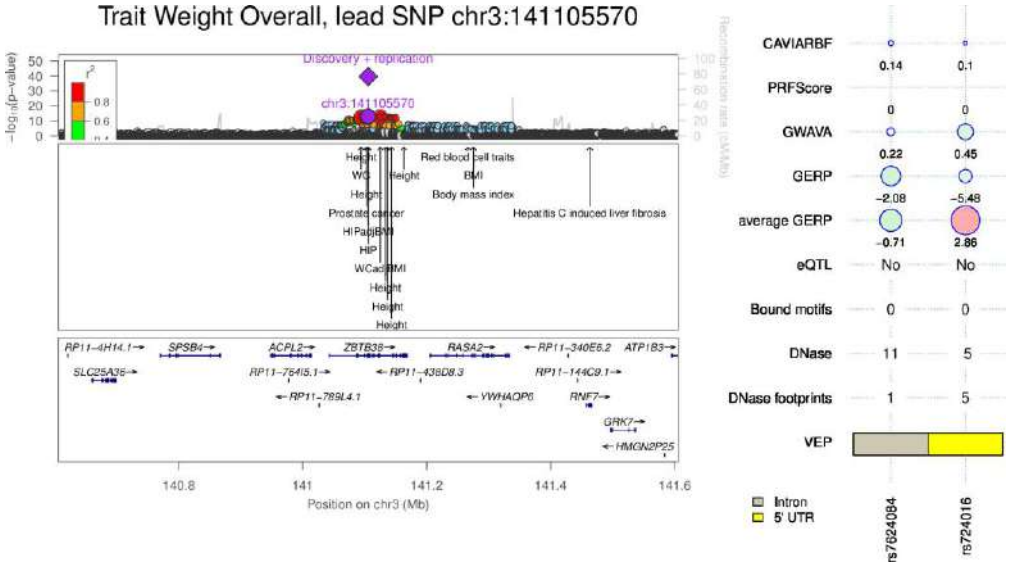
Trait Weight Overall, lead SNP chr20:34183479



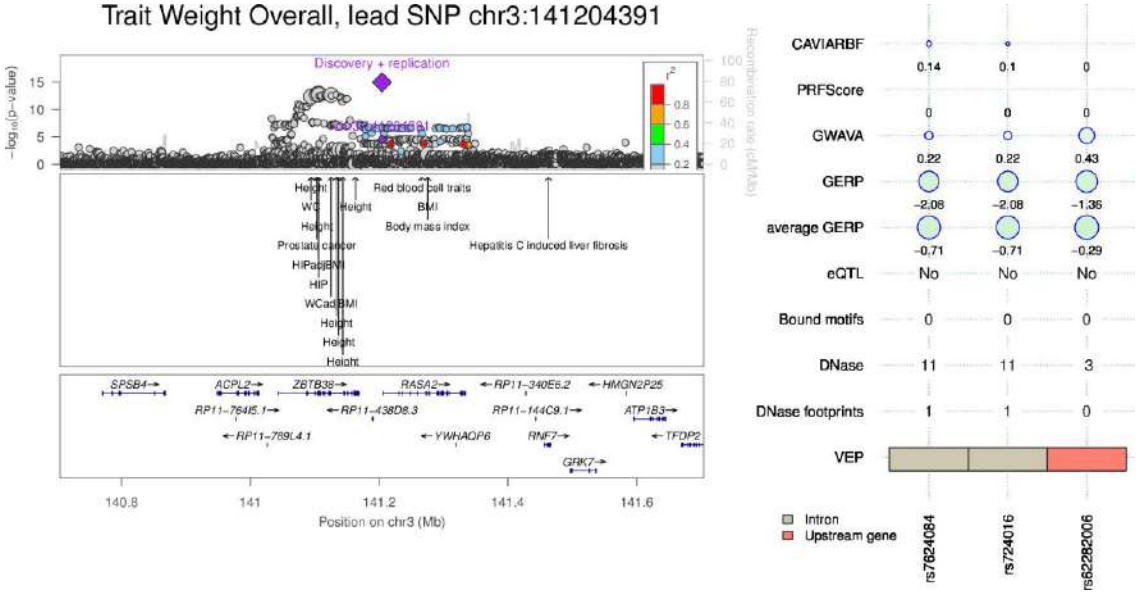
Trait Weight Overall, lead SNP chr3:141053279



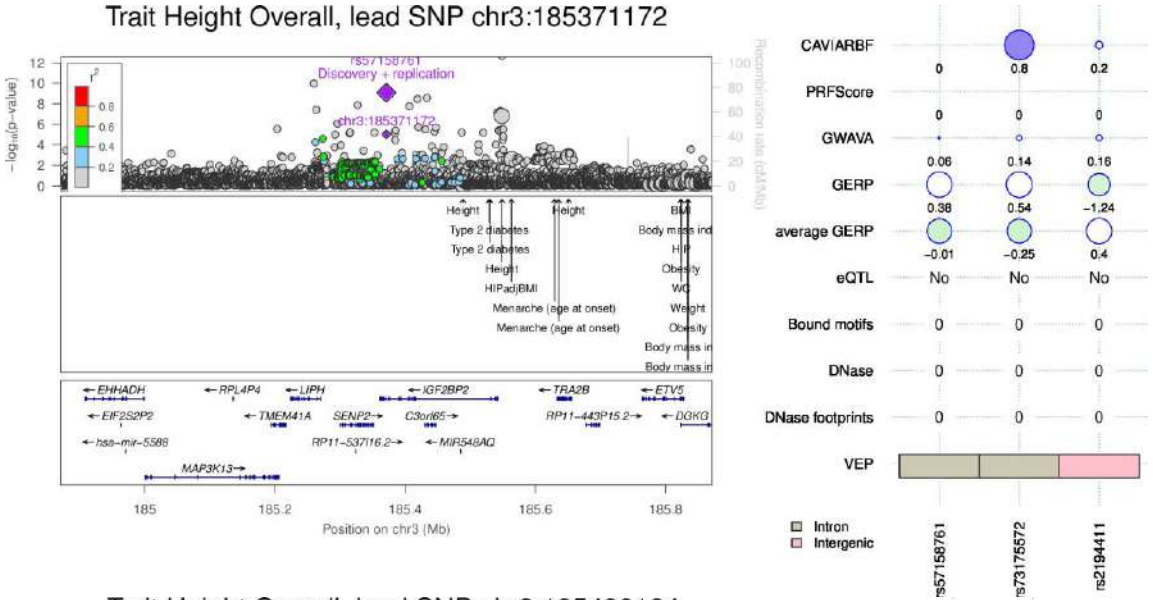
Trait Weight Overall, lead SNP chr3:141105570



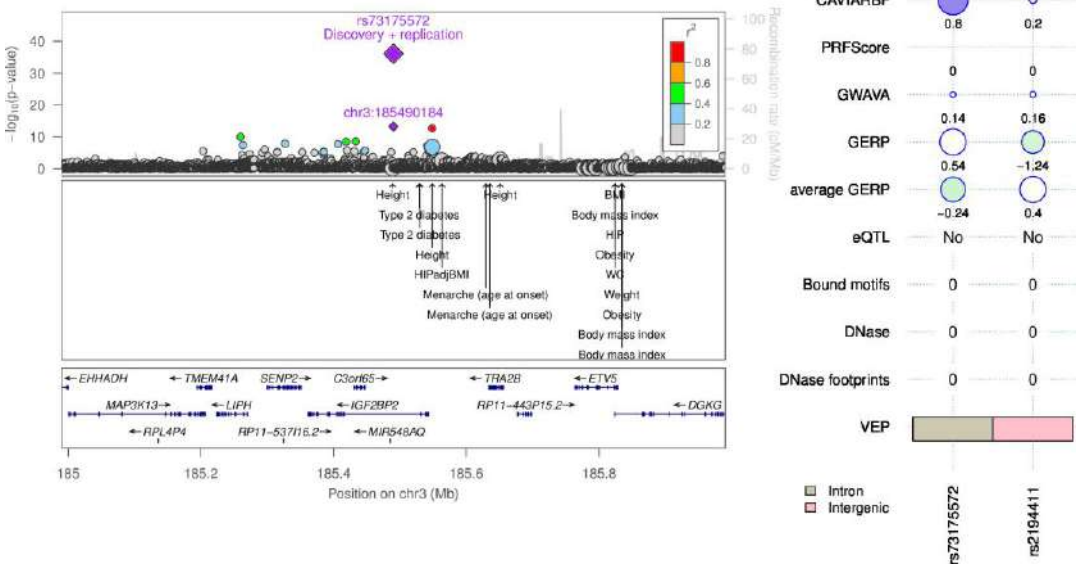
Trait Weight Overall, lead SNP chr3:141204391

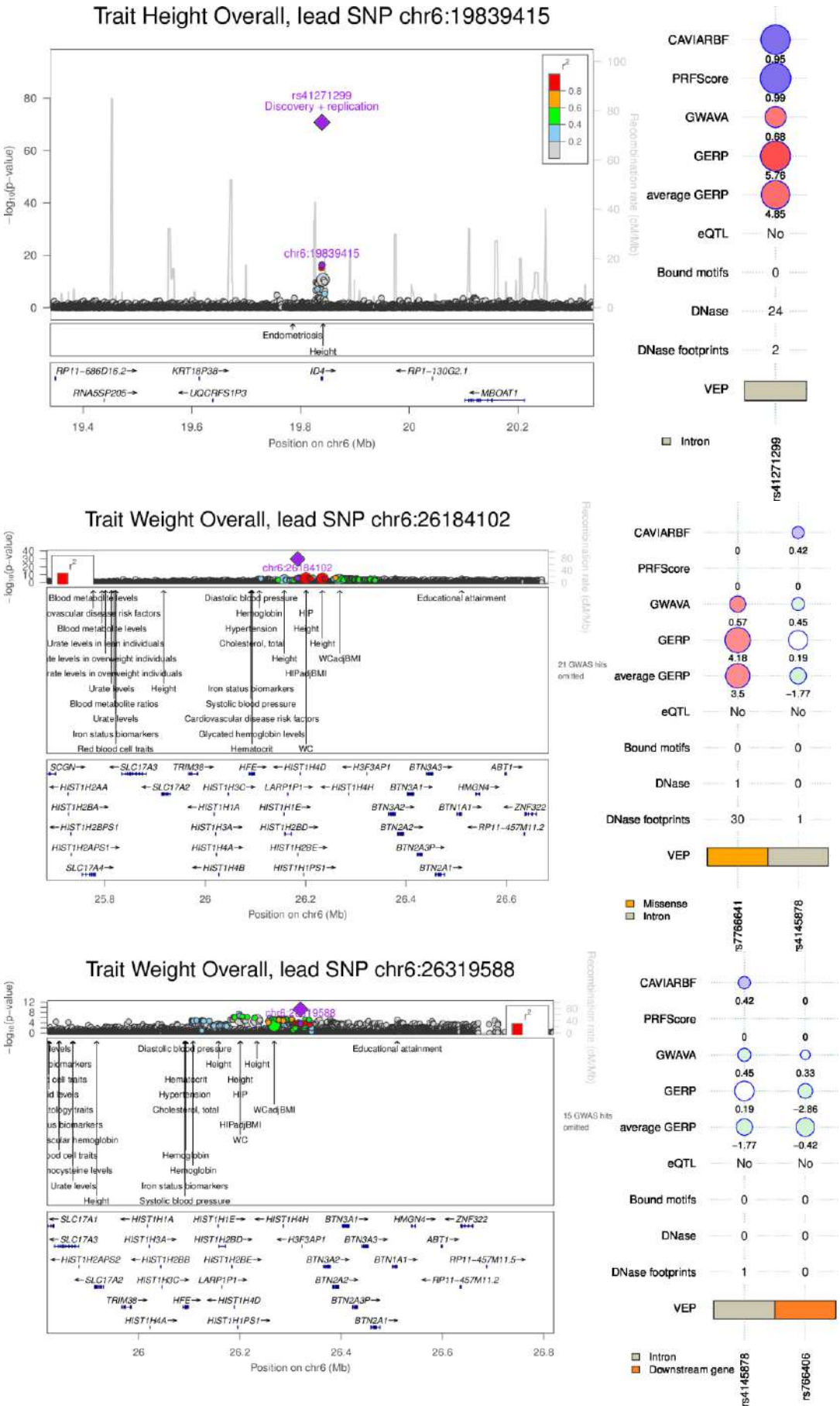


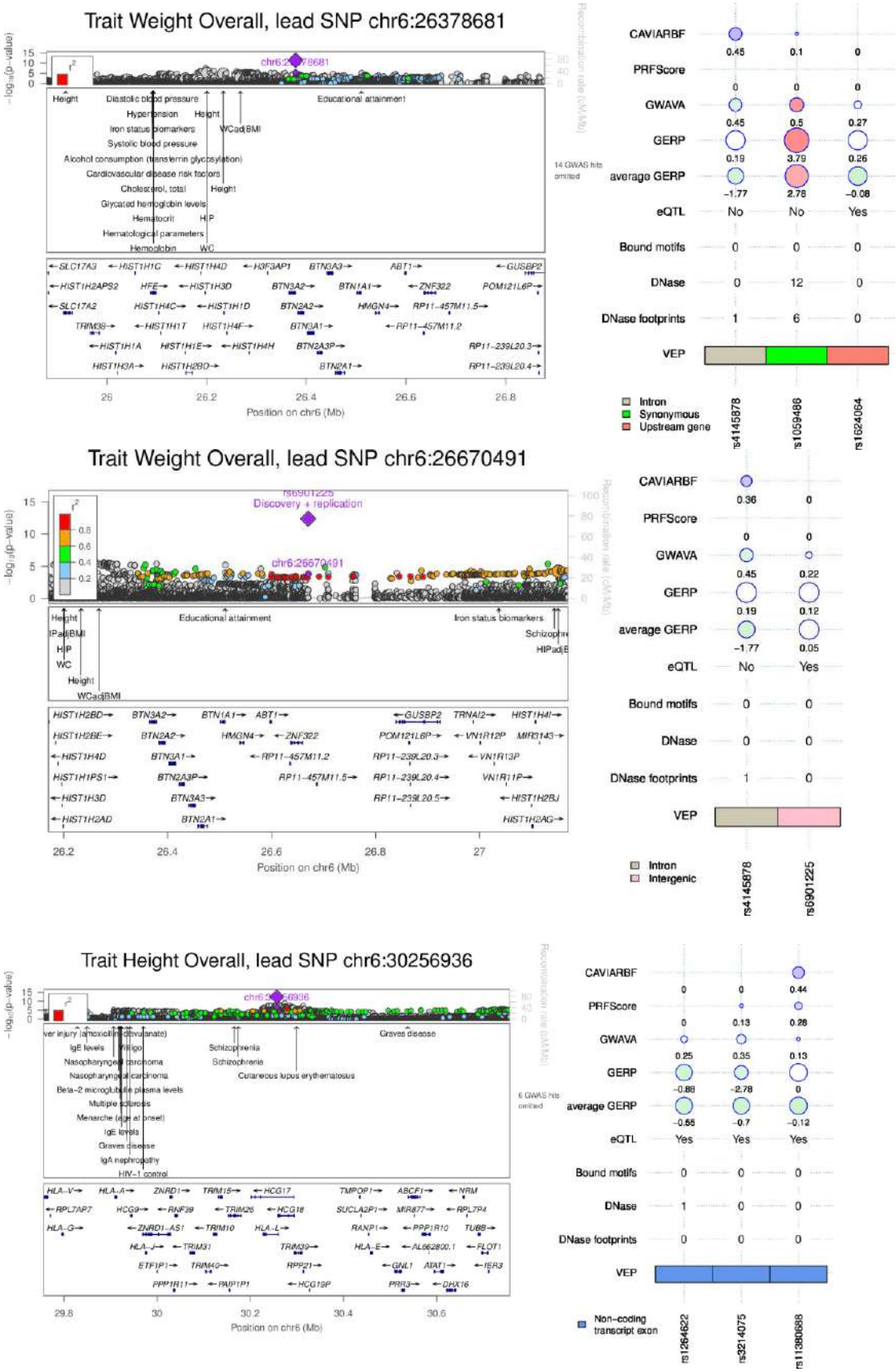
Trait Height Overall, lead SNP chr3:185371172



Trait Height Overall, lead SNP chr3:185490184




Trait Height Overall, lead SNP chr6:19839415
rs41271299
Discovery + replication
chr6:19839415
Endometriosis
Height
Position on chr6 (Mb)
CAVIARBF
PRFScore
GWAVA
GERP
average GERP
eQTL
Bound motifs
DNase
DNase footprints
VEP
Intron
Trait Weight Overall, lead SNP chr6:26184102
chr6:26184102
21 GWAS hits omitted
Missense
Intron
Trait Weight Overall, lead SNP chr6:26319588
chr6:26319588
15 GWAS hits omitted
Intron
Downstream gene


Trait Weight Overall, lead SNP chr6:26378681
Trait Weight Overall, lead SNP chr6:26670491
Trait Height Overall, lead SNP chr6:30256936
CAVIARBF
PRFScore
GWAVA
GERP
average GERP
eQTL
Bound motifs
DNase
DNase footprints
VEP
Intron
Synonymous
Upstream gene
Intergenic
Non-coding transcript exon
rs4145878
rs1059466
rs1624064
rs6901225
rs1264622
rs3214075
rs11380688
Position on chr6 (Mb)

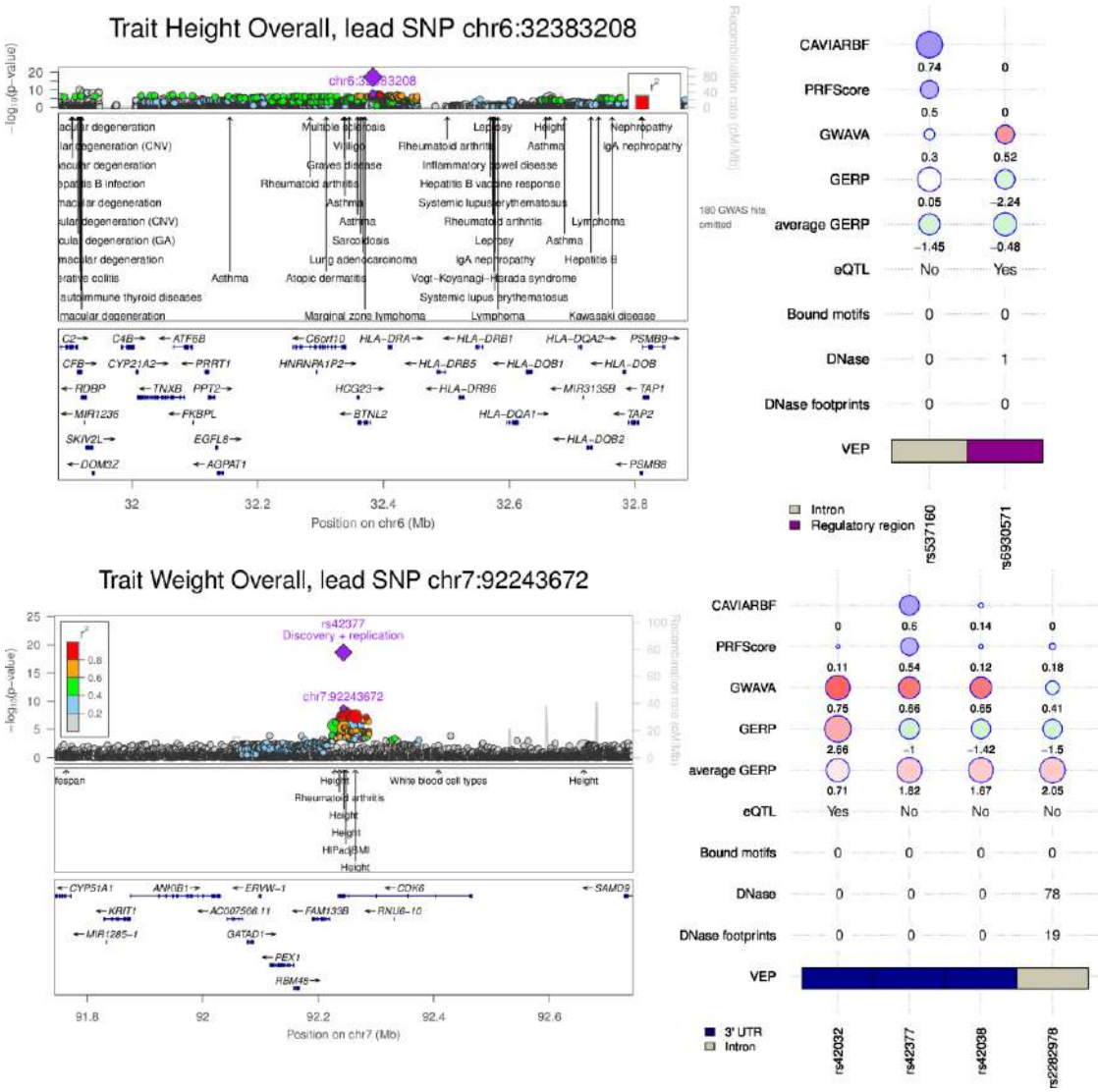
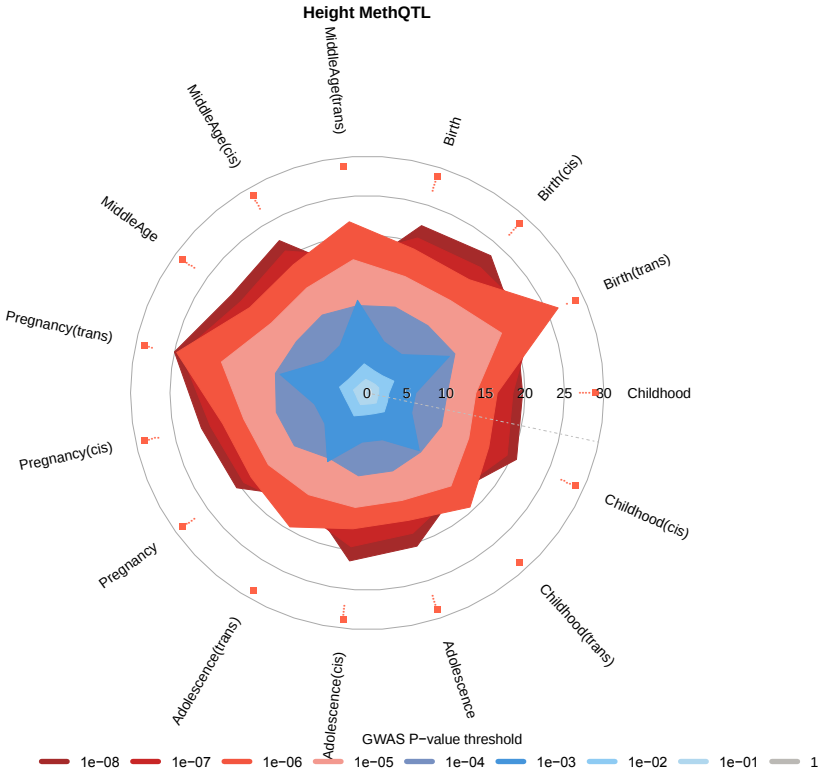
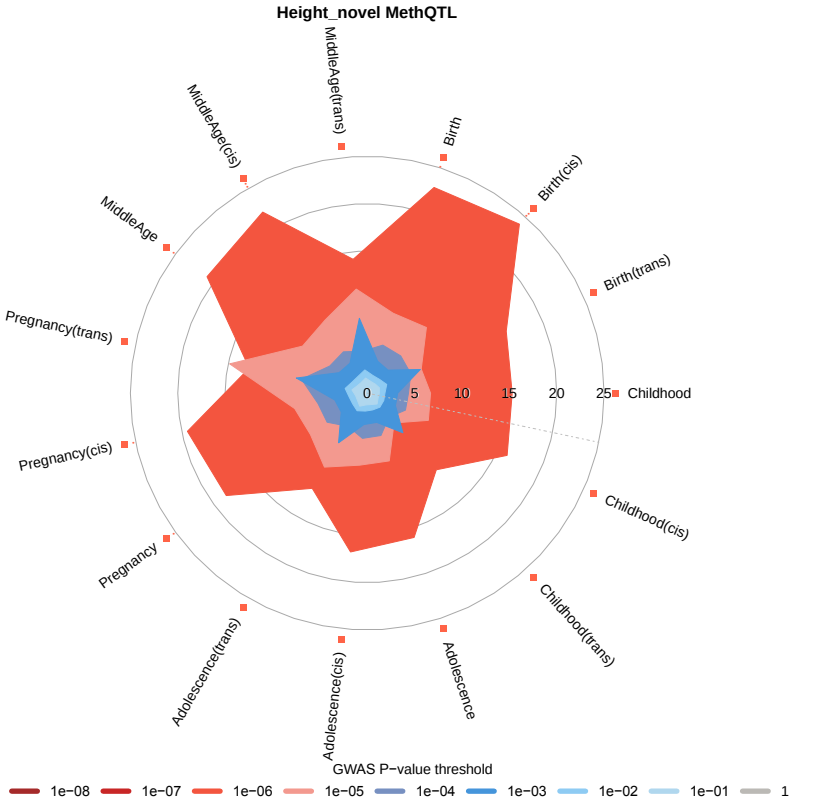
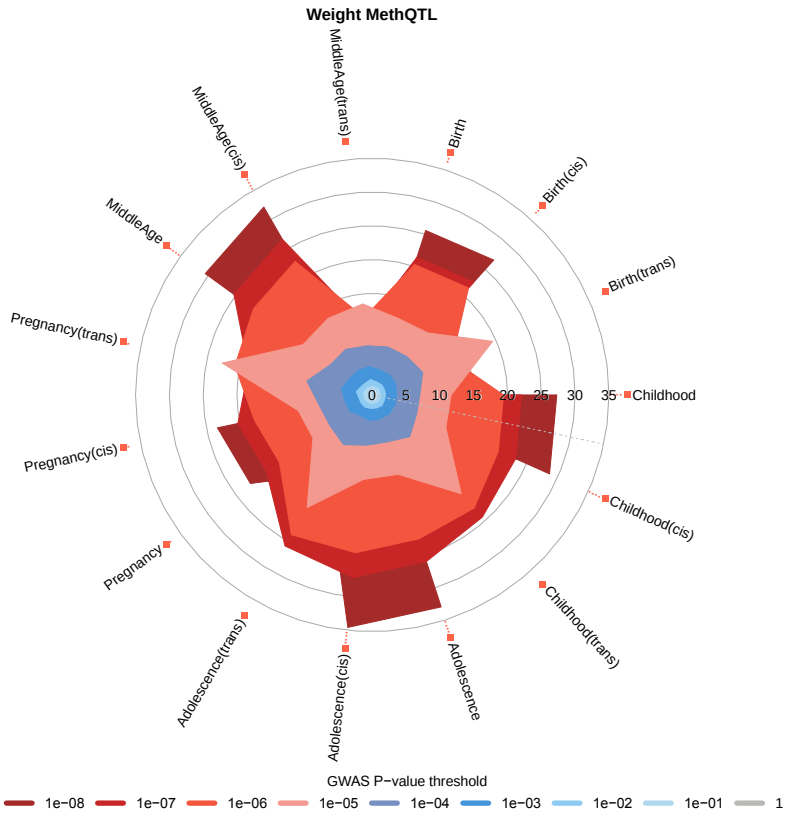


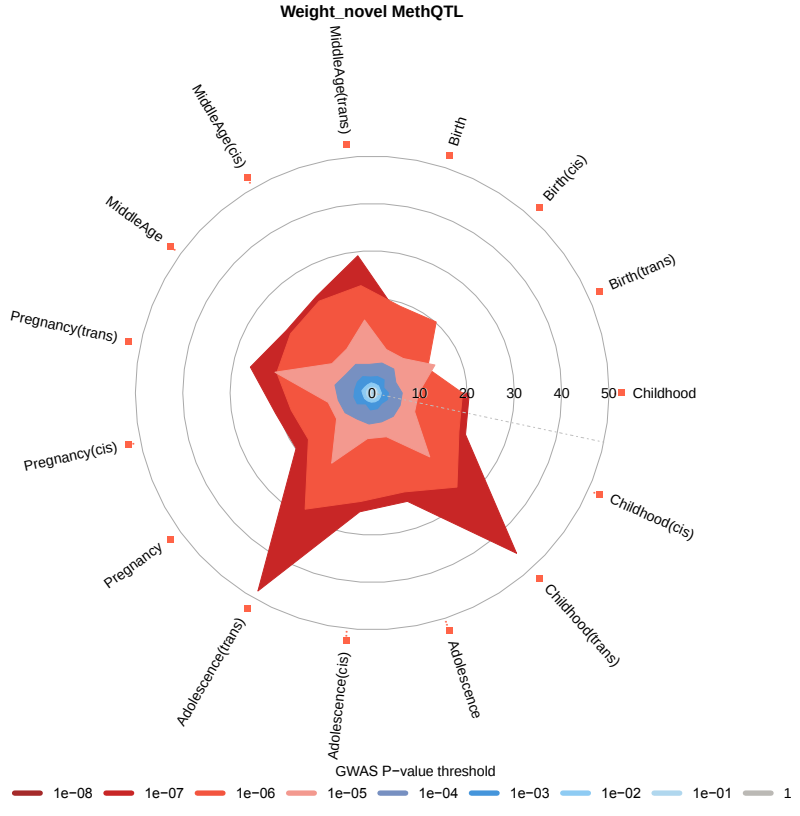
Figure S28: Combined information from two fine-mapping methods, functional prediction scores and eQTL analysis to assess the overall evidence supporting functional and causal interpretation at 30 fine-mapped regions (Table S5) of the 106 newly indentifind variants.

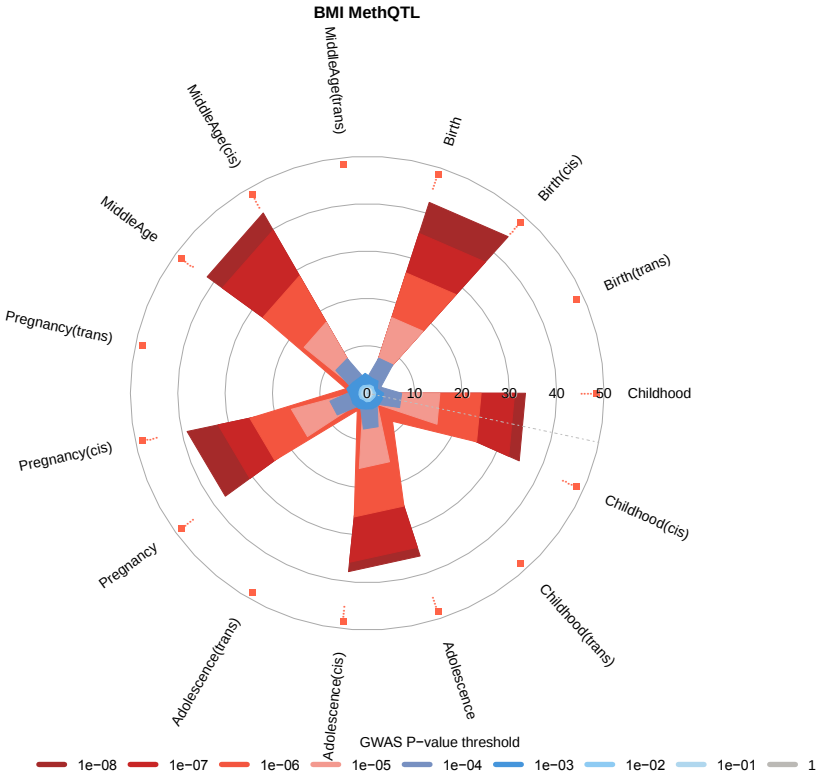
The panels (from top to bottom) show the LocusZoom regional association plot; posterior probability (PP) statistics from the fine-mapping methods CAVIARBF and PRFScore (only variants with PP>0.1 in either methods are shown); Genome Wide Annotation of Variants (GWAVA) scores ; Genomic Evolutionary Rate Profiling (GERP) scores; average GERP (in a 100bp window around each variant) scores; if the variant is an eQTL signal; number of cell lines in which the variant overlaps with a DNase footprints (peak calls from ENCODE); number of overlapping transcriptional factor binding sites based on ENCODE and JASPAR ChIP-seq; number of cell lines in which the queried locus overlaps with a DNase hypersensitivity site (ENCODE data, peaks from Ensembl); and Variant Effect Predictor (VEP) genic annotation. Circle sizes and colors for all scores are scaled with respect to score type and numbers are plotted below each circle. GWAVA scores range between [0,1] and scores over 0.5 indicate functionality (coloured in shades of green for scores <0.5 and red for scores >0.5). GERP scores range between [-12.3,6.17] and scores above zero indicate constrain (coloured in shades of green for scores <0 and red for scores >0).


Height MethQTL
MiddleAge(trans)
Birth
Birth(cis)
Birth(trans)
Childhood
Childhood(cis)
Childhood(trans)
Adolescence
Adolescence(cis)
Adolescence(trans)
Pregnancy
Pregnancy(cis)
Pregnancy(trans)
MiddleAge
MiddleAge(cis)
0
5
10
15
20
25
30
GWAS P−value threshold
1e−08
1e−07
1e−06
1e−05
1e−04
1e−03
1e−02
1e−01
1


Height_novel MethQTL
MiddleAge(trans)
Birth
Birth(cis)
Birth(trans)
Childhood
Childhood(cis)
Childhood(trans)
Adolescence
Adolescence(cis)
Adolescence(trans)
Pregnancy
Pregnancy(cis)
Pregnancy(trans)
MiddleAge
MiddleAge(cis)
0
5
10
15
20
25
GWAS P−value threshold
1e−08
1e−07
1e−06
1e−05
1e−04
1e−03
1e−02
1e−01
1


Weight MethQTL
MiddleAge(trans)
Birth
Birth(cis)
Birth(trans)
Childhood
Childhood(cis)
Childhood(trans)
Adolescence
Adolescence(cis)
Adolescence(trans)
Pregnancy
Pregnancy(cis)
Pregnancy(trans)
MiddleAge
MiddleAge(cis)
0
5
10
15
20
25
30
35
GWAS P−value threshold
1e−08
1e−07
1e−06
1e−05
1e−04
1e−03
1e−02
1e−01
1


Weight_novel MethQTL
MiddleAge(trans)
Birth
Birth(cis)
Birth(trans)
Childhood
Childhood(cis)
Childhood(trans)
Adolescence
Adolescence(cis)
Adolescence(trans)
Pregnancy
Pregnancy(cis)
Pregnancy(trans)
MiddleAge
MiddleAge(cis)
0
10
20
30
40
50
GWAS P−value threshold
1e−08
1e−07
1e−06
1e−05
1e−04
1e−03
1e−02
1e−01
1



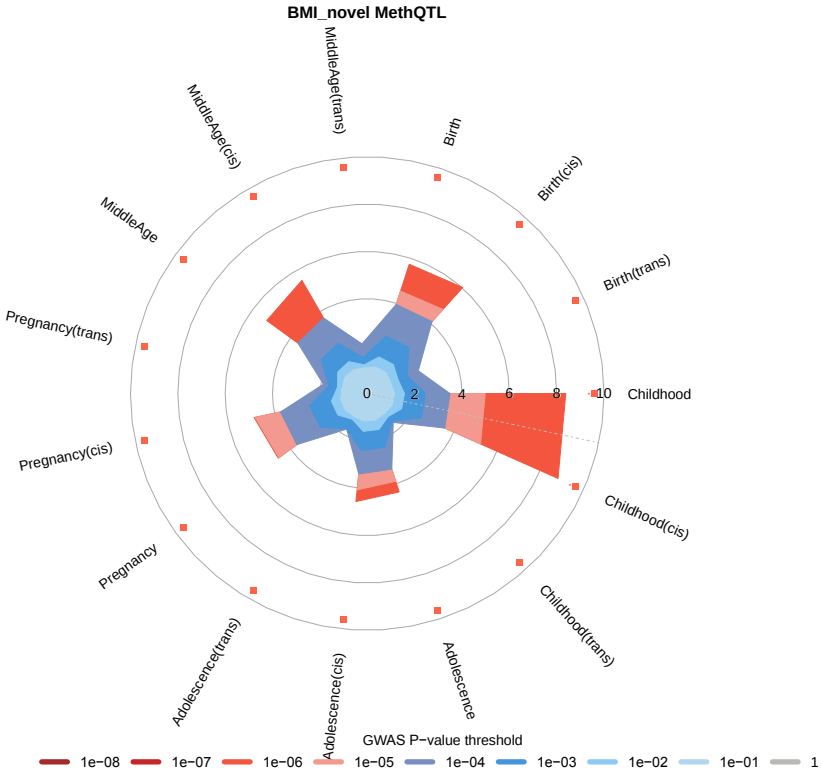


Figure S29: Garfield plots for mQTL enrichment.
Radial plots show the fold enrichment for each time-point where methylation profiles were measured at different GWAS significance thresholds. Small dots on the outer side of the plots show if the observed enrichment is significant for thresholds 10^{-5}, 10^{-6}, 10^{-7}, 10^{-8} in direction from outside to inside.

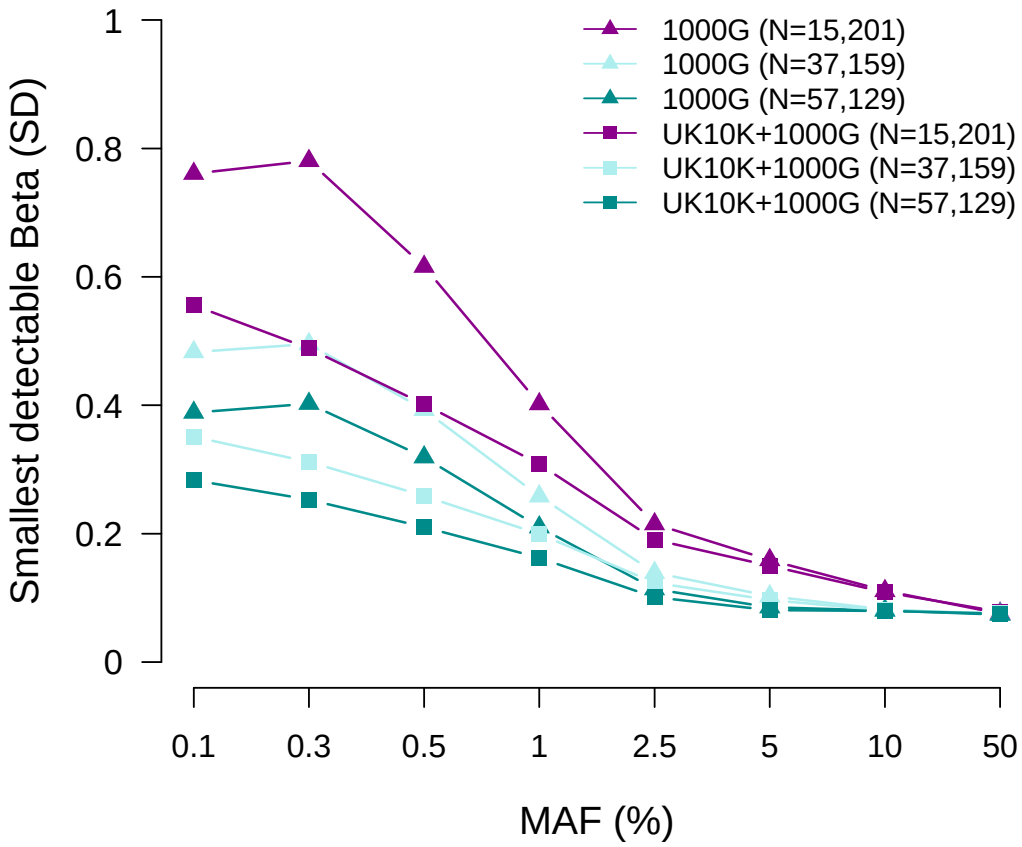
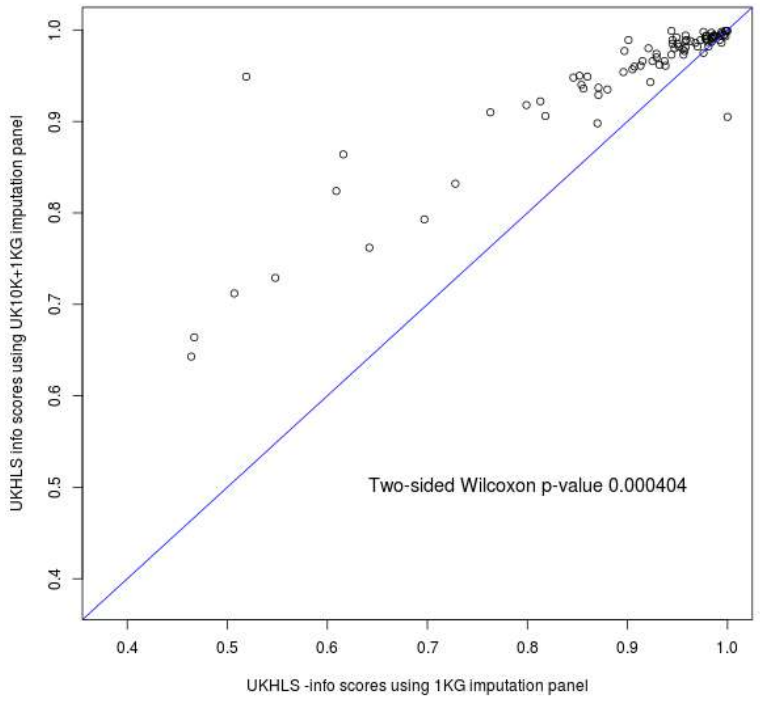


Figure S30: Power benefits due to imputation with UK10K+1000GP compared to 1000GP alone. Strength of single-variant associations detectable at 80% power as a function of Minor Allele Frequency (MAF) and sample size. Using data from chromosome 20, we calculated the smallest value of the strength of association beta (measured in standard deviations), that would be detectable under a linear dosage model at the genome-wide significance threshold ($P<1.85 \times 10^{-9}$), given the MAF and r^2 of each variant imputable from both the 1000GP and the UK10K+1000GP reference panels, for three representative sample sizes of our discovery stage (N=15,201 representing TFM, TLM, TRFM; N=37,159 representing WHR and hip circumference adjusted/unadjusted for BMI; and N=57,129 representing height, BMI, weight, waist circumference adjusted/unadjusted for BMI). The averages of these minimum detectable beta values by MAF and sample size are shown.



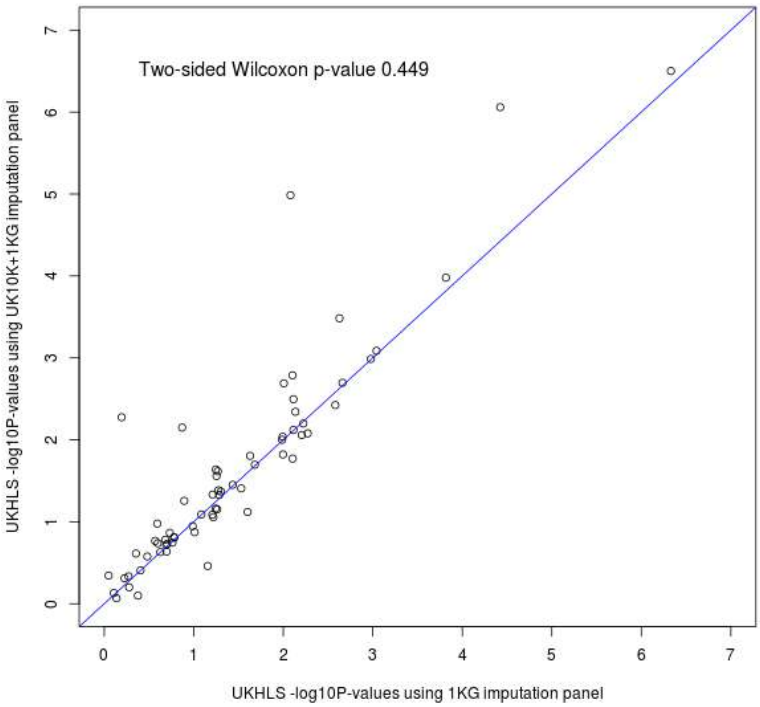
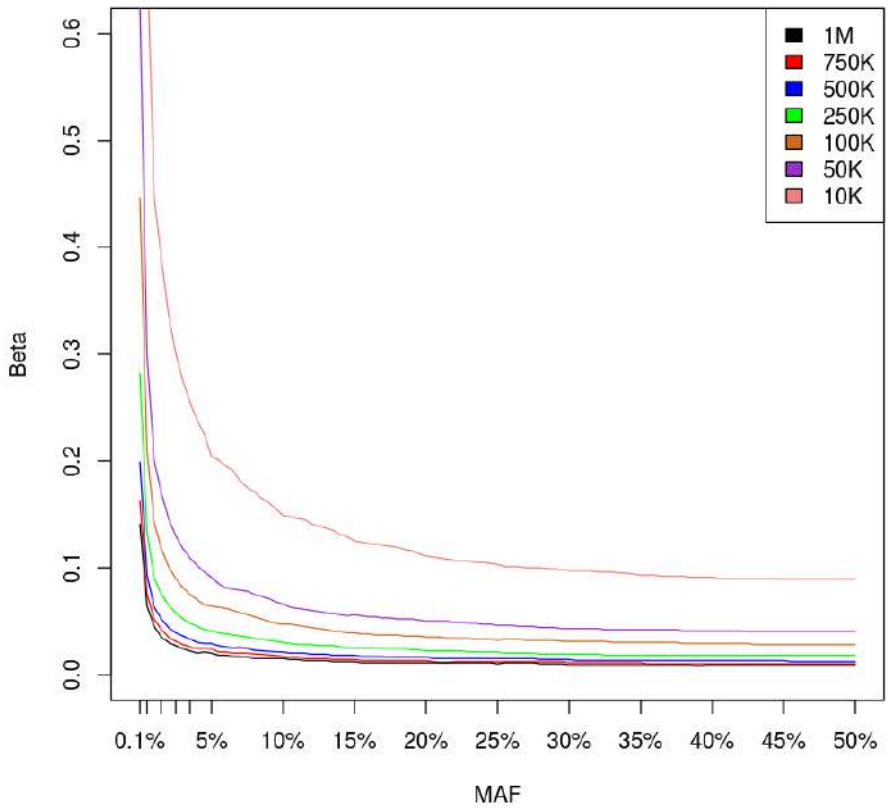


Figure S31: Imputation accuracy scores (top) and *P-values* (bottom) of variants imputed in UKHLS using UK10K+1000GP compared to 1000GP alone.



Effect size	MAF											
Sample size	**0.001**	**0.01**	**0.05**	**0.1**	**0.15**	**0.2**	**0.25**	**0.3**	**0.35**	**0.4**	**0.45**	**0.5**
10K	1.407	0.447	0.204	0.149	0.125	0.111	0.103	0.097	0.093	0.091	0.089	0.089
50K	0.63	0.2	0.091	0.066	0.056	0.05	0.046	0.043	0.042	0.041	0.04	0.04
100K	0.446	0.142	0.064	0.047	0.039	0.035	0.032	0.031	0.03	0.029	0.028	0.028
250K	0.282	0.09	0.041	0.03	0.025	0.022	0.021	0.019	0.019	0.018	0.018	0.018
500K	0.199	0.063	0.029	0.021	0.018	0.016	0.015	0.014	0.013	0.013	0.013	0.012
750K	0.163	0.052	0.024	0.017	0.014	0.013	0.012	0.011	0.011	0.01	0.01	0.01
1M	0.141	0.045	0.02	0.015	0.012	0.011	0.01	0.009	0.009	0.009	0.009	0.009

Figure S32: Effect sizes detectable with 80% power at the genome-wide significance threshold, *P*<5x10^{-8}, as a function of minor allele frequencies and sample size.

Trait	BMI	Weight	Height	TFM	TLM	TRFM	Waist	Hip	WHR	WaistBMIadj	HipBMIadj	WHRBMIadj
ALSPAC WGS	1791	1812	1794	1683	1683	1683	1807	1808	1806	1785	1786	1784
TwinsUK WGS	1747	1747	1747	1716	1716	1716	1265	1266	1265	1265	1266	1265
ALSPAC GWA	4101	4132	4103	3815	3815	3815	4121	4115	4116	4121	4115	4116
TwinsUK GWA	3539	3539	3540	3275	3275	3275	2585	2582	2582	2583	2580	2580
1958 Birth Cohort	8015	8053	8080	--	--	--	8106	8091	8105	8027	8014	8025
INGI Friuli Venezia Giulia	1170	1172	1197	--	--	--	791	701	791	790	831	790
INCIPE 1	934	933	937	--	--	--	934	--	--	932	--	--
INCIPE 2	2035	2056	2056	--	--	--	2050	--	--	2043	--	--
LURIC	1569	1570	1570	--	--	--	1546	1547	1543	1546	1547	1543
Rotterdam 1	5954	5970	5961	2387	2386	2513	5665	5660	5660	5565	5561	5561
Rotterdam 2	2148	2148	2151	747	747	747	1938	1937	1937	1935	1934	1934
Rotterdam 3	3017	3017	3018	1578	1578	2488	2930	2931	2928	2919	2921	2917
TEENAGE	701	703	703	--	--	--	698	701	697	698	701	697
INGI-Val Borbera	1778	1779	1785	--	--	--	1754	--	--	1754	--	--
INGI Carlantino	472	472	471	--	--	--	397	400	388	397	400	388
HELIC MANOLIS	1019	1051	1043	--	--	--	1060	1050	1053	1005	998	1001
HELIC Pomak	932	942	933	--	--	--	887	883	879	875	871	867
arcOGEN	3908	3923	3925	--	--	--	--	--	--	--	--	--
UKHLS	8560	8620	8700	--	--	--	8727	--	--	8513	--	--
FINRISK	1249	1249	1249	--	--	--	1254	1254	1254	1247	1247	1247
LOLIPOP_EW610	915	916	927	--	--	--	914	916	919	909	909	909
LOLIPOP_EW_A	589	589	589	--	--	--	587	587	587	587	587	587
LOLIPOP_EW_P	650	650	650	--	--	--	649	649	649	649	649	649
Total discovery (stage 1)	**56793**	**57043**	**57129**	**15201**	**15200**	**16237**	**50665**	**37078**	**37159**	**50145**	**36917**	**36860**
Fenland	9101	9103	9106	8662	8661	8662	9100	9079	9082	9094	9077	9076
Copenhagen	28710	28736	28745	--	--	--	28687	28668	28677	28643	28631	28632
GenerationR	--	--	--	2008	2015	2005	--	--	--	--	--	--
SardiNIA	6481	6480	6480	--	--	--	6483	6481	6481	6483	6481	6481
GoT2D	32022	--	27544	--	--	--	29328	28680	28686	29320	28678	28684
UK Biobank	134509	134570	134798	--	--	--	134798	134650	134795	134584	134455	134594
Total follow-up (stage 2)	**210823**	**178889**	**206673**	**106701**	**106761**	**106672**	**208396**	**207558**	**207721**	**208124**	**207322**	**207467**
Total discovery + follow-up (stage 1 + stage 2)	**267616**	**235932**	**263802**	**258712**	**258762**	**269042**	**259061**	**244636**	**244880**	**258269**	**244239**	**244327**

BMI: body mass index; WHR: waist to hip ratio; WaistBMIadj: waist circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass

Table S1: Sample sizes for the 12 anthropometric traits studied

Trait	Independent known variants	Same direction of effect	Binomial test *P*	Source of known variants
BMI	97	96	$<2.2\times10^{-16}$	Locke et al 2015
Weight	14	14	6.1×10^{-5}	Thorleifsson et al 2009
Height	619	610	$<2.2\times10^{-16}$	Wood et al 2015
TFM	12	12	2.44×10^{-4}	Lu et al 2016
Waist	45	44	1.31×10^{-12}	Shungin et al 2015
Hip	63	61	$<2.2\times10^{-16}$	Shungin et al 2015
WHR	28	27	1.08×10^{-7}	Shungin et al 2015
WaistBMIadj	70	70	$<2.2\times10^{-16}$	Shungin et al 2015
HipBMIadj	89	89	$<2.2\times10^{-16}$	Shungin et al 2015
WHRBMIadj	39	39	1.82×10^{-12}	Shungin et al 2015

BMI: body mass index; WHR: waist to hip ratio; WaistBMIadj: waist circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass

Table S13: Comparison of direction of effect between betas from our discovery phase and known loci. There are 28 variants reported for weight in Table 2 of Thorleifsson et al 2009, 14 of which are independent of each other ($r^2<0.2$ and 500 kb away from each other). From the 697 variants associated with height by Wood et al 2015, we kept the ones that were GWAS significant from the single-point analysis (623 remained) and we further excluded 4 non-distinct signals ($r^2>0.2$ within 500 kb). For body shape phenotypes, we also took forward independent variants identified in European and sex-combined samples from Shungin et al 2015.

Cohorts	N of duplicate pairs (pi-hat>0.98)	N of related pairs (pi-hat>0.2)	N of total pairs (N1 x N2)
1958 Birth Cohort vs UKBB	40	178	5,847x138,990
arcOGEN vs UKBB	63	194	2,762x138,990
GWAS TwinUK vs UKBB	68	243	3,980x138,990
UKHLS vs UKBB	88	450	9,175x138,990
WGS TwinsUK vs UKBB	43	117	1,754x138,990
Total	302	1,182	3,268,766,820

Table S19: Number of overlapping (pi-hat > 0.98) and related (pi-hat > 0.2) pairs between UK-based cohorts and UK Biobank (UKBB).

	Independent number of suggestive associations	Opposite Direction of Effects with BMI or Height	Proportion (%)	Binomial P-value
WaistBMIadj	146	77	52.74	0.280
HipBMIadj	155	57	36.77	1.000
WHRBMIadj	86	49	56.98	0.118
TFM	79	29	36.71	0.994
TLM	79	40	50.63	0.500
TRFM	82	33	40.24	0.970

WaistBMIadj: waist circumference adjusted for BMI; HipBMIadj: hip circumference adjusted for BMI; WHRBMIadj: waist to hip ratio adjusted for BMI; TFM: total fat mass; TLM: total lean mass; TRFM: trunk fat mass

Table S21: No evidence of collider bias for waist circumference adjusted for BMI analysis.
Number of independent (pairwise r^2<0.2 and further than 500kb) variants associated with WaistBMIadj, HipBMIadj, WHRBMIadj, TFM, TLM, TRFM in the discovery meta-analysis with *P-value*<10^{-5}; number and proportion of those variants that had opposite direction of effects for WaistBMIadj, HipBMIadj, WHRBMIadj versus effect sizes for BMI and TFM, TLM, TRFM versus Height; binomial *P-value* of significance.

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