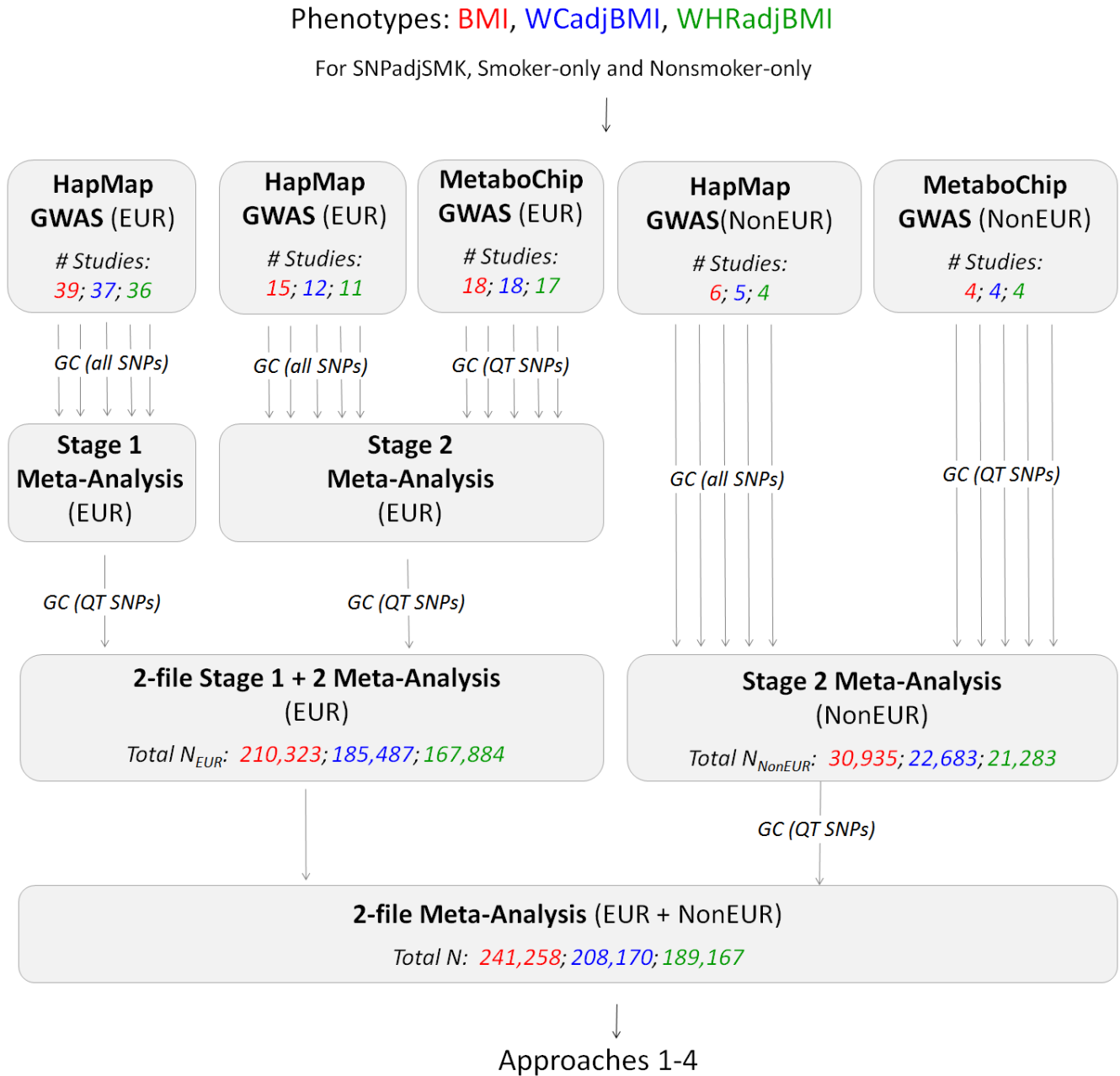
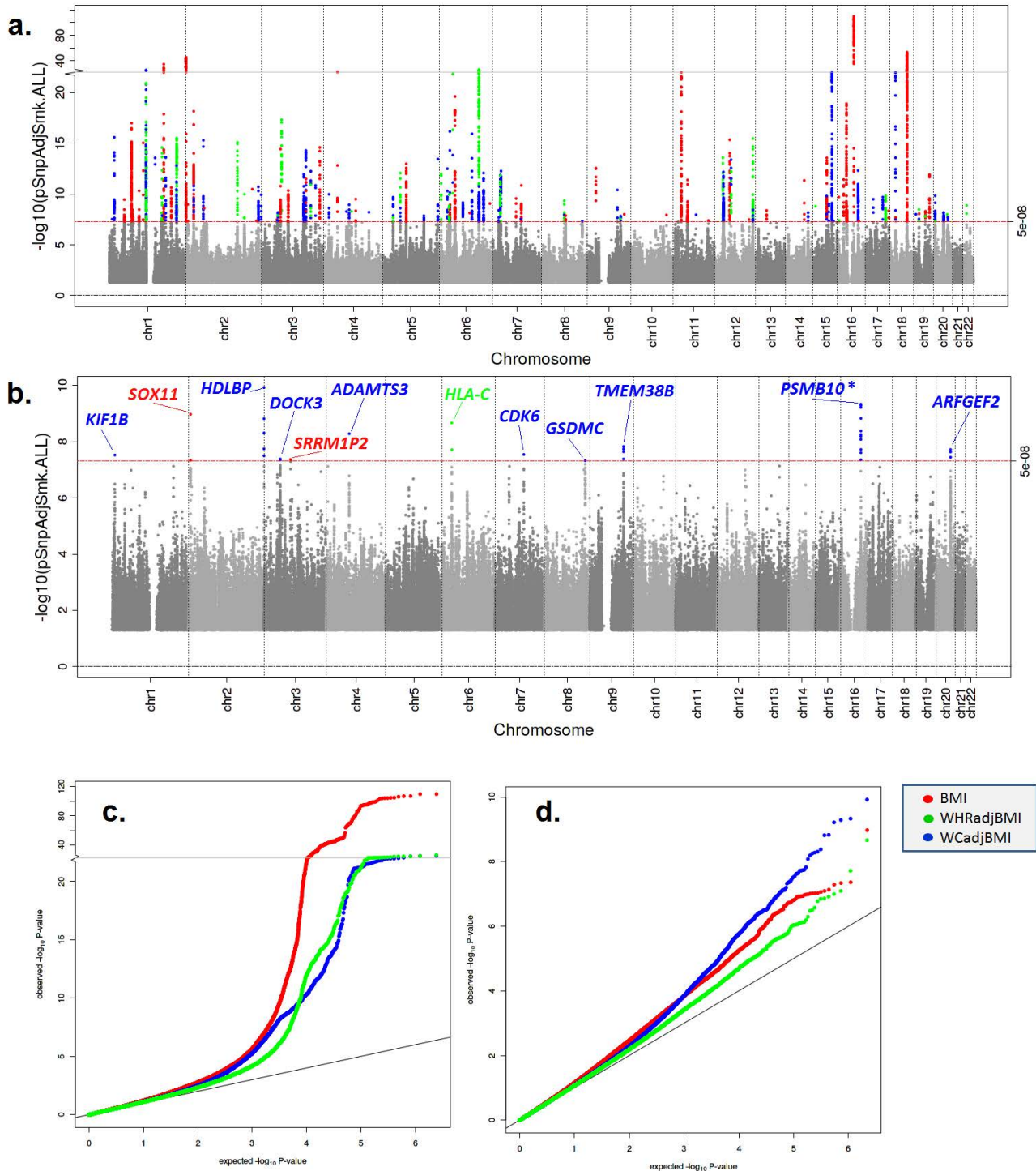


**Supplementary Figure 1. Summary of overall study design and workflow for meta-analyses.** All numbers provided represent the maximum number specific for that trait (BMI-red, WCadjBMI-blue, and WHRadjBMI-green) and strata (EUR-European descent participants, nonEUR-excluding European descent participants). Three studies provided GWAS data for EUR and nonEUR participants.

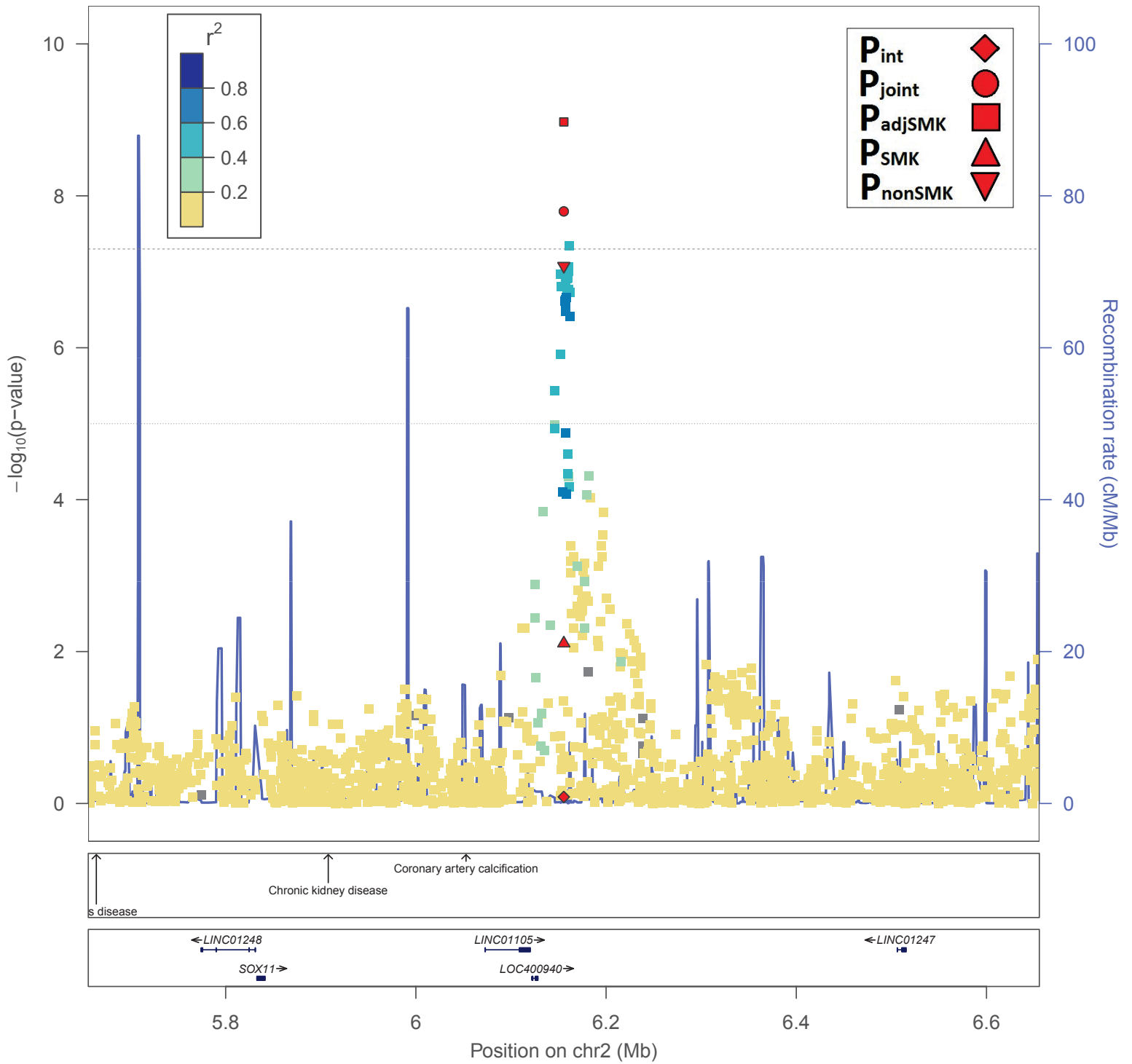


**Supplementary Figure 2. Summary plots of discovery meta-analysis for Approach 1 primary meta-analyses. (a)** Manhattan plot showing the loci identified in Approach 1 in primary meta-analyses, used to identify significant main effects loci (SNPadjSMK), in the primary meta-analyses association  $-\log_{10}$ P-values for BMI-red, WCadjBMI-blue, and WHRadjBMI-green; **(b)** Manhattan plot showing the loci identified in Approach 1 excluding known regions  $\pm 500$  kb and labeled with the nearest gene to the index SNP; **(c)** QQ-plot showing the Approach 1 P-values as observed against those expected under the null for each phenotypes separately (colored); **(d)** QQ-plot for Approach 1 after excluding known association regions. \**PSMB10* locus is  $>500$   $\pm$  kb from previously identified index SNPs, but is not independent of known GWAS signals.

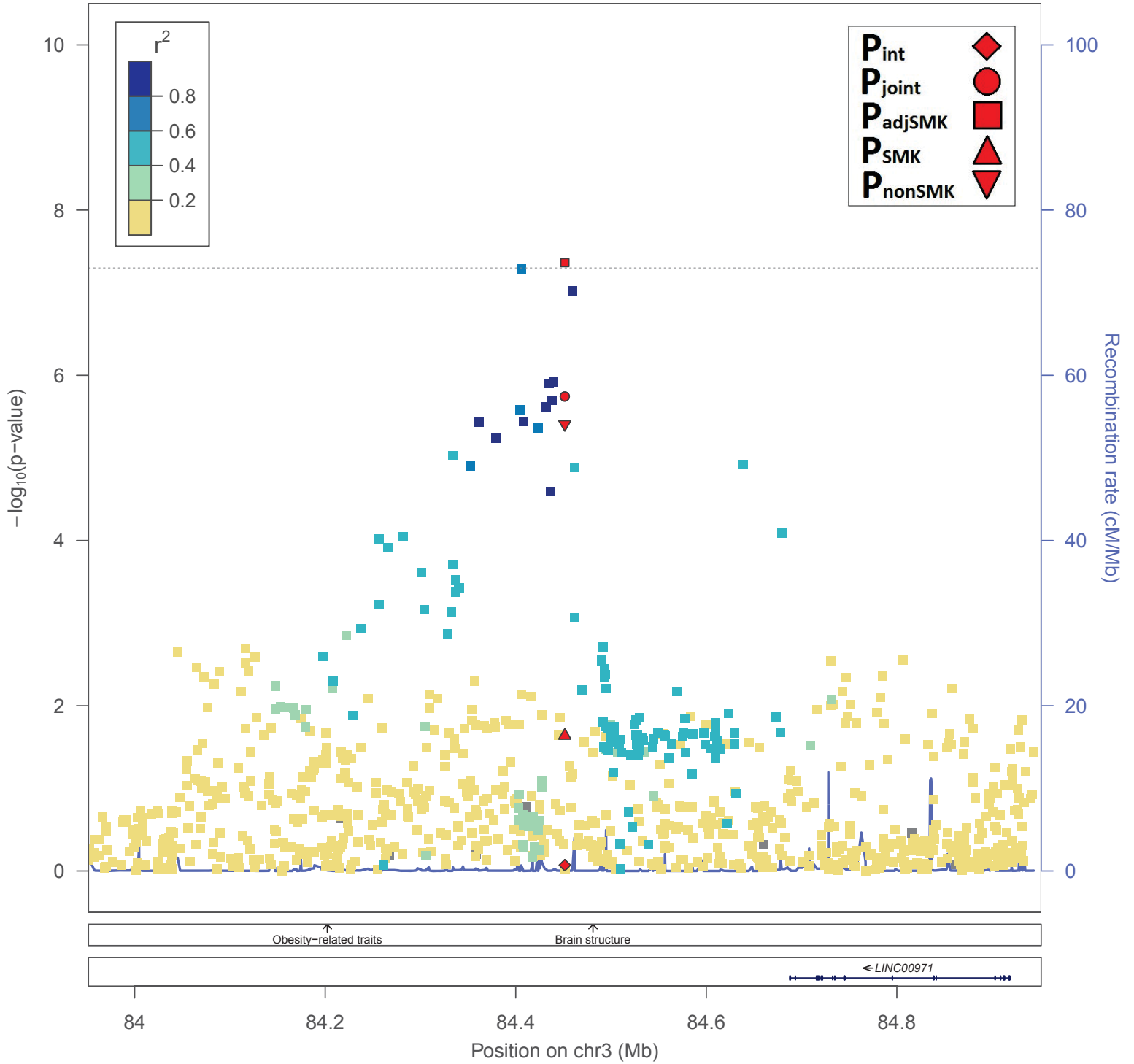


**Supplementary Figure 3. Regional association plots for Approach 1 primary meta-analyses.** Regional association plots for all novel loci identified in Approach 1 (SNP<sub>adjSMK</sub>) in primary meta-analyses for BMI: (a) rs10929925, (b) rs6794880; WC<sub>adjBMI</sub>: (c) rs17396340, (d) rs6743226, (e) rs4378999, (f) rs7697556, (g) rs10269774, (h) rs6470765, (i) rs9409082, (j) rs6012558; and WHR<sub>adjBMI</sub>: (k) rs1049281, and ordered as they appear in Table 1. LD has been calculated using the combined ancestries from the 1000 Genomes Phase 1 reference panel. For comparison, each plot highlights the p-value for the tag SNP in Approach 1 ( $P_{\text{adjSMK}}$ ), Approach 2 ( $P_{\text{joint}}$ ), Approach 3 ( $P_{\text{int}}$ ), current smokers ( $P_{\text{SMK}}$ ), and in nonsmokers ( $P_{\text{nonSMK}}$ ).

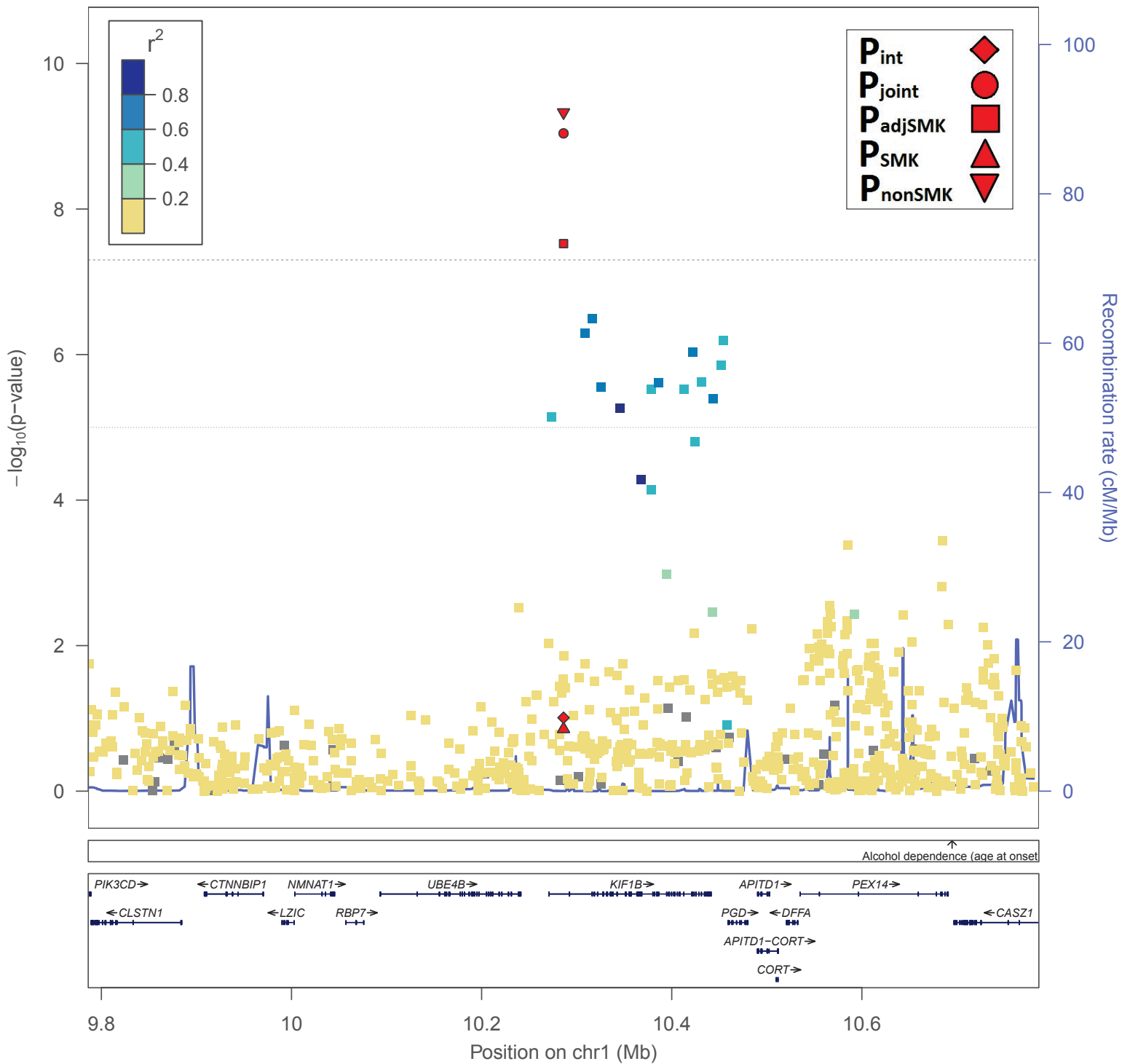
a. BMI: rs10929925



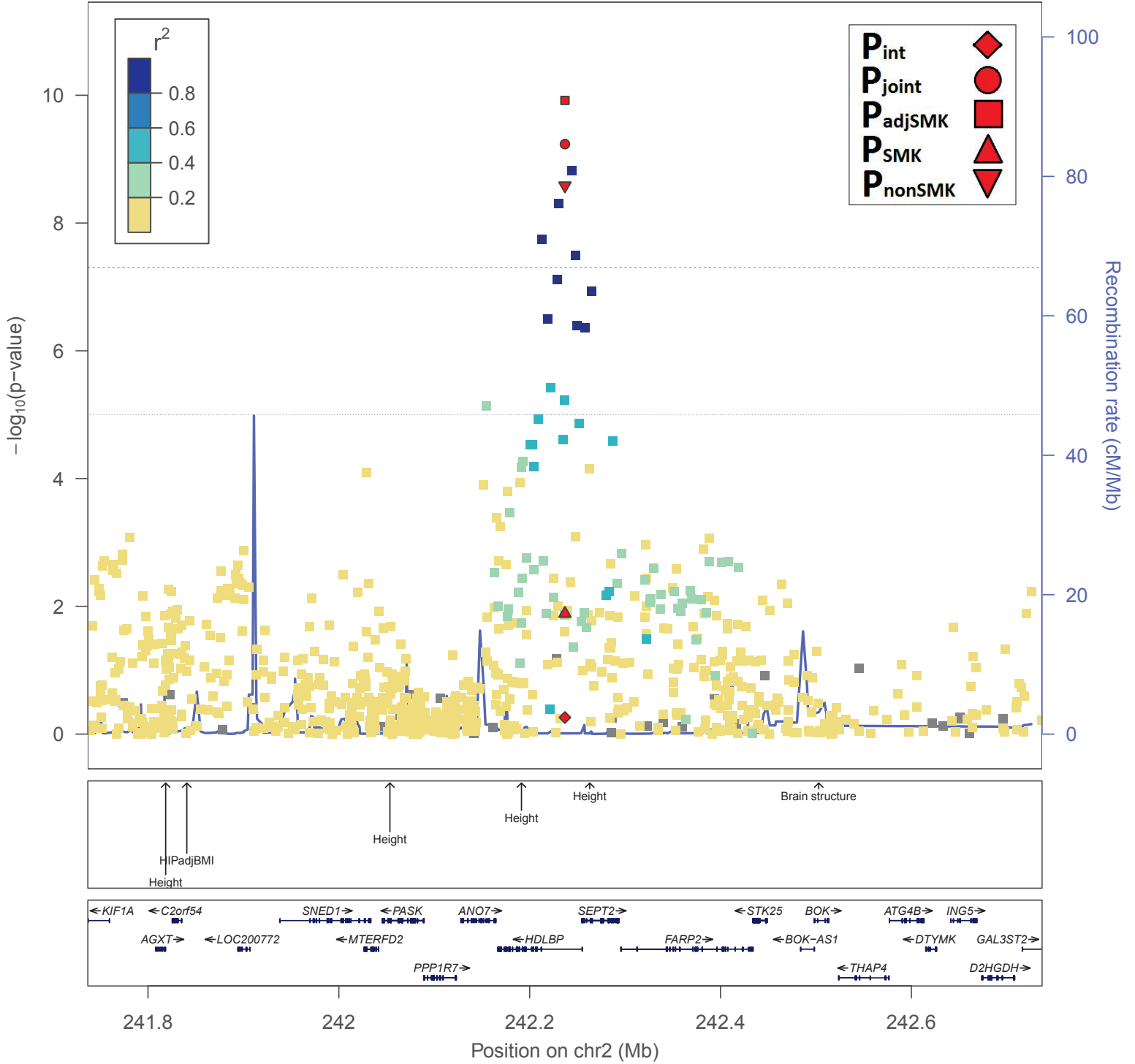
b. BMI: rs6794880



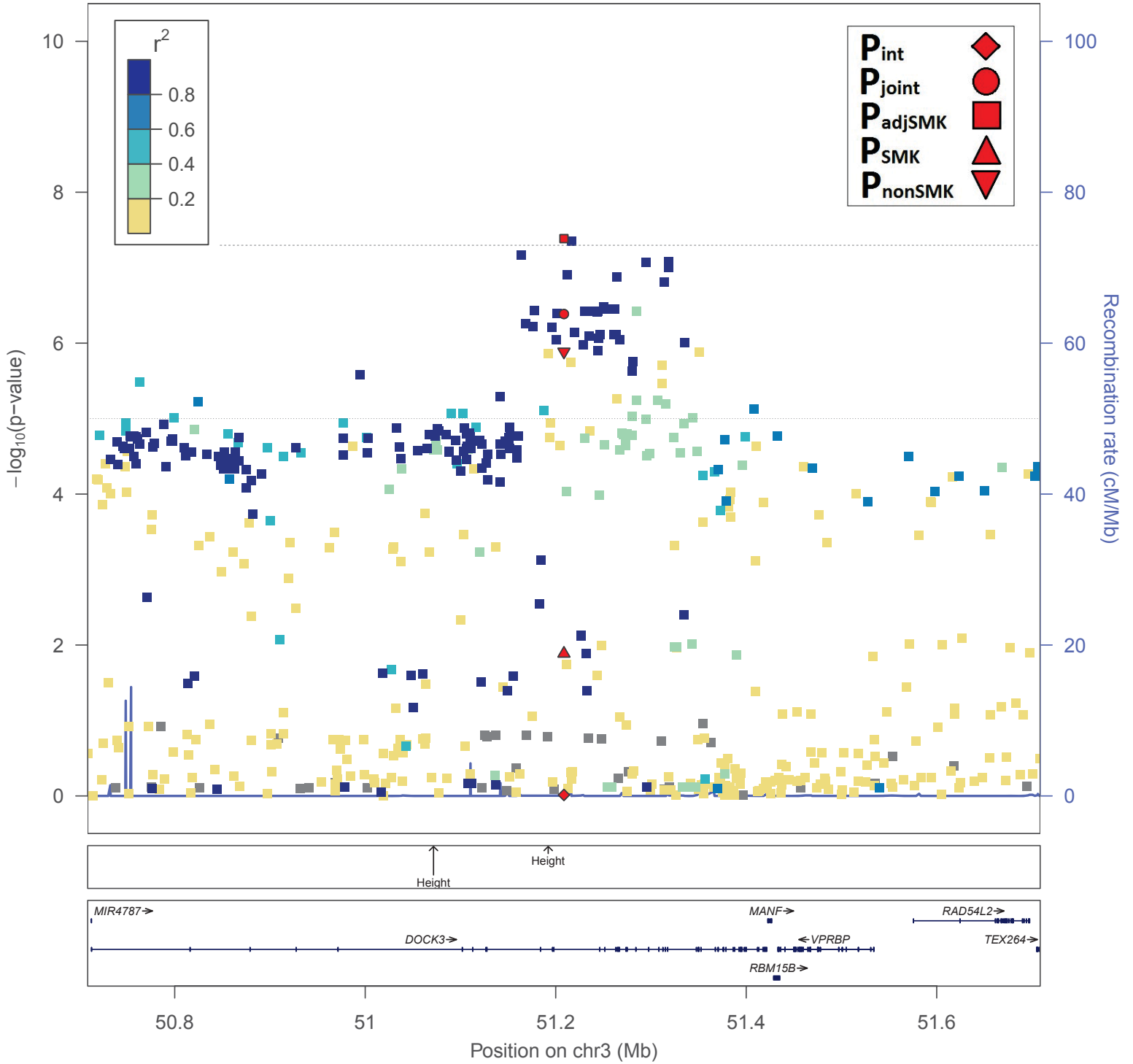
c. WCadjBMI: rs17396340 -  $\alpha$  &  $\beta$



d. WCadjBMI: rs6743226 -  $r^2$  | [  $\alpha$  &  $\beta$  ]

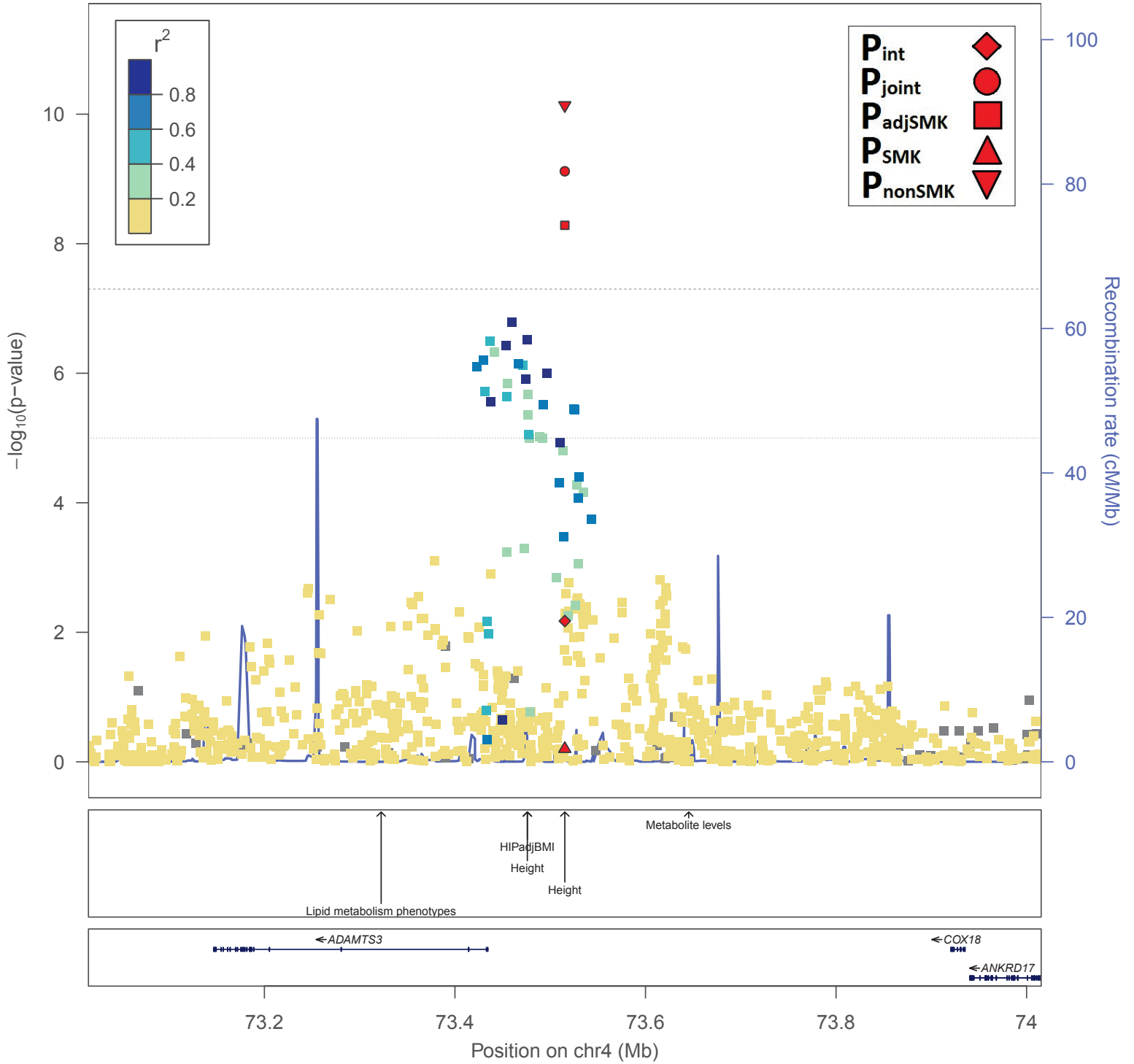


e. WCadjBMI: rs4378999 -  $r^2$  | [  $\alpha$  &  $\beta$  ]

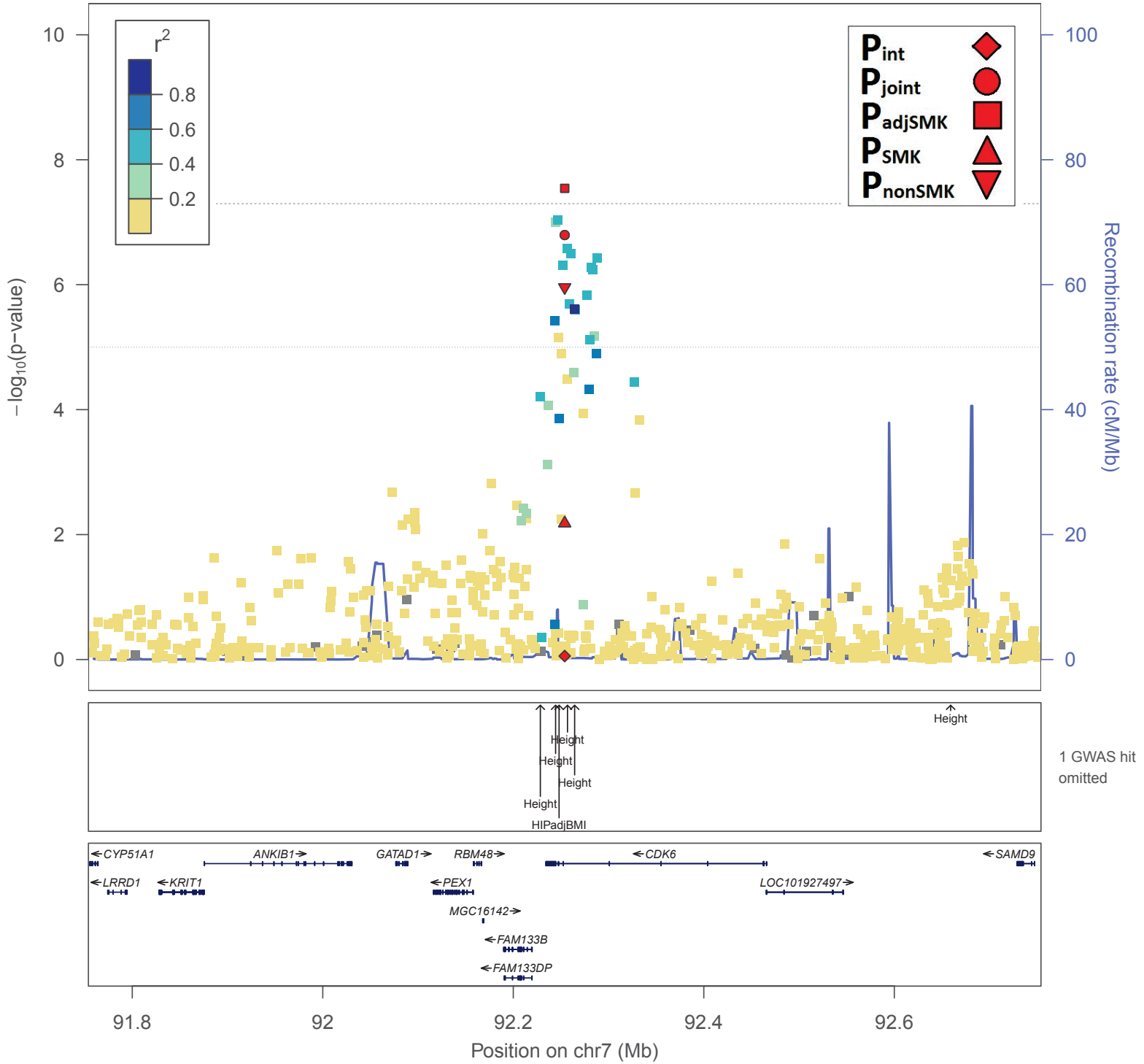




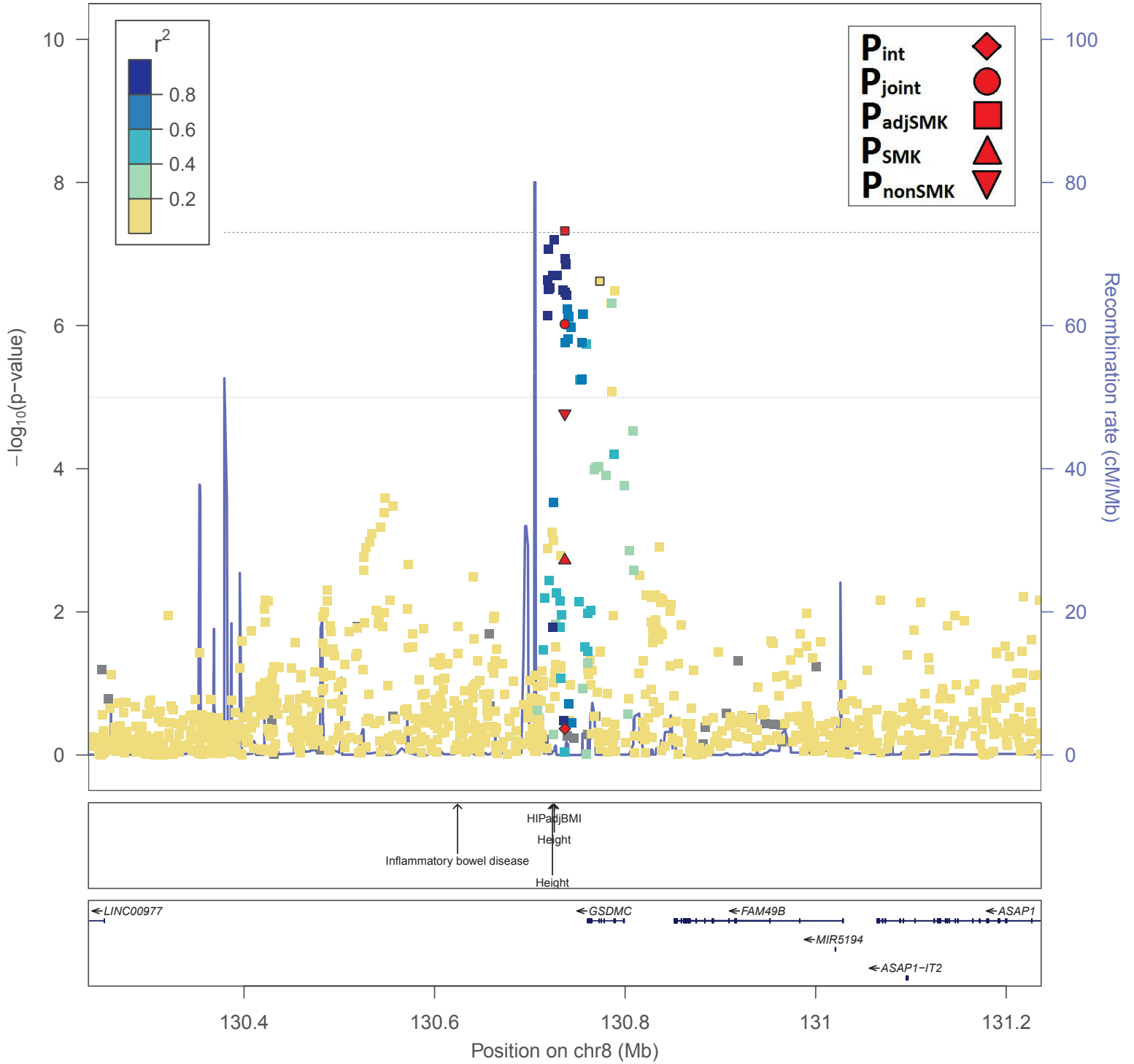
f. WCadjBMI: rs7697556 -  $r^2$  |  $P_{int}$  |  $P_{joint}$  |  $P_{adjSMK}$  |  $P_{SMK}$  |  $P_{nonSMK}$



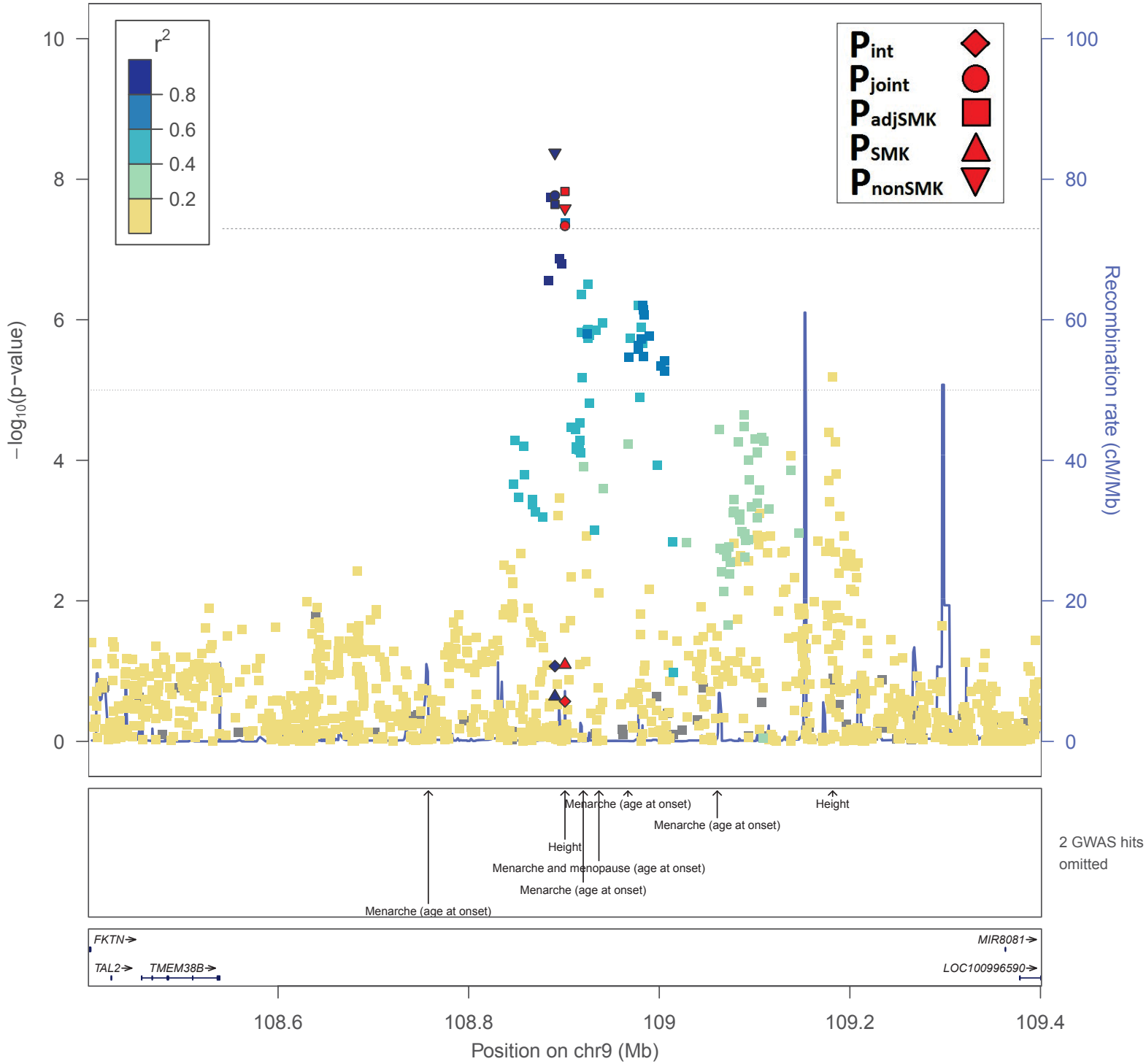
# g. WCadjBMI: rs10269774 - 0.71 | [ a&@A



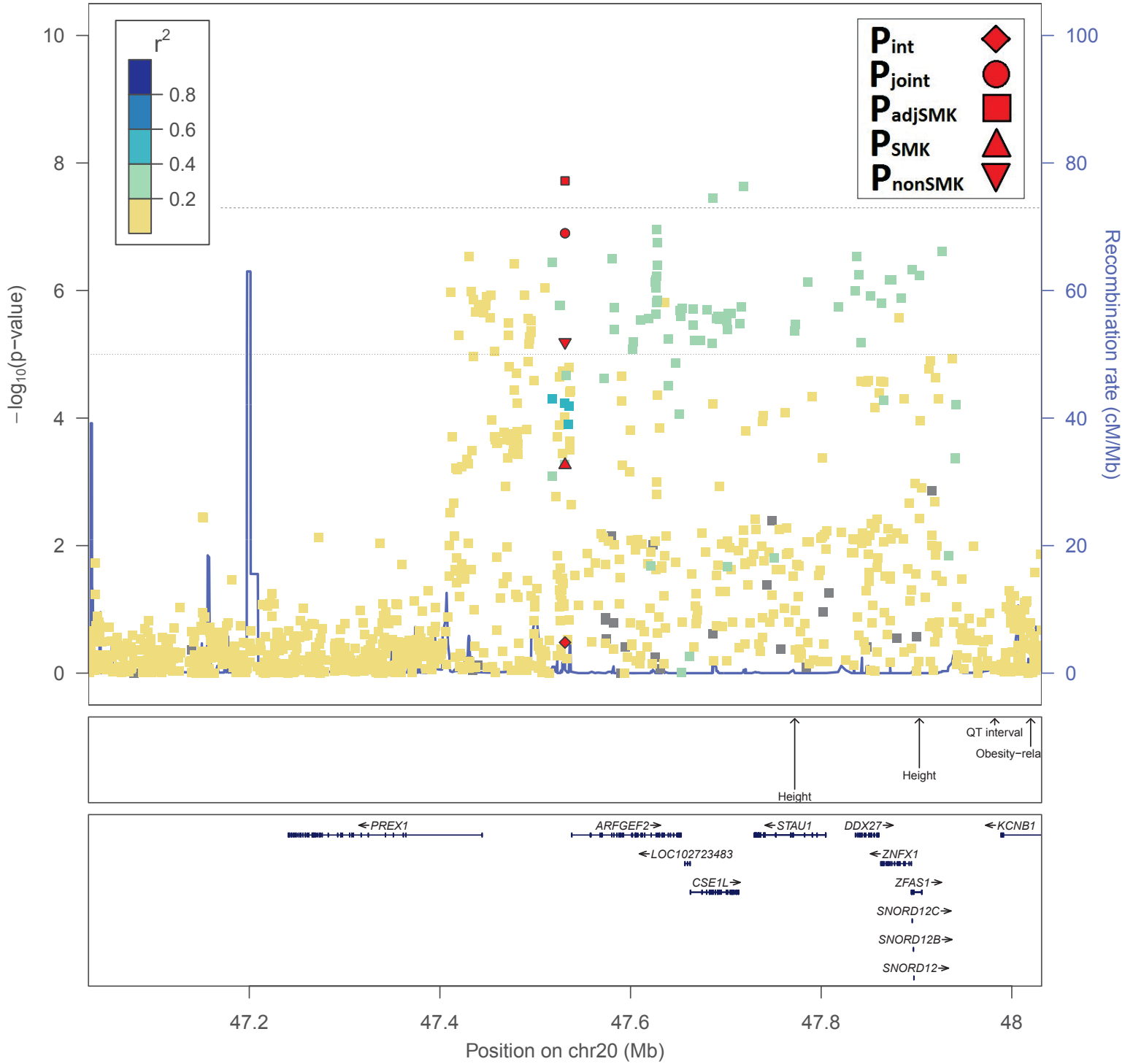
# h. WCadjBMI: rs6470765 - 0.71 [ 0.68 & 0.71



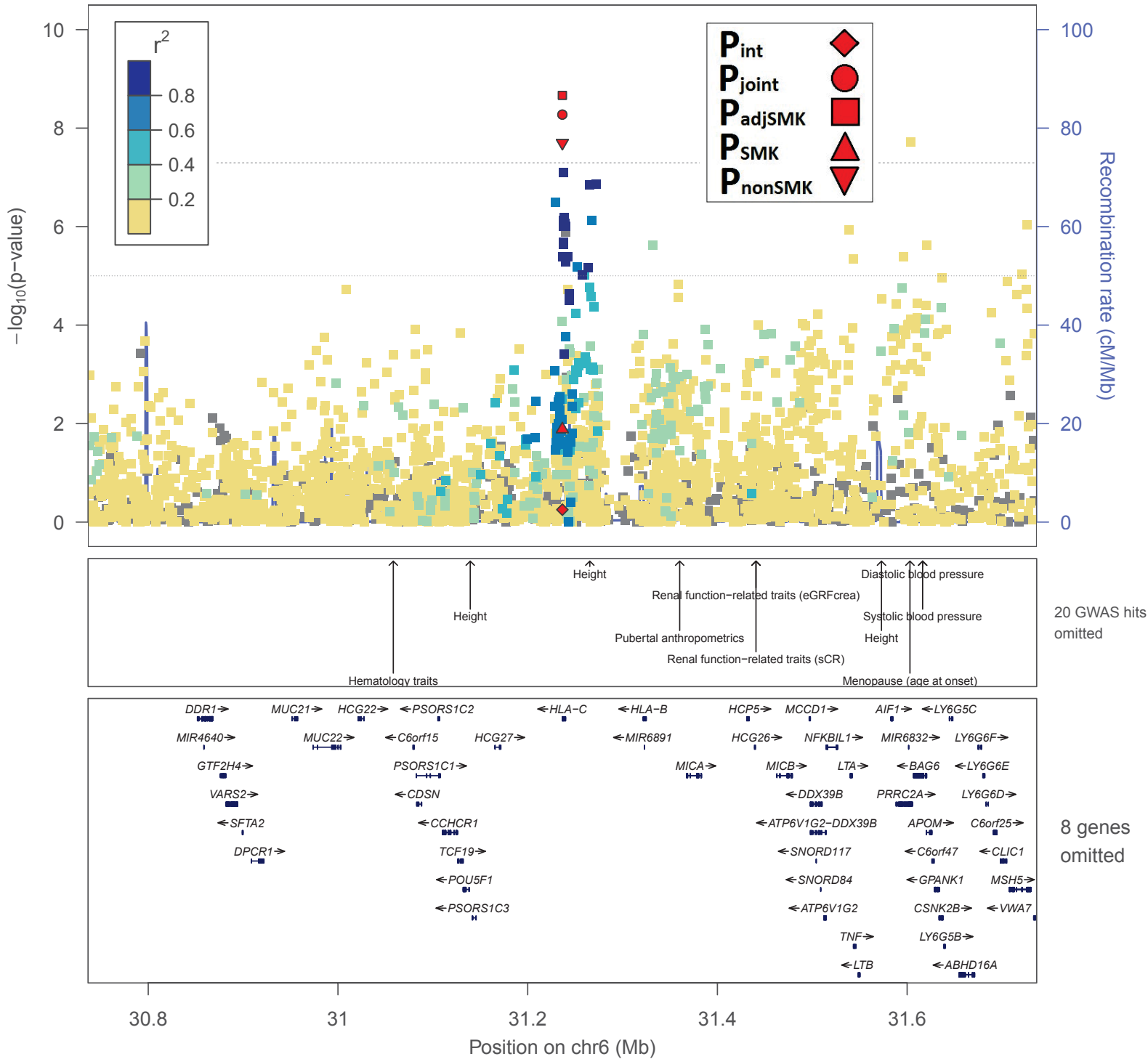
# i. WCadjBMI: rs9409082 - 0.71 [ a&@F



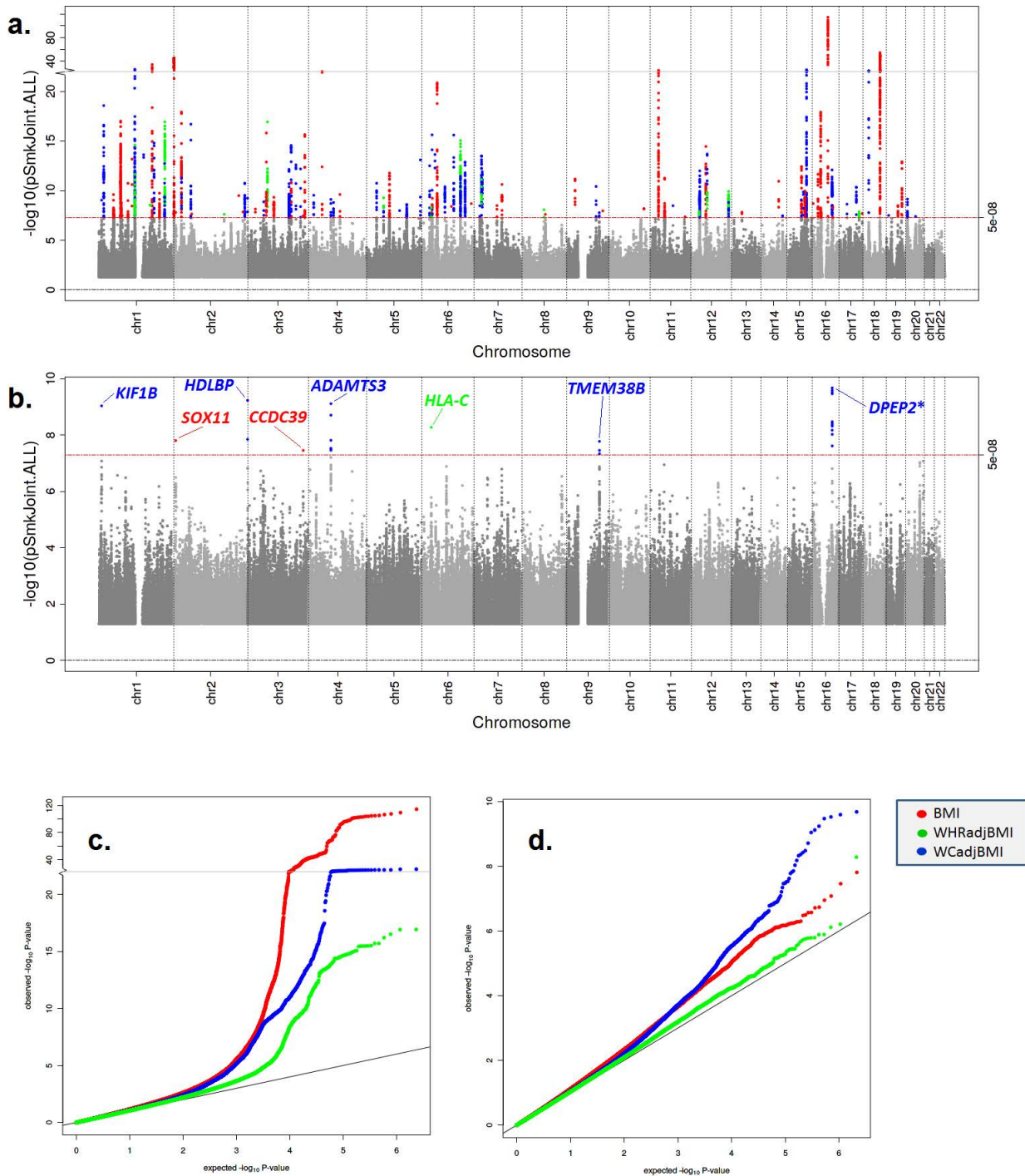
# j. WCadjBMI: rs6012558 - 0.71 | [ a&@A



# k. WHRadjBMI: rs1049281 - 0.71 | r<sup>2</sup> | 0.96



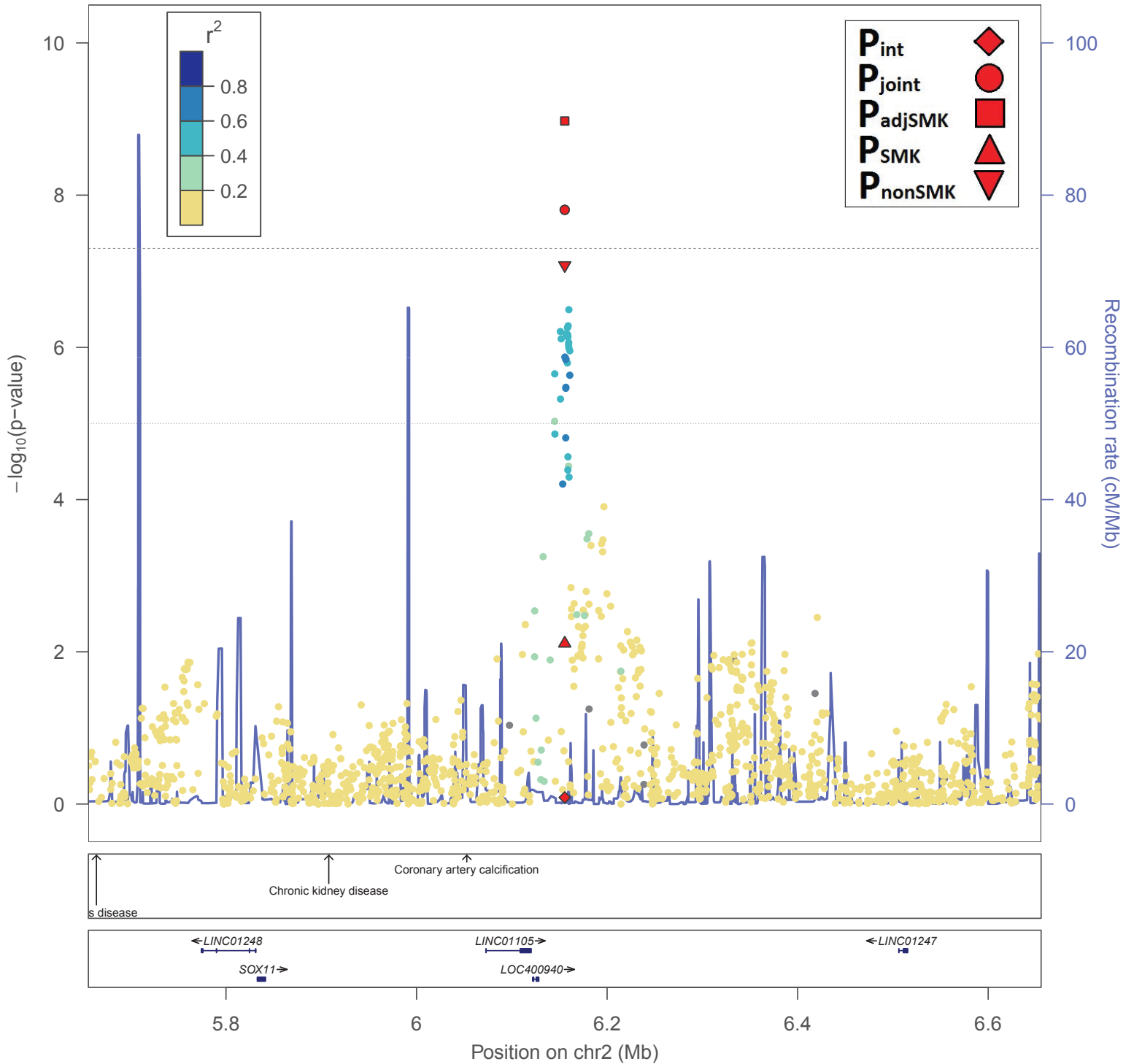
**Supplementary Figure 4. Summary plots of discovery meta-analysis for Approach 2 primary meta-analyses. (a)** Manhattan plot showing the loci identified in Approach 2 in primary meta-analyses, used to identify significant joint main+interaction effects loci (SNPjoint), in the primary meta-analyses association  $-\log_{10}P$ -values for BMI-red, WCadjBMI-blue, and WHRadjBMI-green; **(b)** Manhattan plot showing the loci identified in Approach 2 excluding known regions +/- 500 kb and labeled with the nearest gene to the index SNP; **(c)** QQ-plot showing the Approach 2 P-values as observed against those expected under the null for each phenotypes separately (colored); **(d)** QQ-plot for Approach 2 after excluding known association regions.



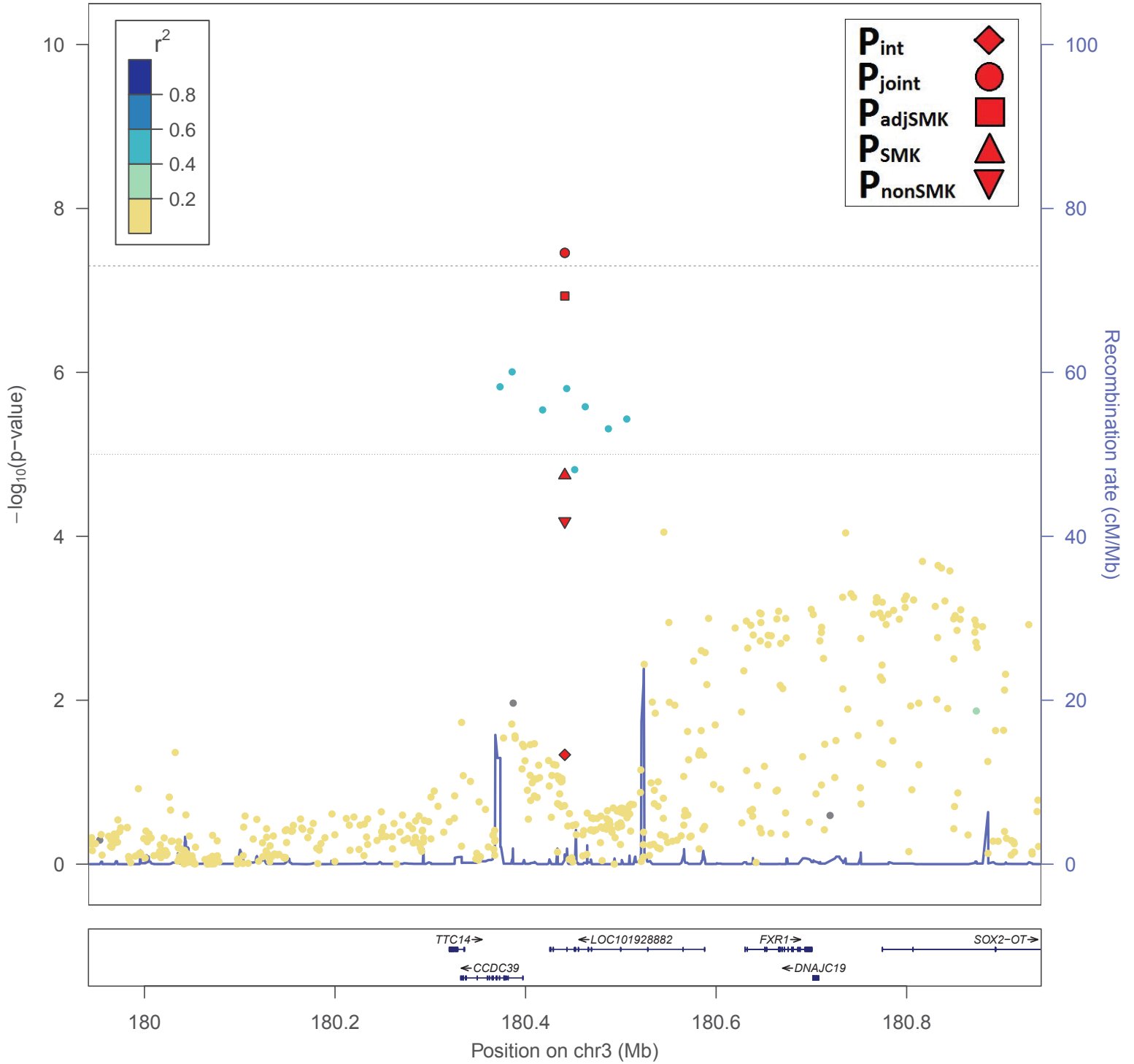
**Supplementary Figure 5. Regional association plots for Approach 2 primary meta-analyses.** Regional association plot for all novel loci identified in Approach 2 (SNPjoint) in the primary meta-analyses for BMI: (a) rs10929925, (b) rs13069244; WCadjBMI: (c) rs17396340, (d) rs6743226, (e) rs7697556, (f) rs9408815, and WHRadjBMI: (g) rs1049281, and ordered as they appear in Table 1. LD has been calculated using the combined ancestries from the 1000 Genomes Phase 1 reference panel. For comparison, each plot highlights the p-value for the tag SNP in Approach 1 ( $P_{\text{adjSMK}}$ ), Approach 2 ( $P_{\text{joint}}$ ), Approach 3 ( $P_{\text{int}}$ ), current smokers ( $P_{\text{SMK}}$ ), and in nonsmokers ( $P_{\text{nonSMK}}$ ).



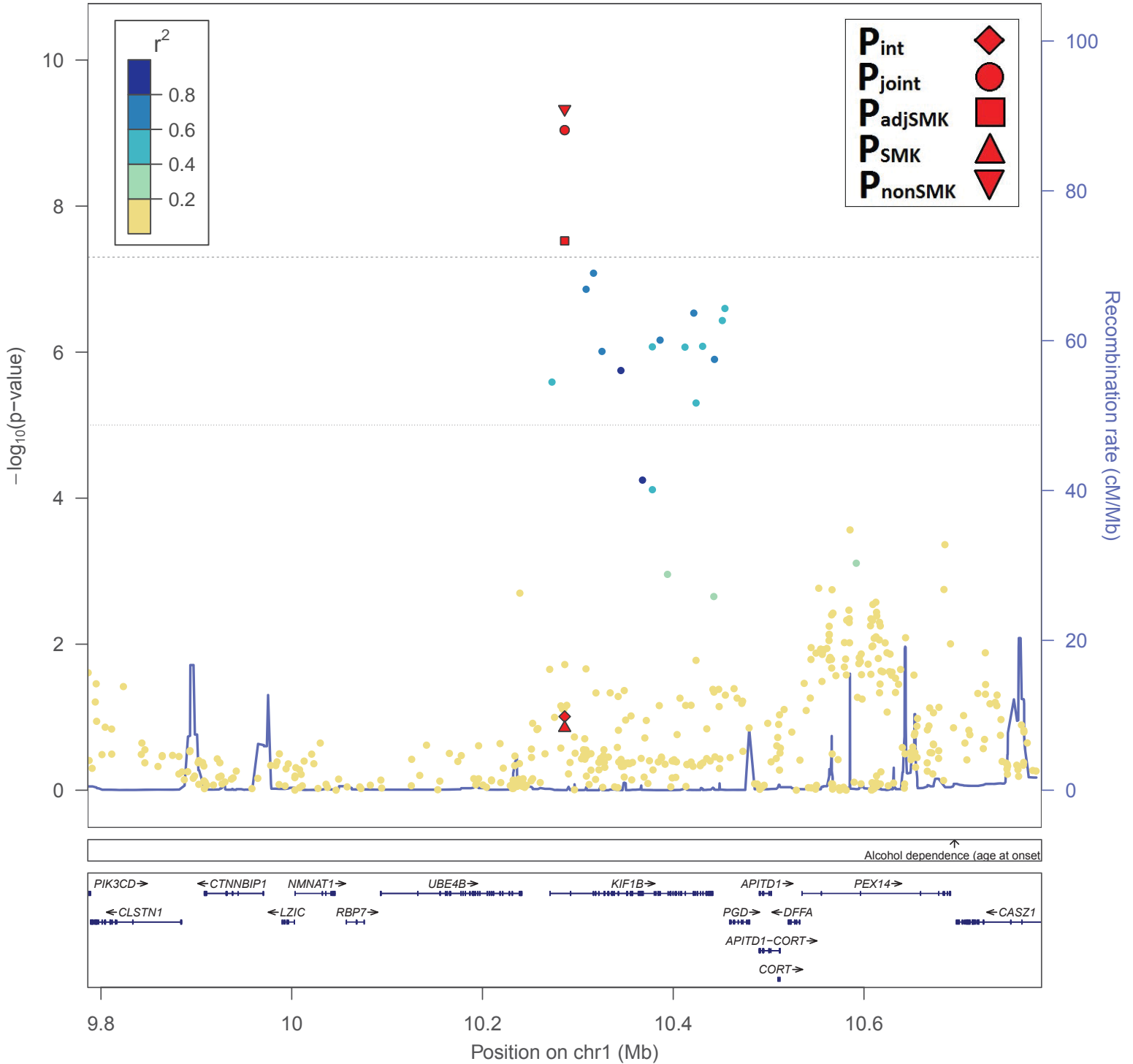
### a. BMI: rs10929925 – Approach 2



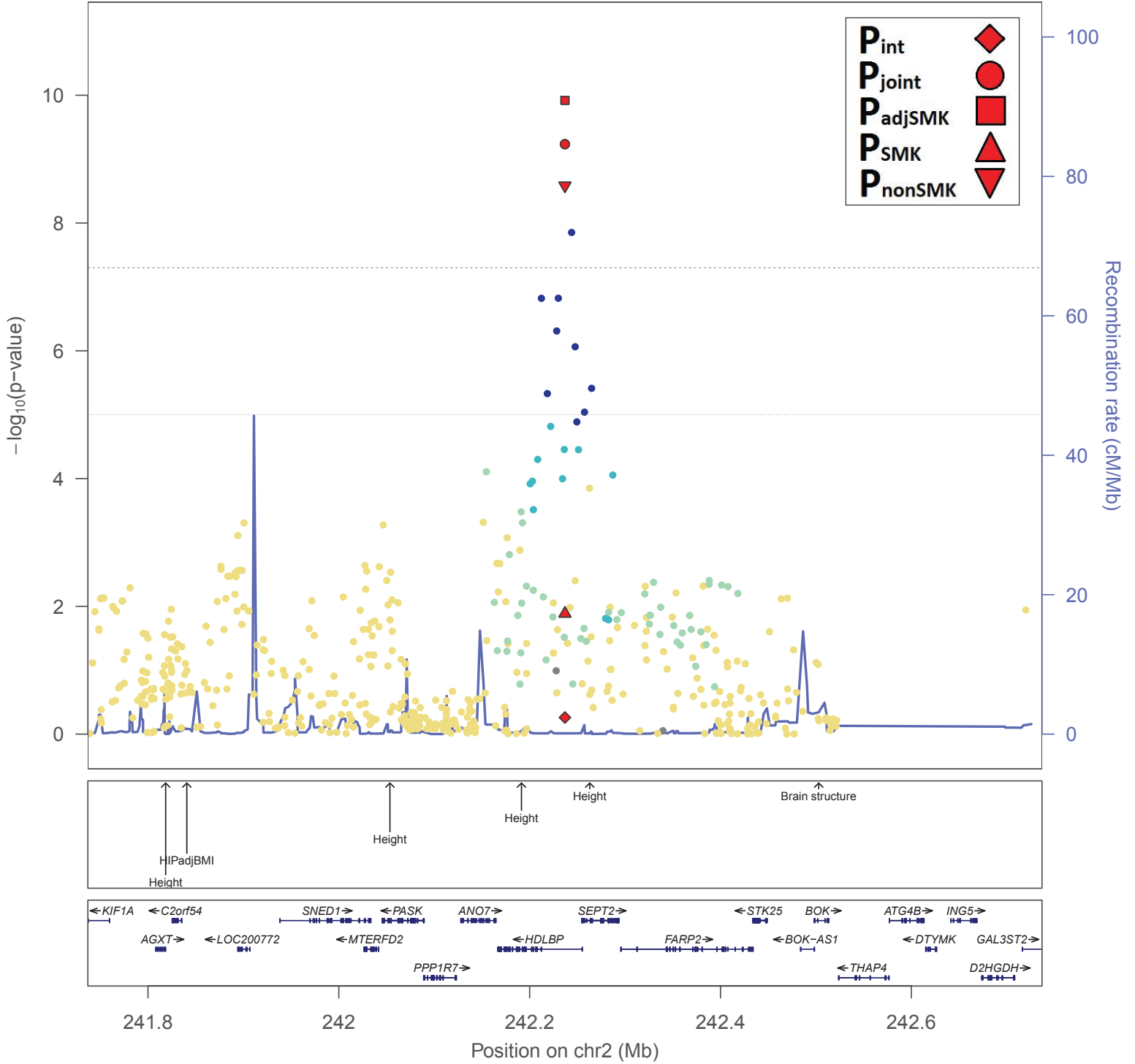
## b. BMI: rs13069244 – Approach 2



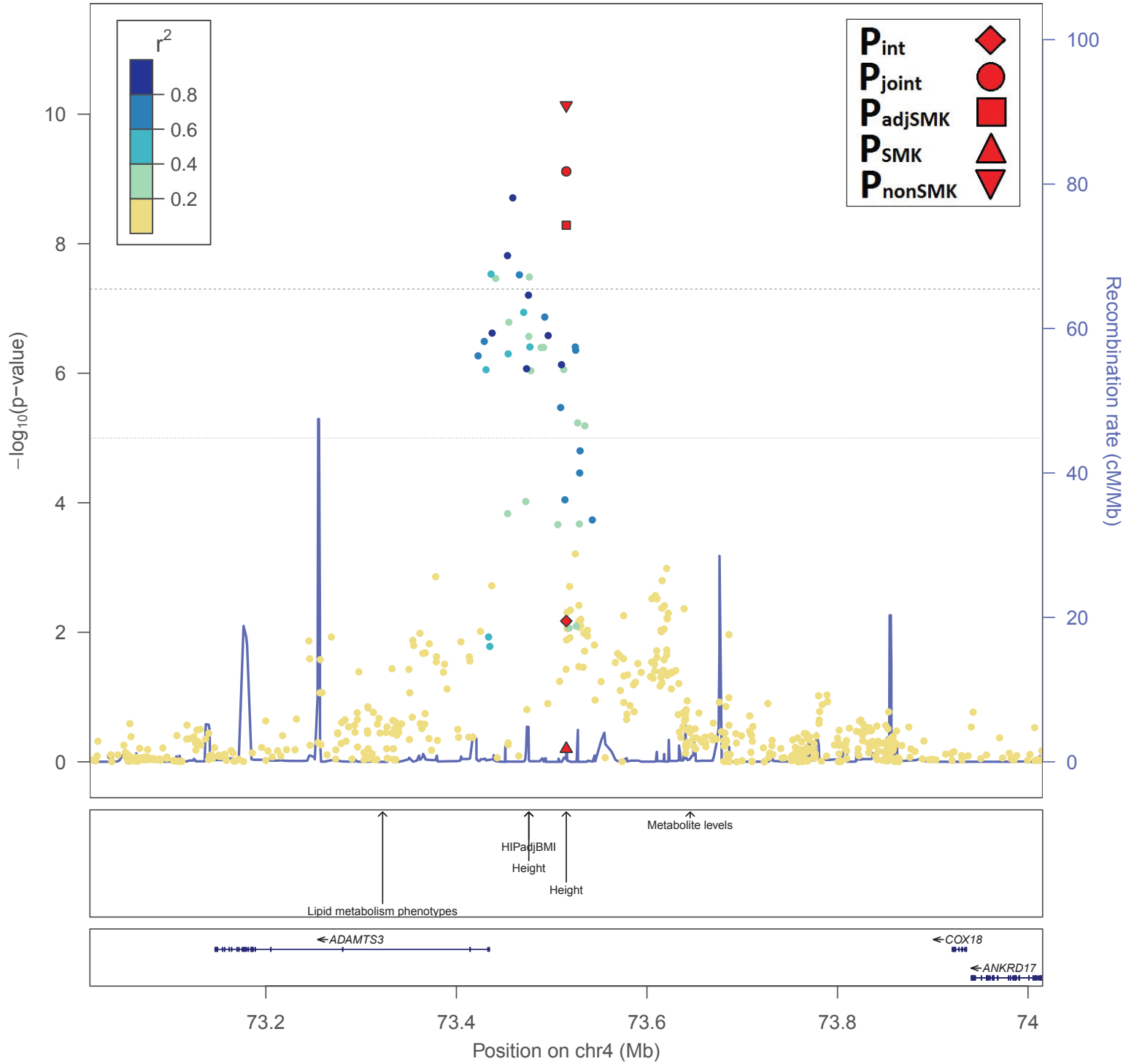
### c. WCadjBMI: rs17396340 – Approach 2



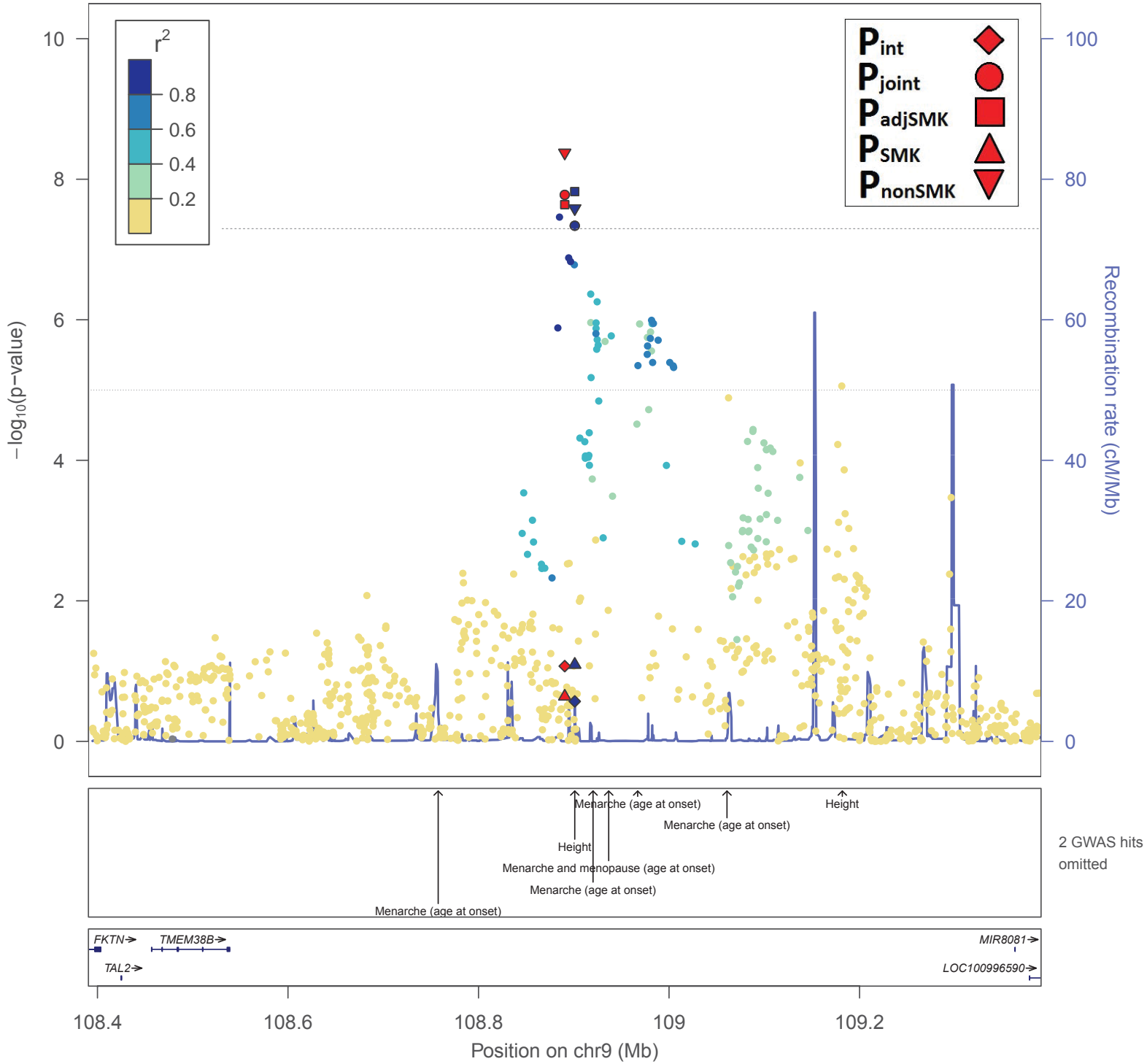
### d. WCadjBMI: rs6743226 – Approach 2



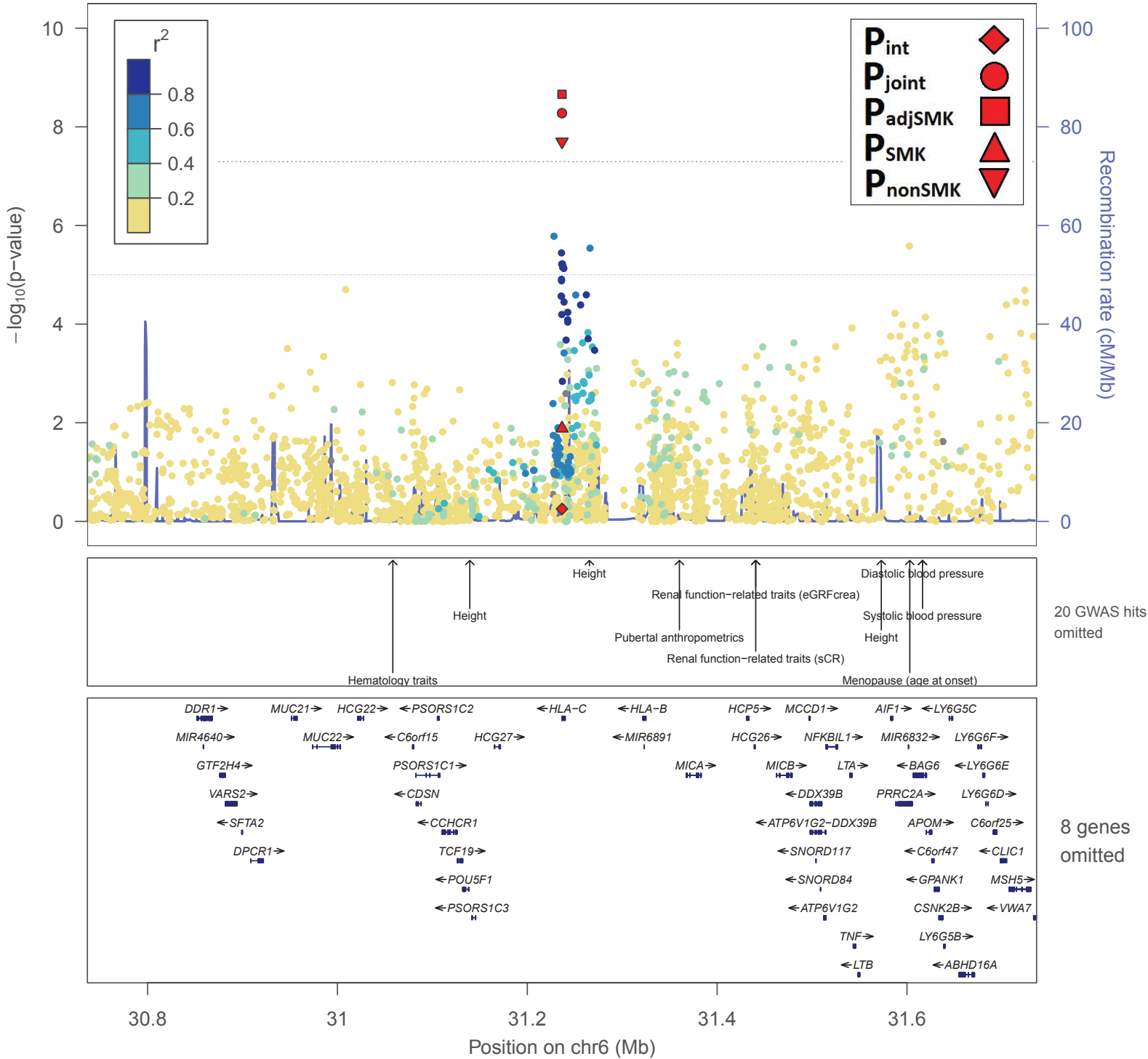
### e. WCadjBMI: rs7697556 – Approach 2



## f. WCadjBMI: rs9408815 – Approach 2



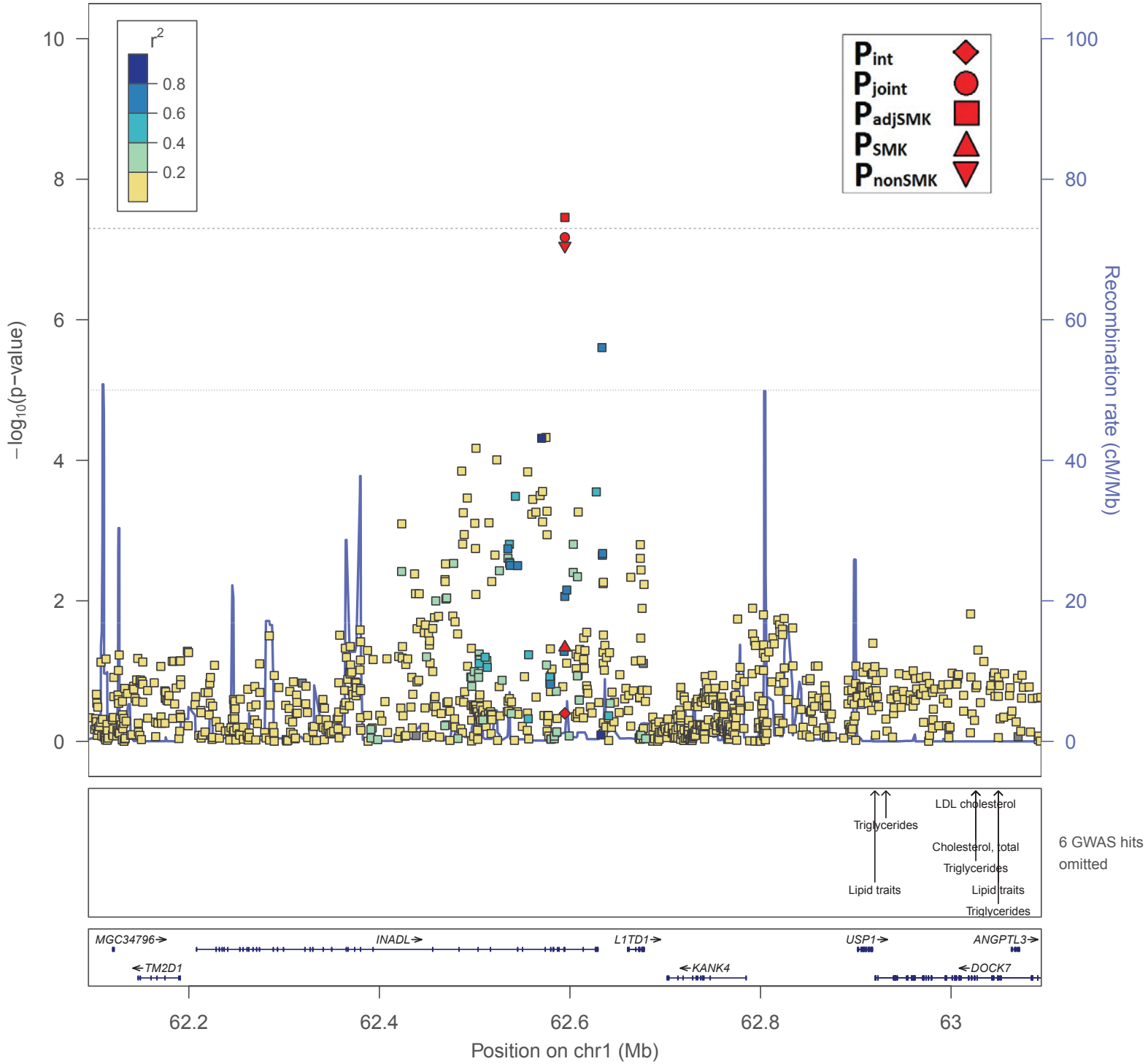
# g. WHRadjBMI: rs1049281 – Approach 2



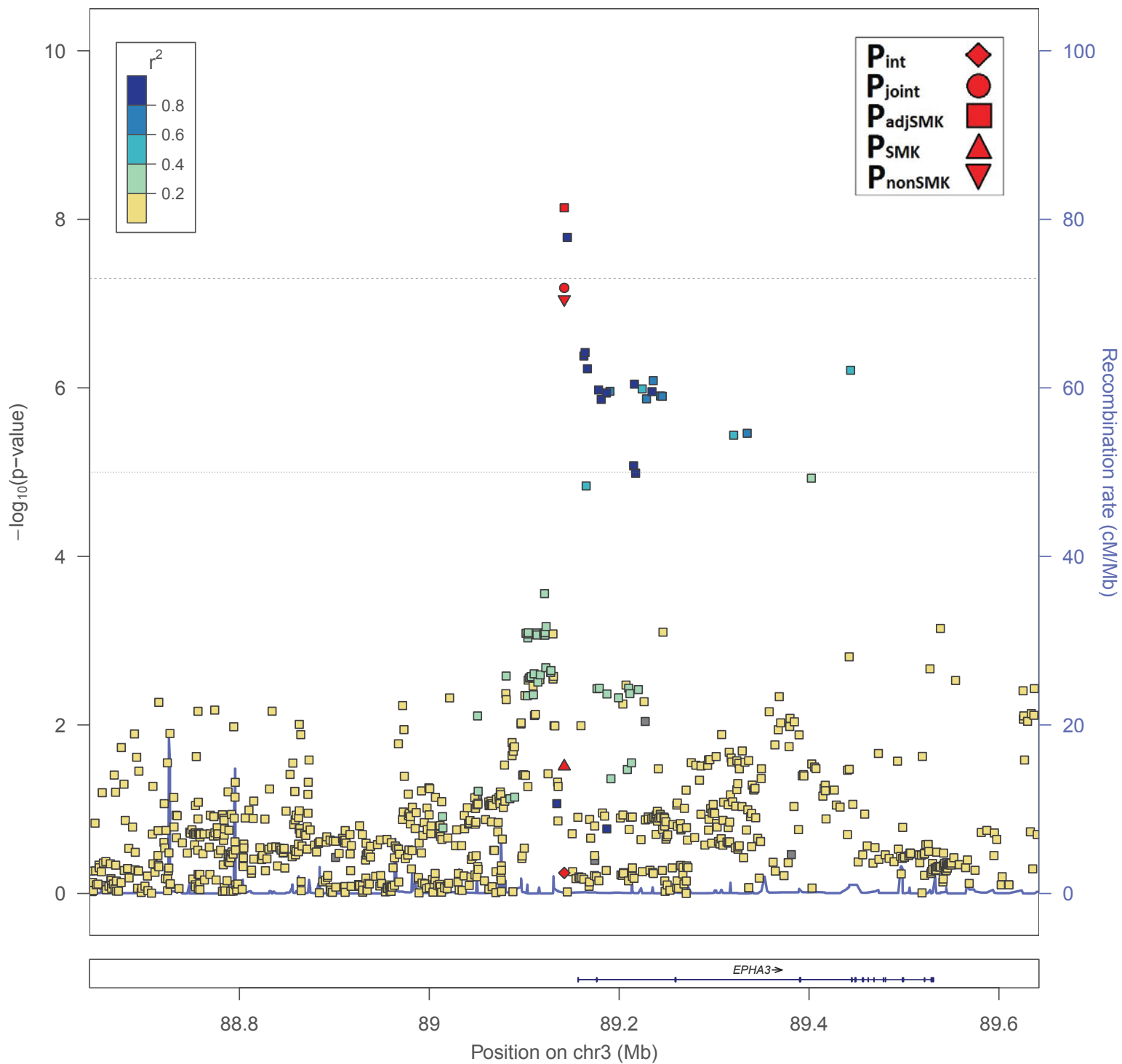
**Supplementary Figure 6. Regional association plots for Approaches 1-3 secondary meta-analyses.** Regional association plot for additional novel loci identified in Approaches 1 (SNP<sub>adjSMK</sub>), Approach 2 (SNP<sub>joint</sub>), or Approach 3 (SNP<sub>int</sub>) secondary meta-analyses for BMI: (a) rs2481665, (b) rs2173039, (c) rs12629427; WC<sub>adjBMI</sub>: (d) rs1545348, (e) rs6076699 (Approach 2), (f) rs6076699 (Approach 3), (g) rs670752; and WHR<sub>adjBMI</sub>: (h) rs589428, (i) rs1856293, (j) rs2001945, (k) rs17065323. LD has been calculated using the combined ancestries from the 1000 Genomes Phase 1 reference panel. For comparison, each plot highlights the p-value for the tag SNP in Approach 1 ( $P_{adjSMK}$ ), Approach 2 ( $P_{joint}$ ), Approach 3 ( $P_{int}$ ), current smokers ( $P_{SMK}$ ), and in nonsmokers ( $P_{nonSMK}$ ). P-values are shown from the strata in which the signal was identified (e.g. European-only women). EUR- European-only meta-analyses; ALL- all ancestries combined meta-analyses.



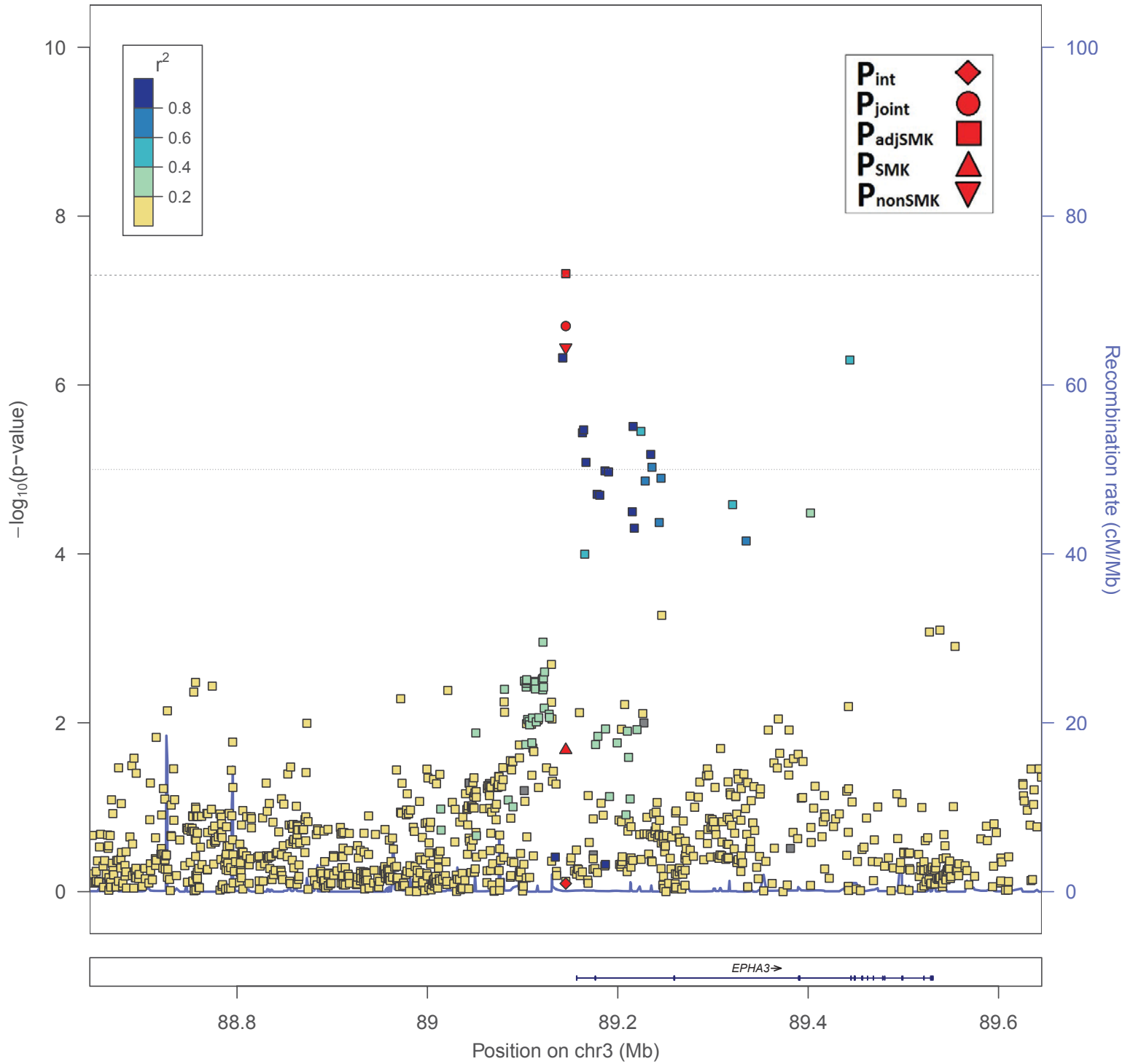
# a. BMI: rs2481665 – Approach 1, EUR, Combined Sexes



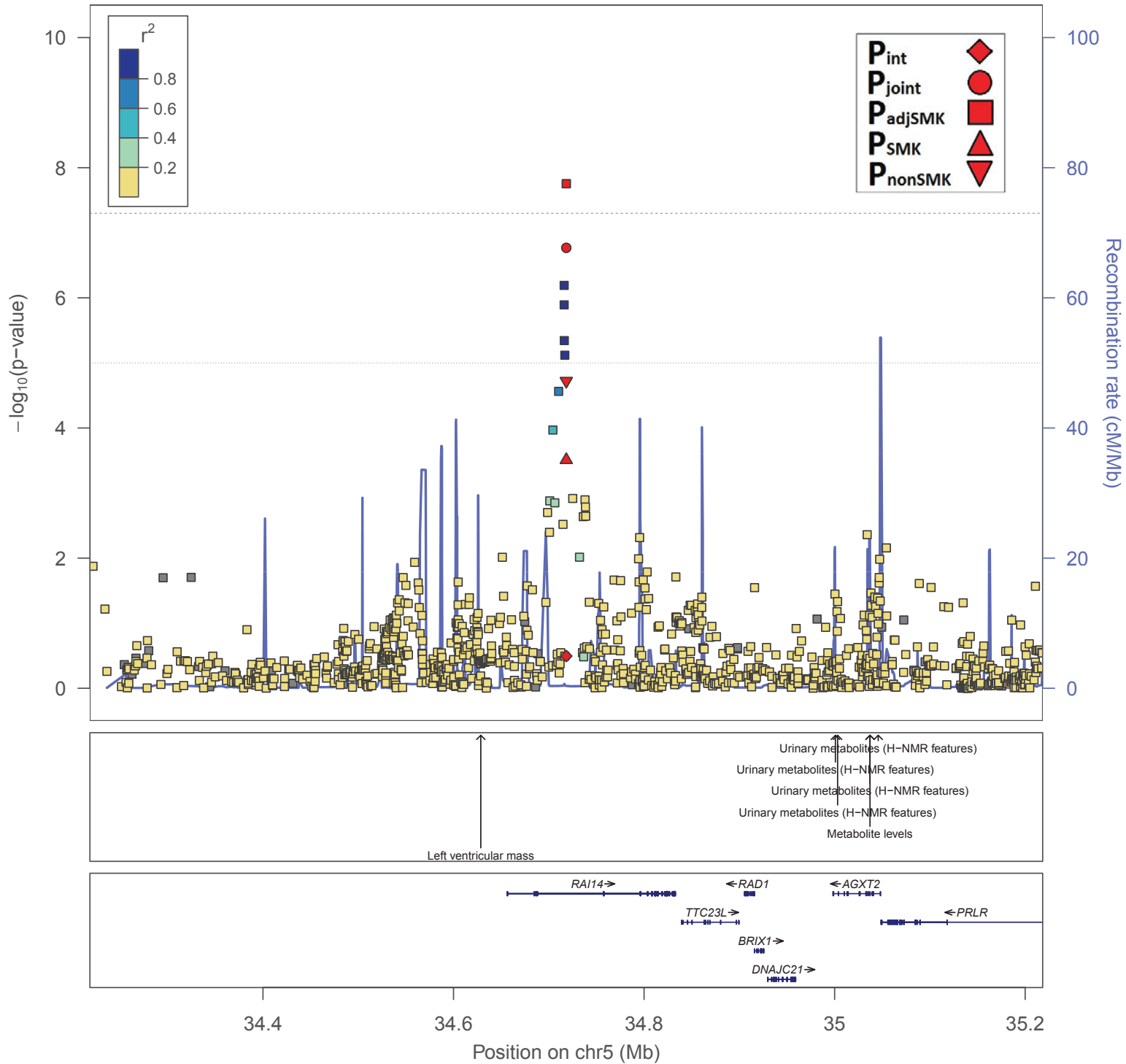
## b. BMI: rs2173039 – Approach 1, ALL Women



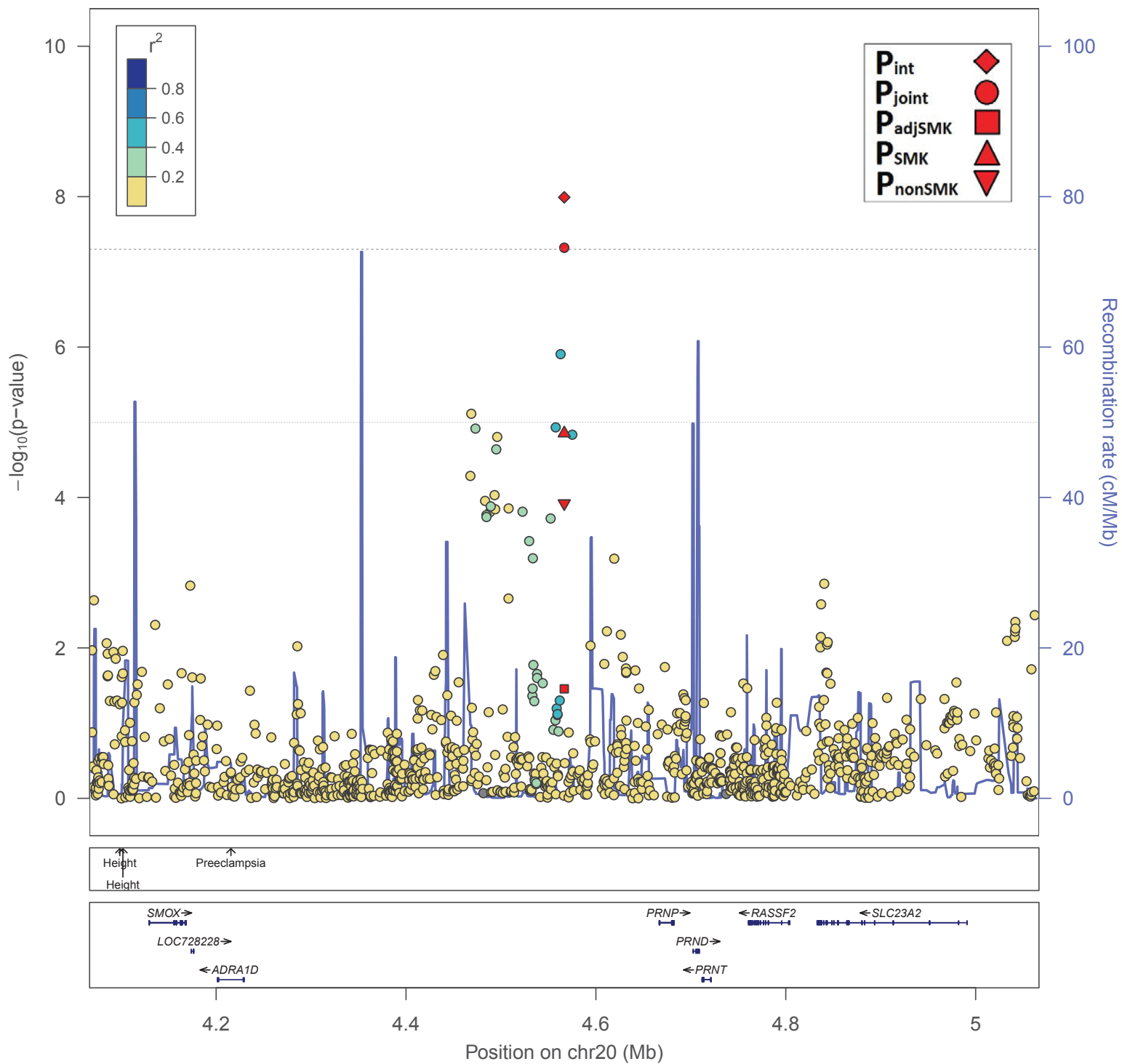
### c. BMI: rs12629427 – Approach 1, EUR Women



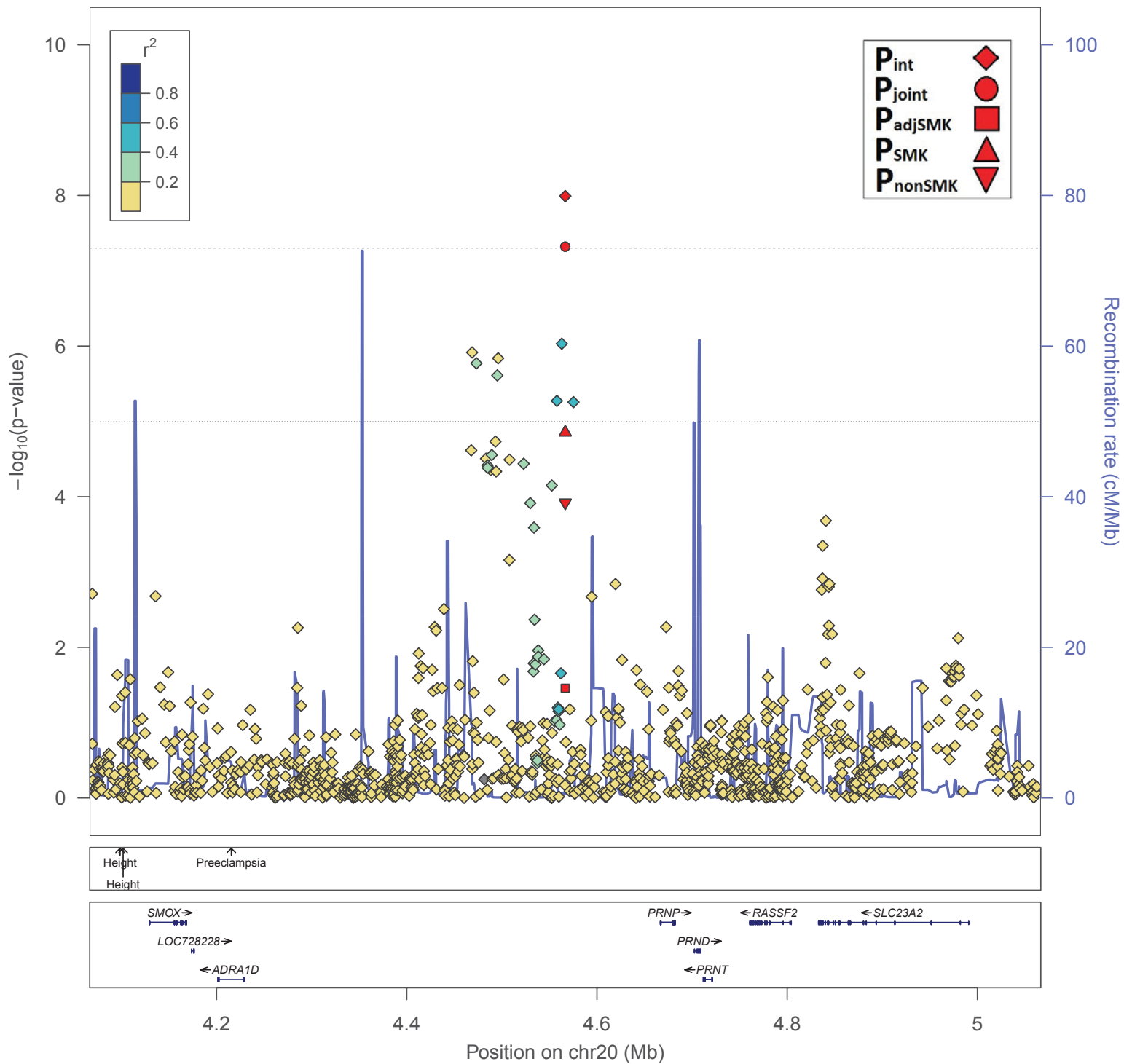
### d. WCadjBMI: rs1545348 – Approach 1, EUR Men



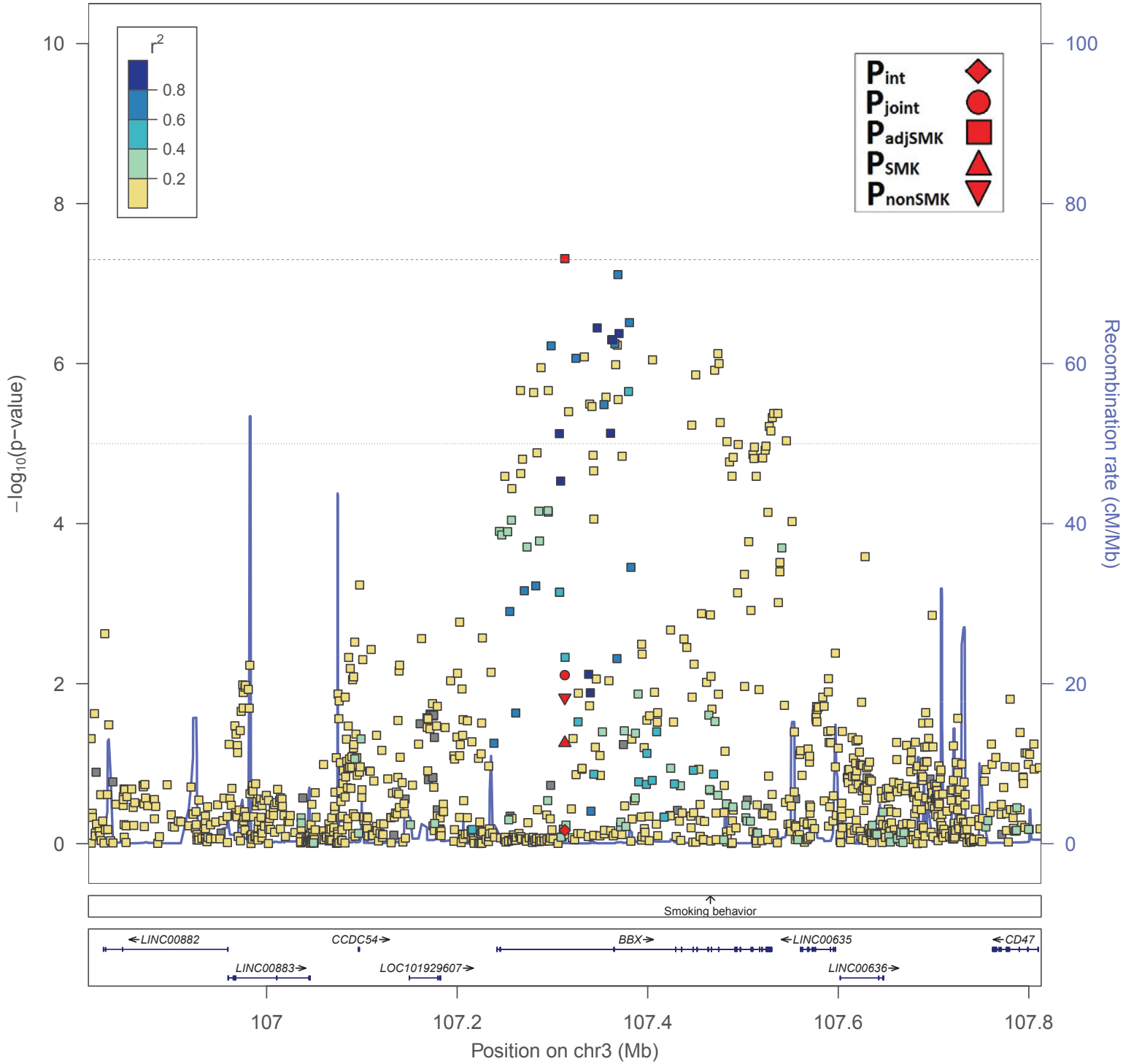
### e. WCadjBMI: rs6076699 – Approach 2, EUR Women



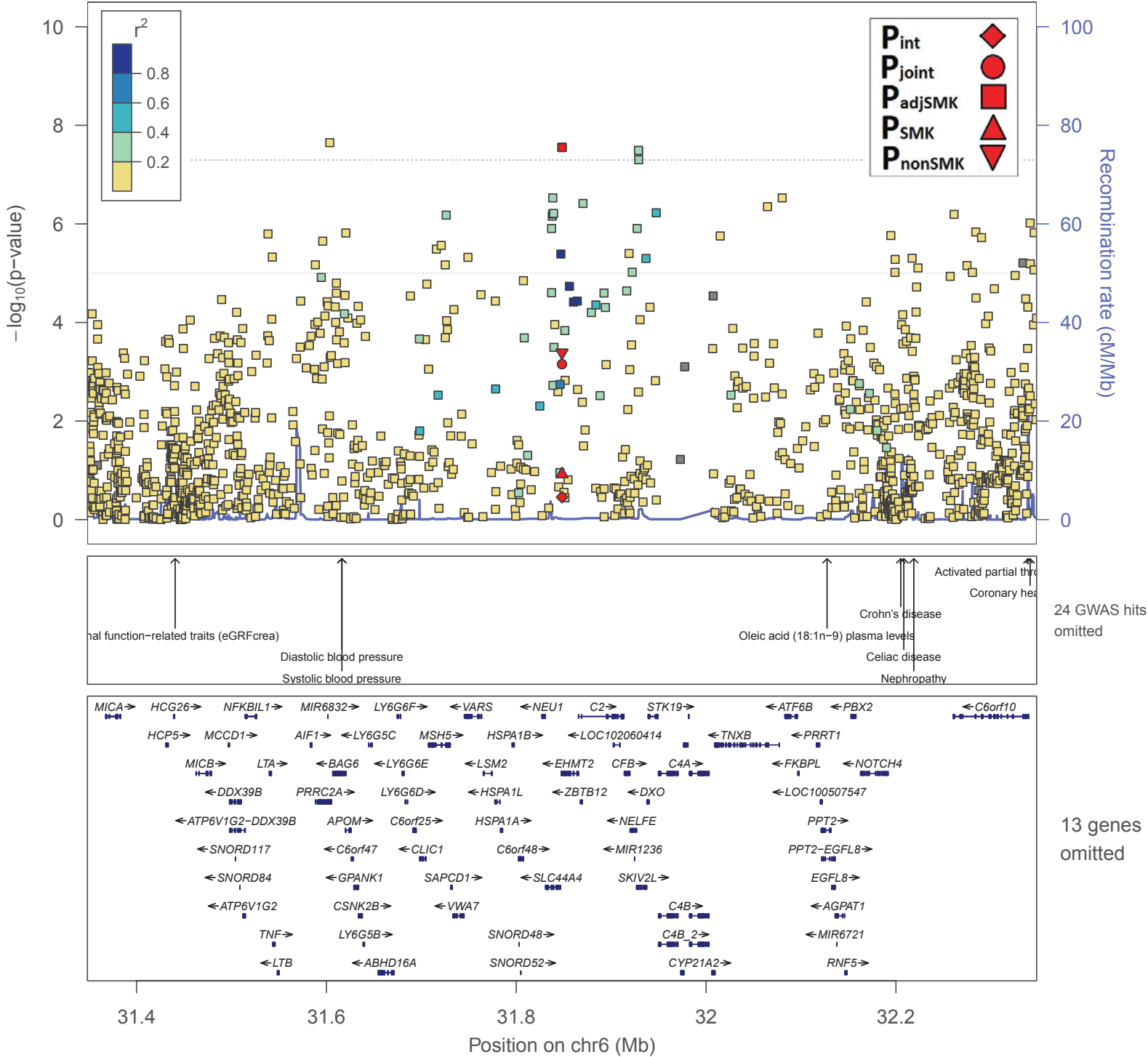
# f. WCadjBMI: rs6076699 – Approach 3, EUR Women



# g. WHRadjBMI: rs670752 – Approach 1, ALL Women

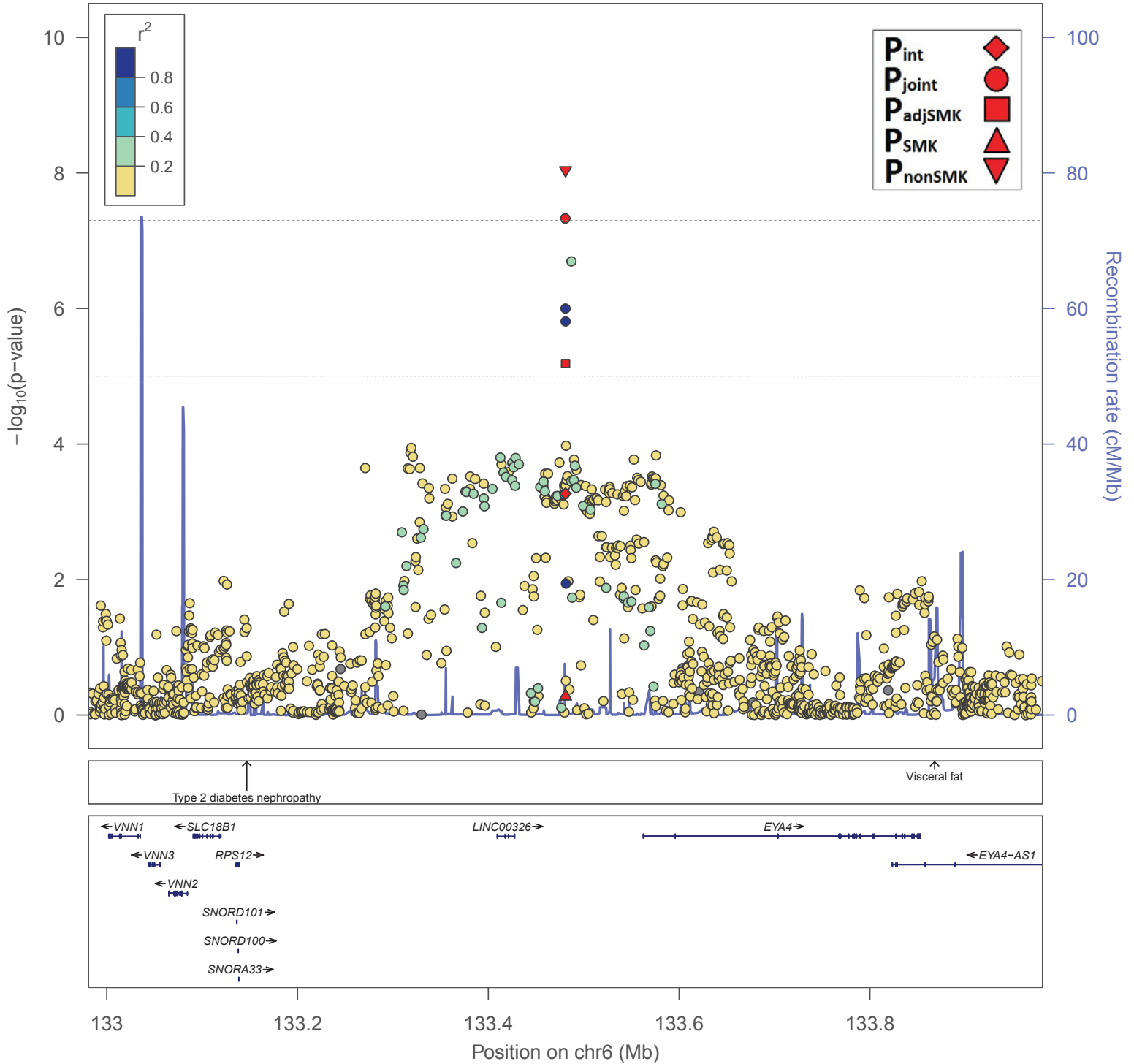


# h. WHRadjBMI: rs589428 – Approach 1, EUR Combined Sexes

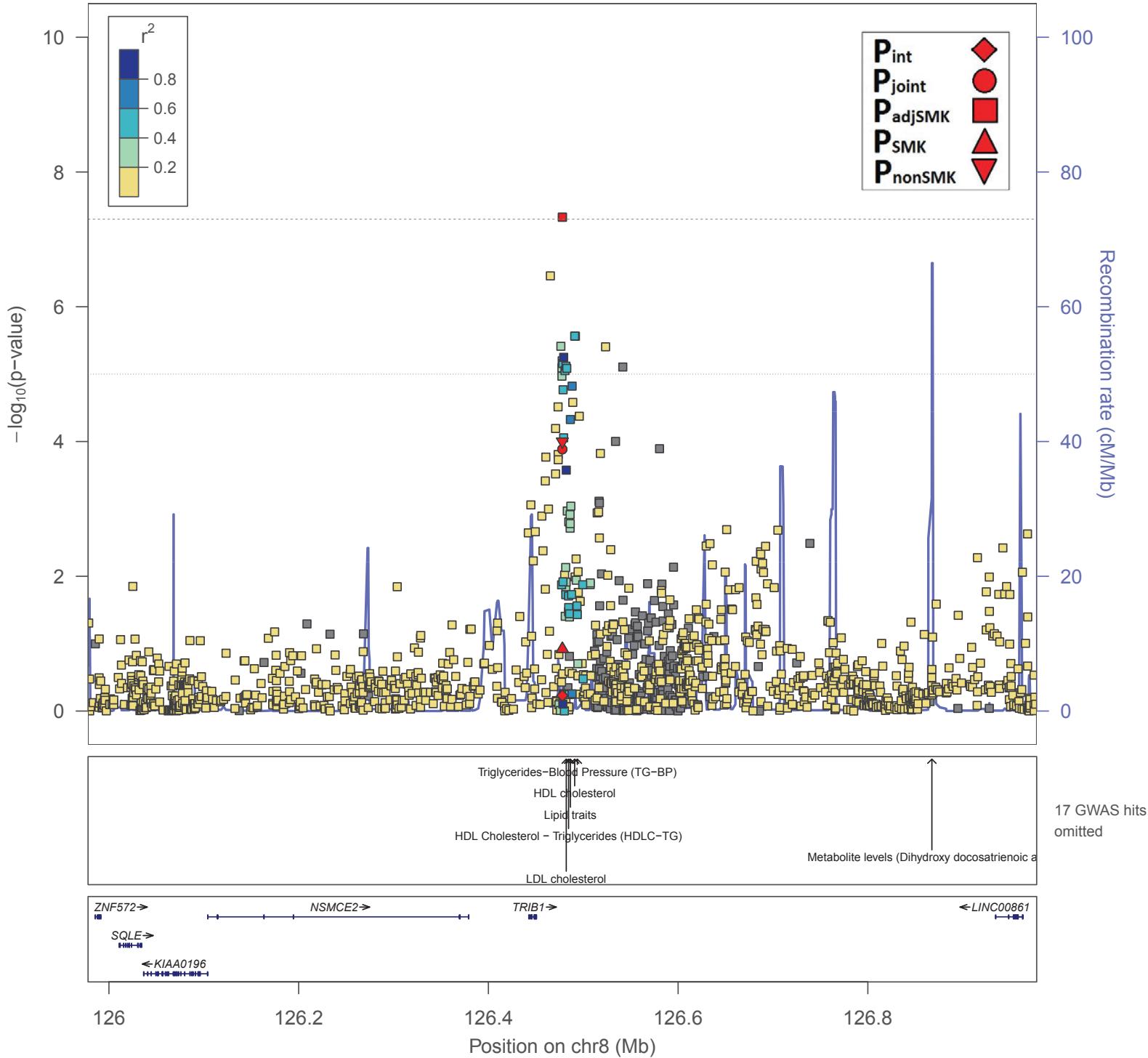




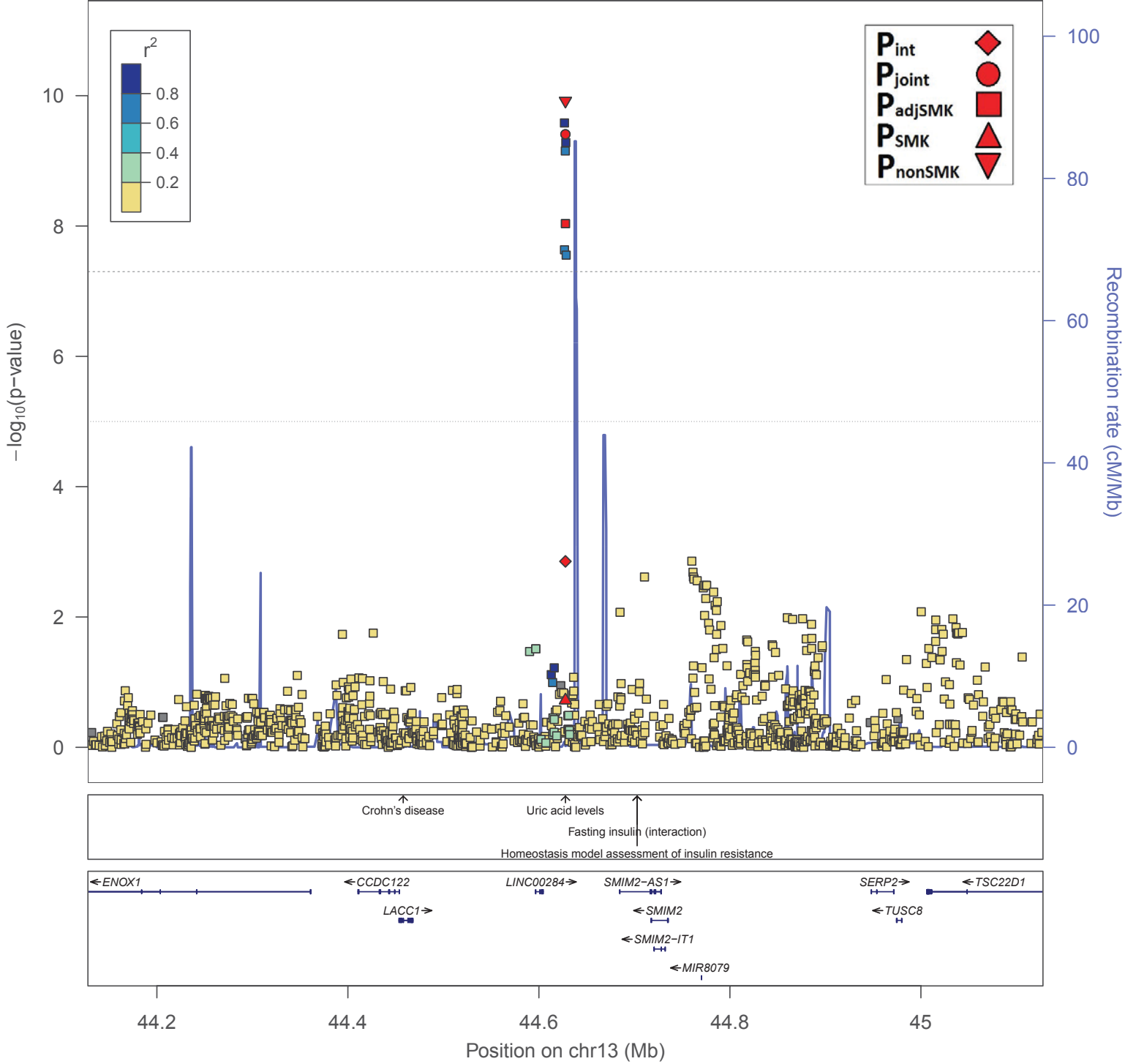
# i. WHRadjBMI: rs1856293 – Approach 2 EUR Combined Sexes



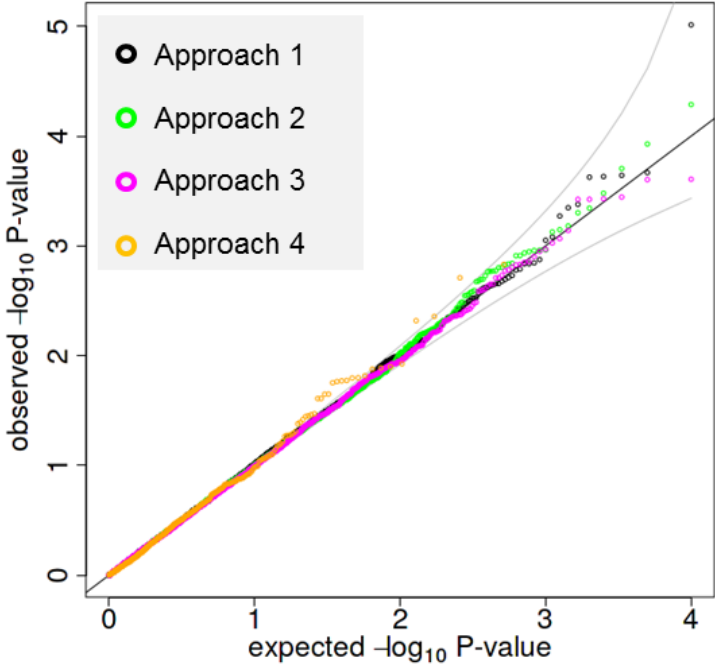
# j. WHRadjBMI: rs2001945 – Approach 1, ALL Women



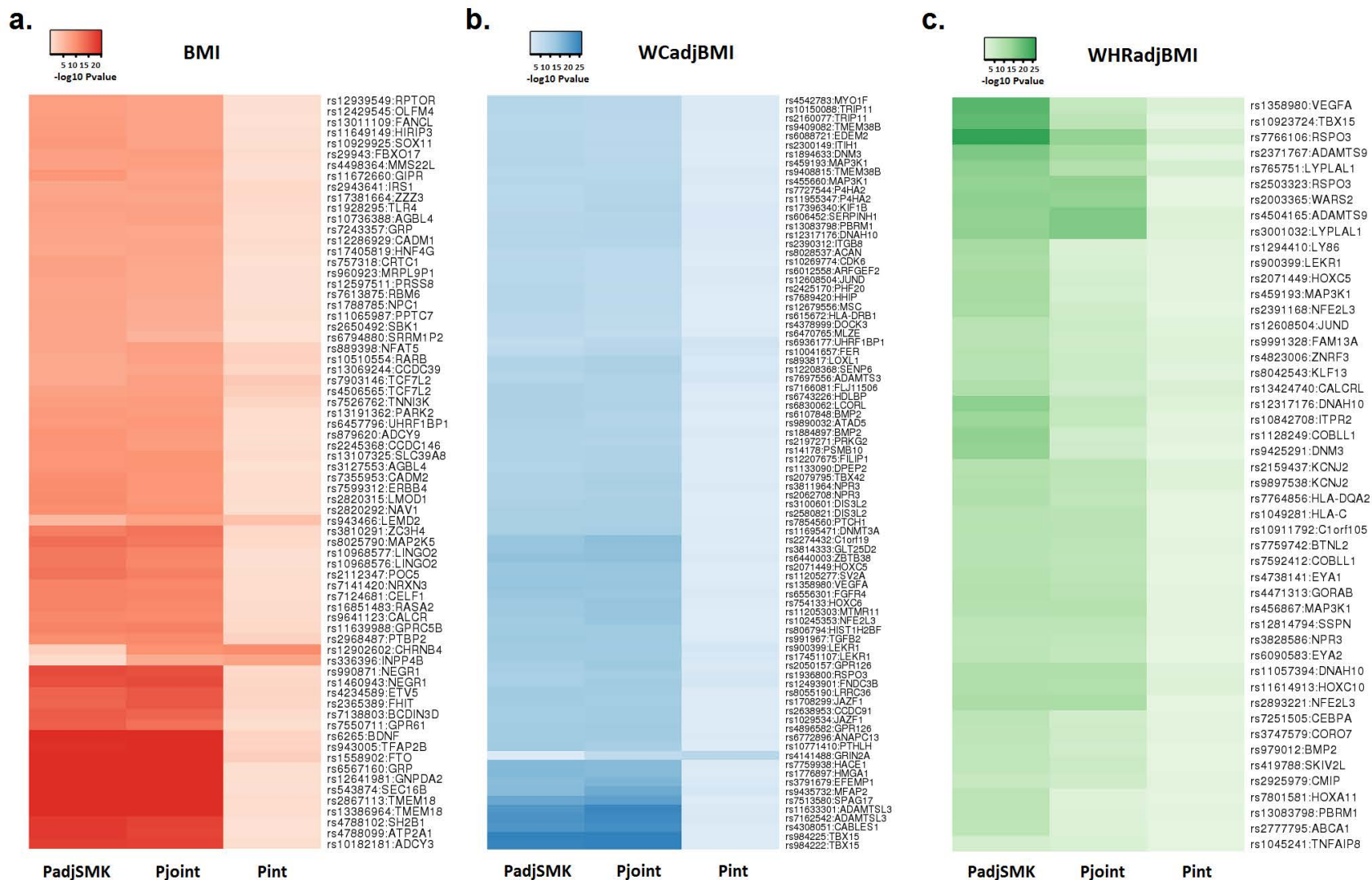
# k. WHRadjBMI: rs17065323 – Approach 1, EUR Combined Sexes



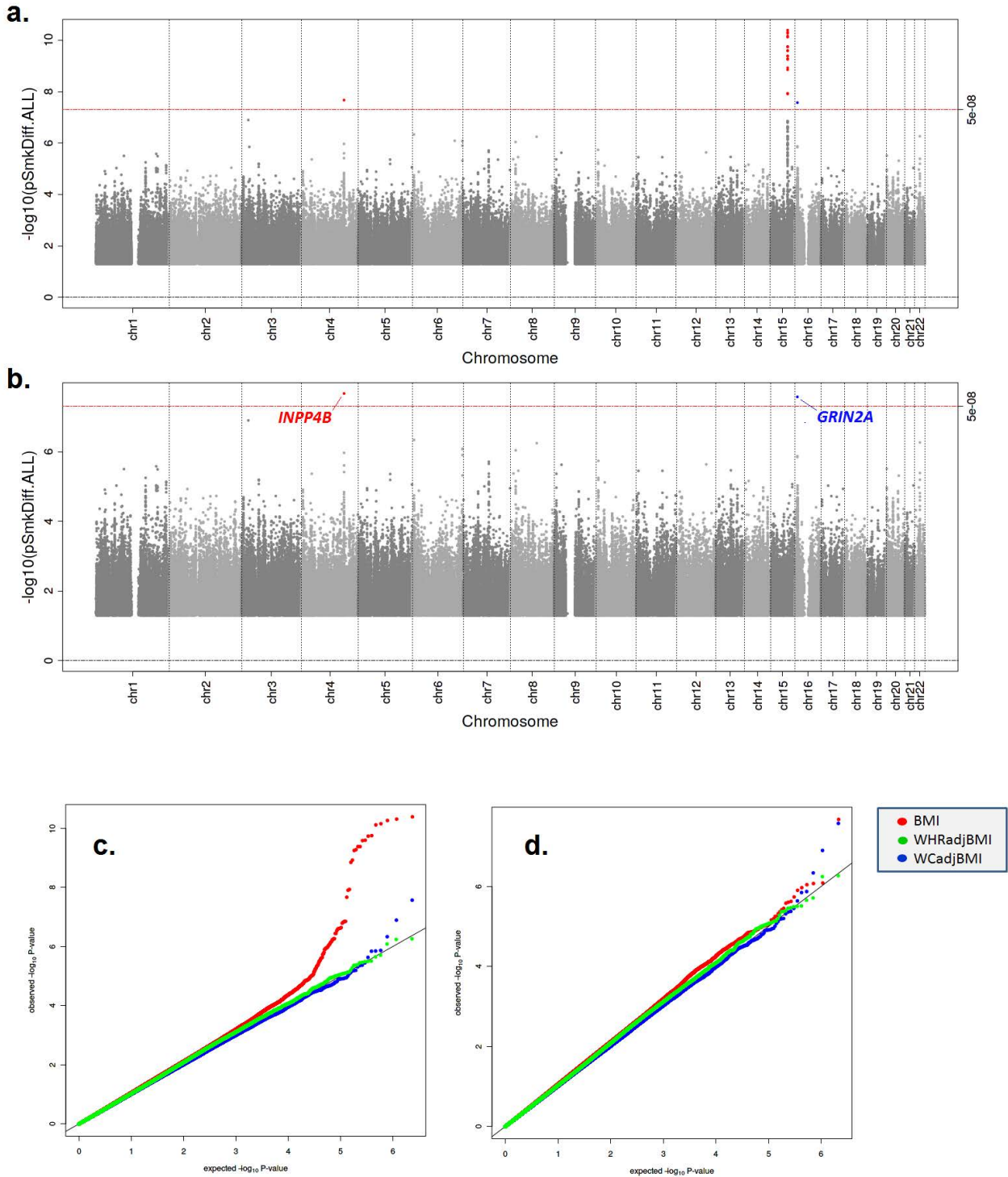
**Supplementary Figure 7. Simulation-based estimation of type 1 error using QQ plots.** Shown are the QQ plots of simulation results for Approach 1 (adjusted effect), Approach 2 (joint effect), Approach 3 and 4 (interaction effects). The simulation was based on MAF=0.05, 50,000 smokers and 180,000 nonsmokers.



**Supplementary Fig. 8.** Heatmap of  $-\log_{10}P$ -values for SNPadjSMK, SNPjoint, and SNPint models. We have included each variant identified in the all ancestries analysis which was significant for Approaches 1-3. Strength of color represents the  $-\log_{10}P$ -value from the all ancestries, combined sexes meta-analysis for (a) BMI in red, (b) WCadjBMI in blue, and (c) WHRadjBMI in green.

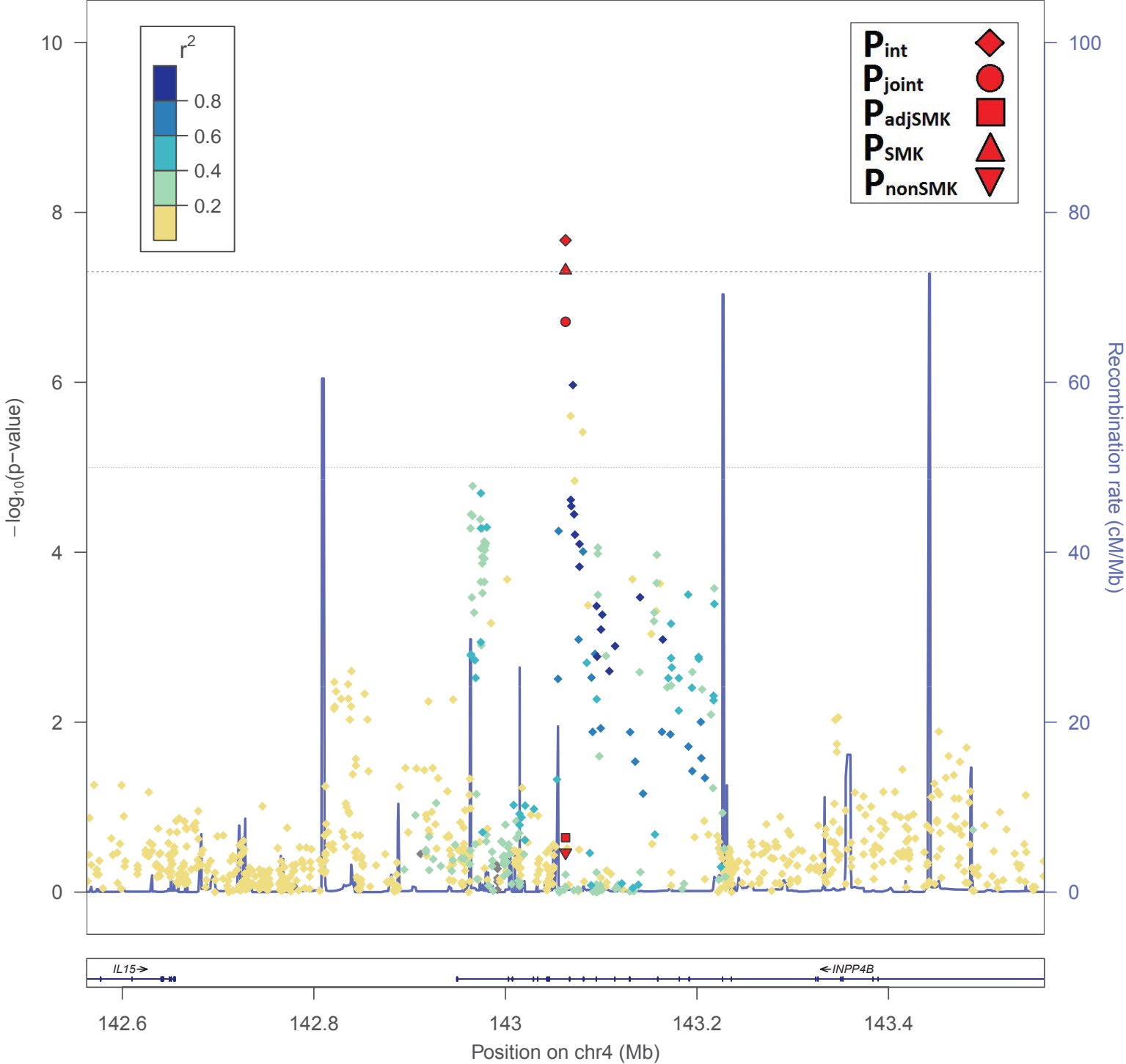


**Supplementary Figure . Summary plots of discovery meta-analysis for Approach 3 primary meta-analyses. (a)** Manhattan plot showing the loci identified in Approach 3 in primary meta-analyses, used to identify significant interaction effects loci (SNPint), in the primary meta-analyses association  $-\log_{10}P$ -values for BMI-red, WCadjBMI-blue, and WHRadjBMI-green; **(b)** Manhattan plot showing the loci identified in Approach 3 excluding known regions  $\pm 500$  kb and labeled with the nearest gene to the index SNP; **(c)** QQ-plot showing the Approach 3 P-values as observed against those expected under the null for each phenotypes separately (colored); **(d)** QQ-plot for Approach 3 after excluding known association regions.



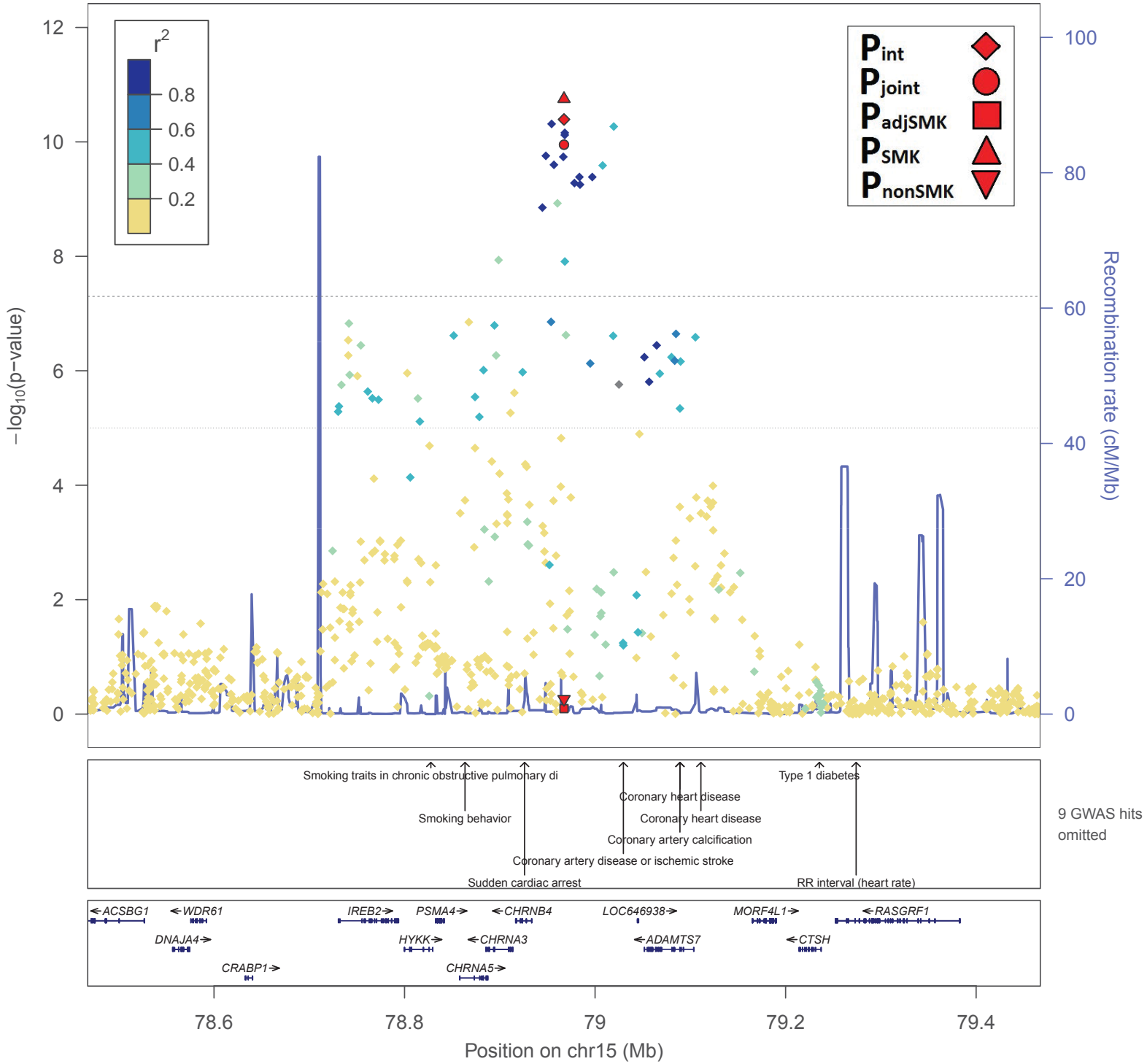
**Supplementary Figure . Regional association plots for Approach 3 primary meta-analyses.** Regional association plot for all loci identified in Approach 3 in primary meta-analyses, used to identify significant interaction (SNP<sub>int</sub>), in the primary meta-analyses for BMI: (a) rs336396, (b) rs12902602; and WCadjBMI: (c) rs4141488, and ordered as they appear in Table 3. LD has been calculated using the combined ancestries from the 1000 Genomes Phase 1 reference panel. For comparison, each plot highlights the p-value for the tag SNP in Approach 1 ( $P_{\text{adjSMK}}$ ), Approach 2 ( $P_{\text{joint}}$ ), Approach 3 ( $P_{\text{int}}$ ), current smokers ( $P_{\text{SMK}}$ ), and in nonsmokers ( $P_{\text{nonSMK}}$ ).

a. BMI: rs336396 – Approach 3

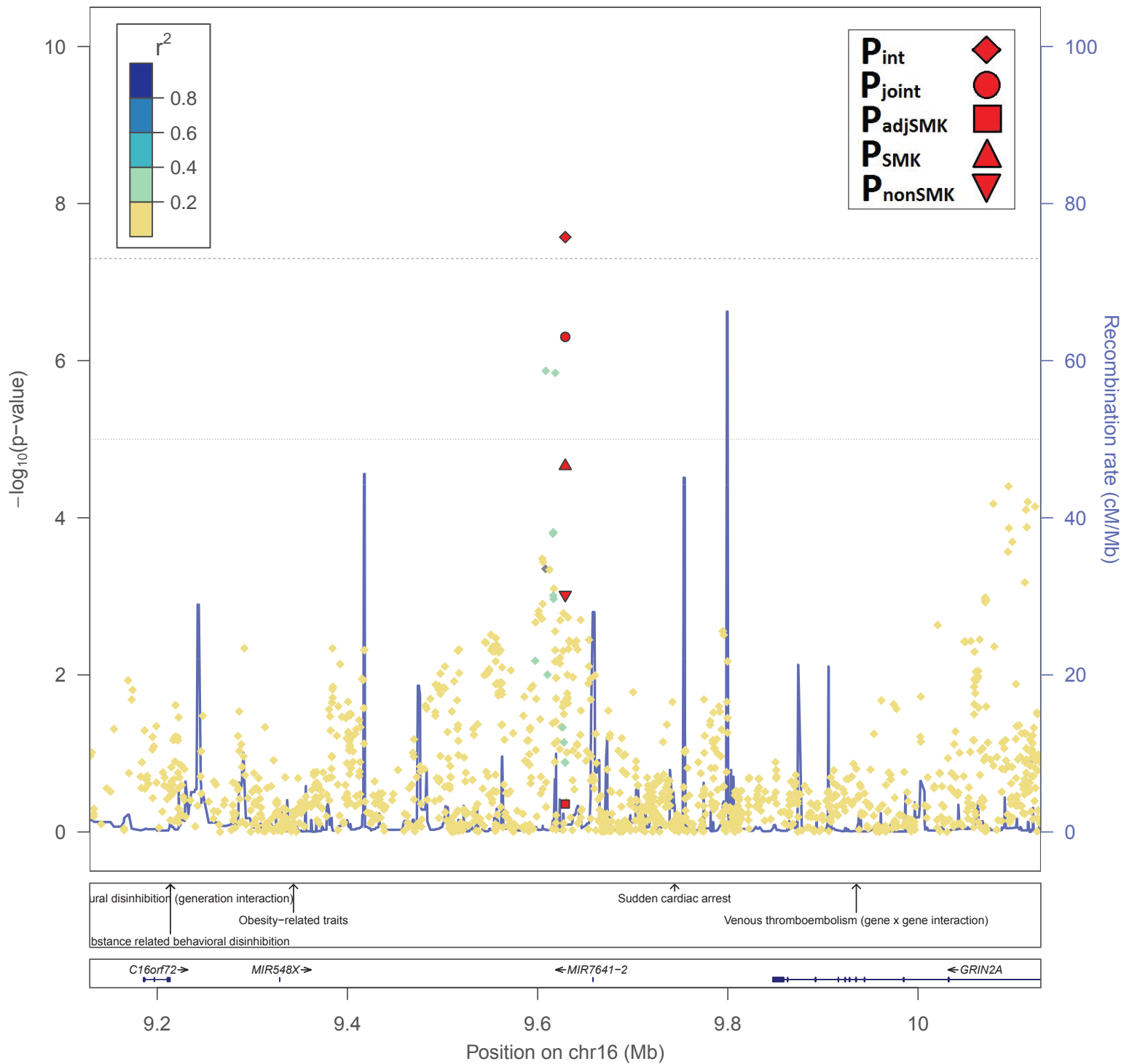




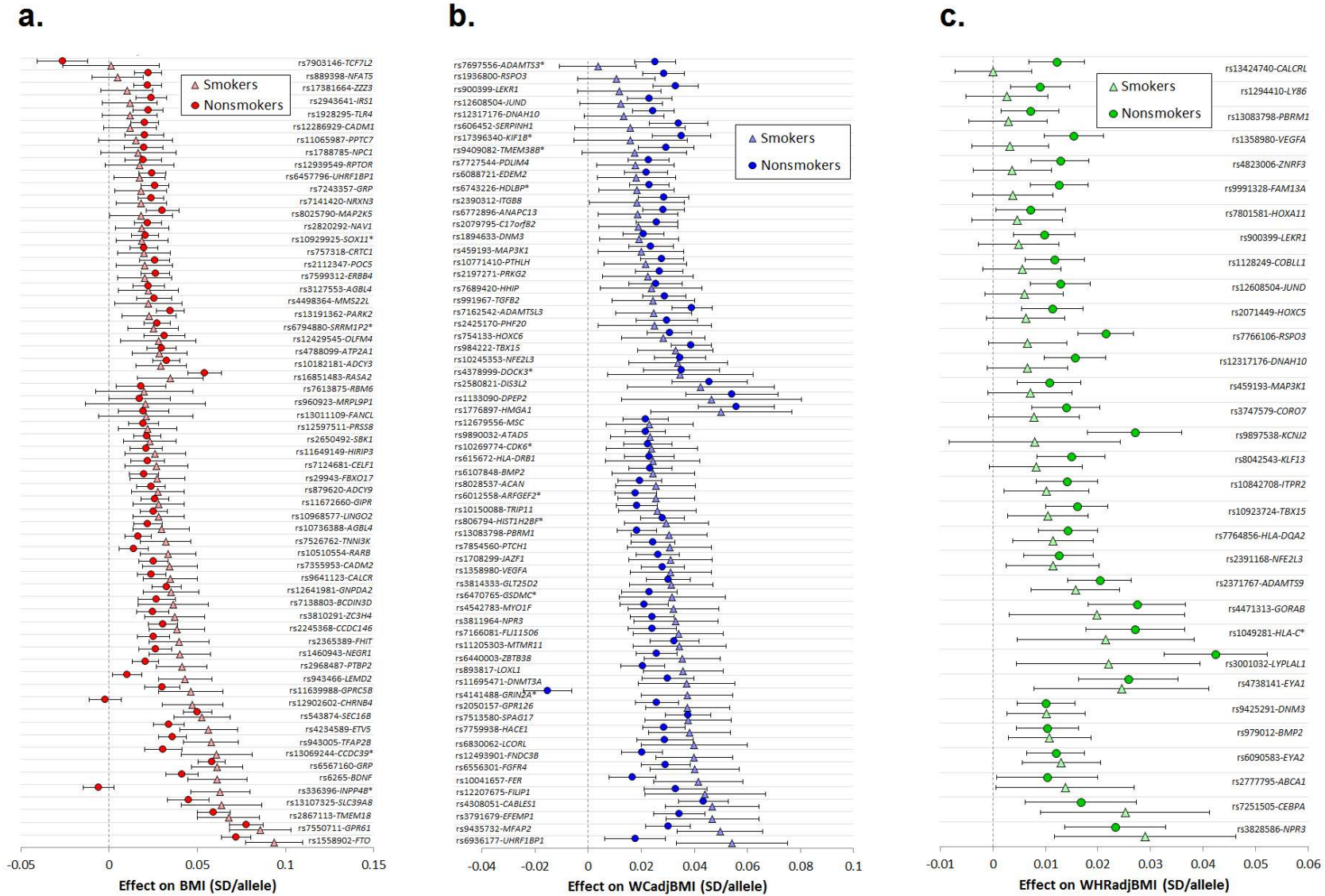
## b. BMI: rs12902602 – Approach 3



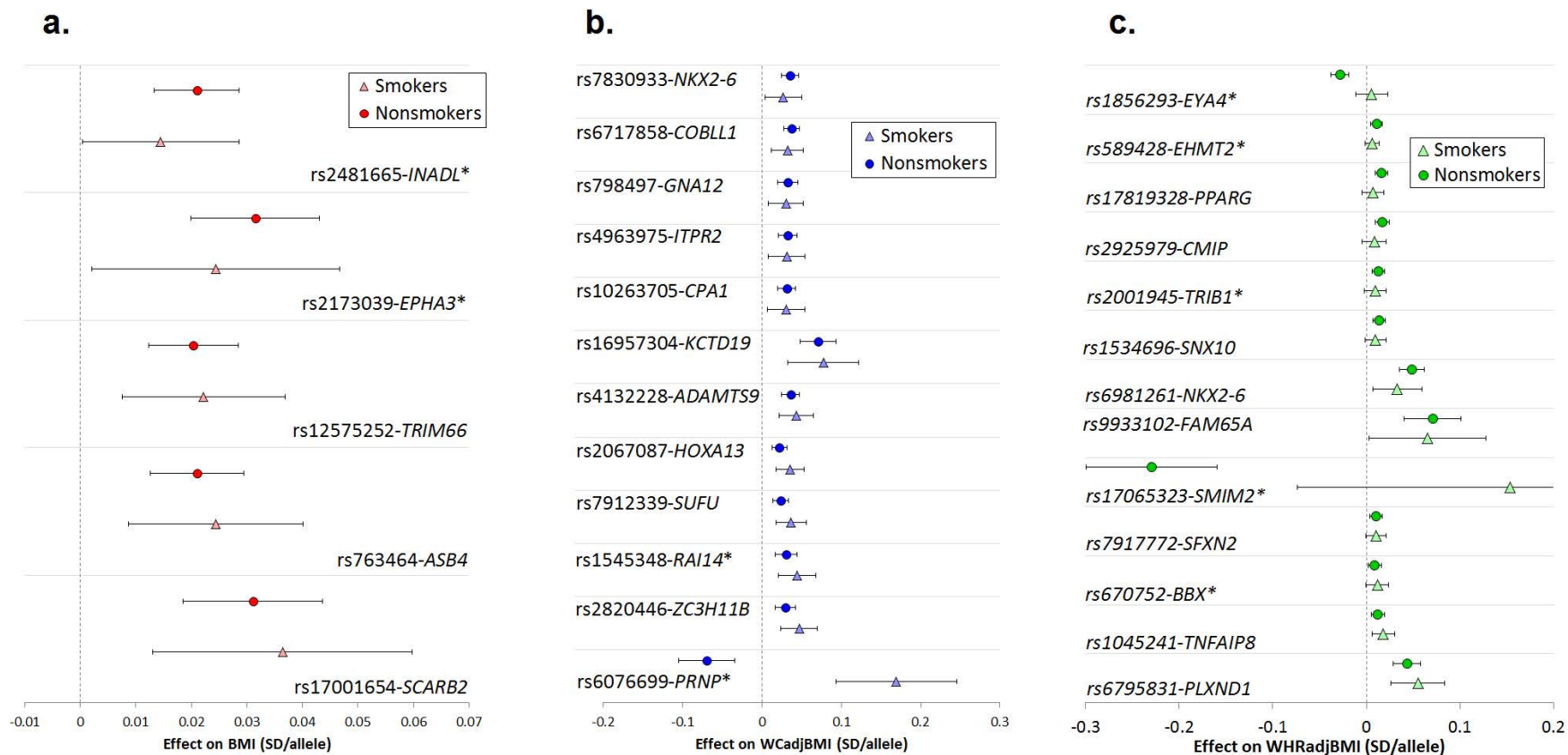
### c. WCadjBMI: rs4141488 – Approach 3



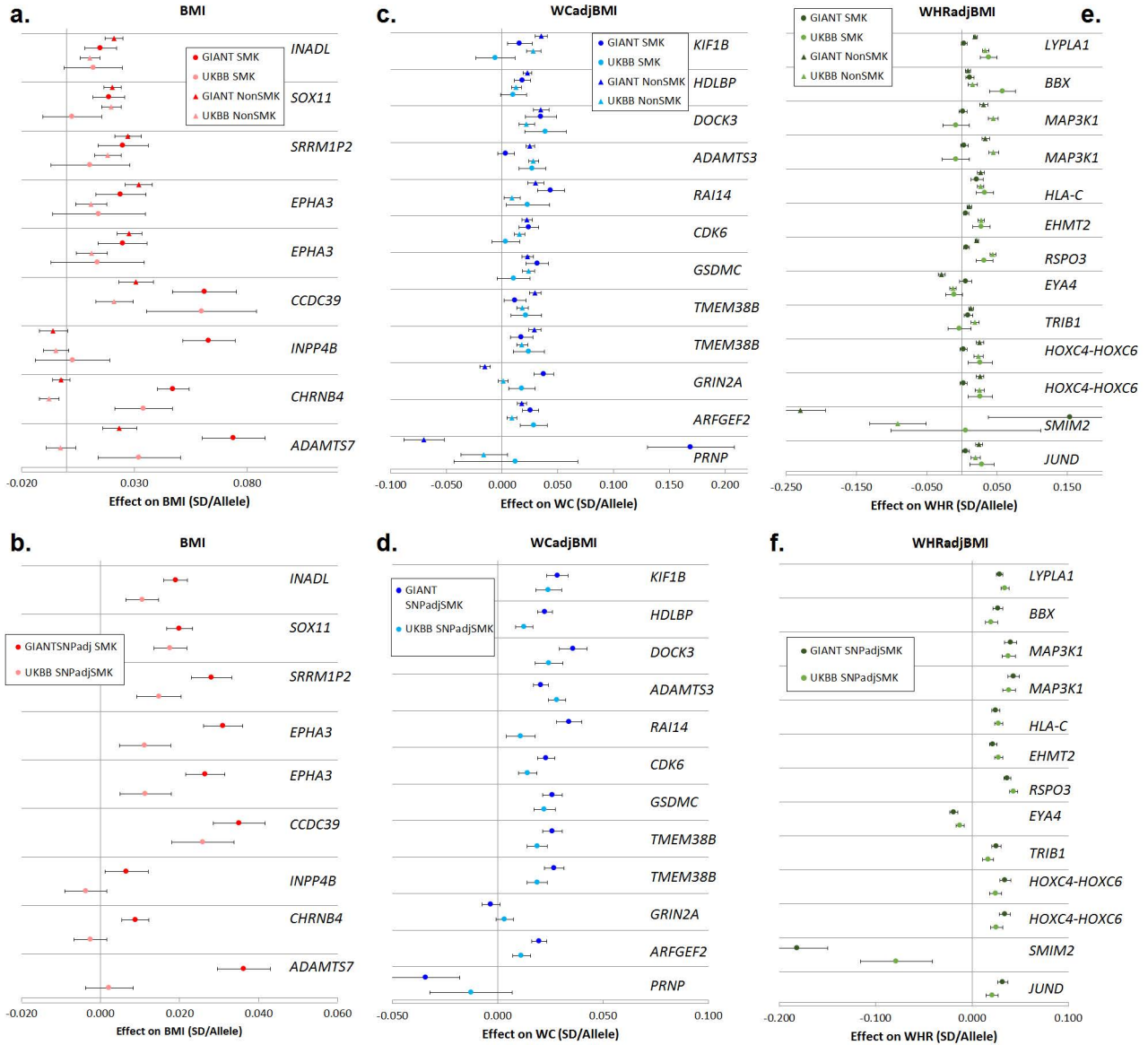
**Supplementary Figure . Forest plot for significant loci stratified by smoking status.** Estimated effects ( $\beta \pm 95\%$  CI) for smokers (N upto 51,080) and nonsmokers (N up to 190,178) per risk allele for (a) BMI, (b) WCadjBMI, and (c) WHRadjBMI for the most significant variant for each locus identified in the primary meta-analyses (combined ancestries and combined sexes) for Approaches 1 (SNPadJSMK), 2 (SNPjoint) and 3 (SNPint). Loci are grouped by those with greater effect in nonsmokers, then smokers and then ordered by magnitude of effect in smokers and labeled with the nearest gene.



**Supplementary Figure 1** . Estimated effects ( $\beta \pm 95\%$  CI) in smokers (N up to 51,080) and nonsmokers (N up to 190,178) per risk allele for (a) BMI, (b) WCadjBMI, and (c) WHRadjBMI for the most significant variant for each locus identified in the secondary meta-analyses (sex-stratified and European-only analyses) for Approaches 1 (SNPadjSMK), 2 (SNPjoint) and 3 (SNPint).



**Supplementary Figure 13.** Comparison of estimated effect estimates (+/-SE) for smokers (GIANT N up to 51,080; UKBB N up to 13,416) and nonsmokers (GIANT N up to 190,178; UKBB N up to 105,218) per risk allele in GIANT only and UKBiobank validation analysis for (a) BMI stratified by smoking status, (b) BMI adjusted for smoking status, (c) WCadjBMI stratified by smoking status, (d) WCadjBMI adjusted for smoking status, (e) WHRadjBMI stratified by smoking status, and (f) WHRadjBMI adjusted for smoking status for each novel and GxSMK SNP in Tables 1-4. All loci are ordered by chromosome and position.



**Supplementary Table 1.** Study design, sample size, and data quality control for contributing genome-wide association study and Metabochip cohorts.

GWAS DATA											
Study		Study design	Ancestry	Region	Total genotyped sample size (N)	Sample QC		Anthropometric assessment method			Study References (PMID)
Short name	Full name					Call rate*	sample exclusion criteria	BMI	WHR	WHR and BMI were assessed at the same time?	
AE	Athero-Express Biobank Study	Cohort-study	European	Utrecht, the Netherlands	690	≥ 97%	1) heterozygosity ( $\hat{H}$ ) $\pm$ 3 standard deviations of the mean 2) ethnic outliers through Principal Component Analysis compared to HapMap 2 (r22) 3) related individuals and duplicates, $\pi > 0.20$ 4) missing body weight and height 5) gender-discrepancies	Self-reported	NA	NA	15678794
AGES	Age, Gene/Environment Susceptibility-Reykjavik Study	Population based	European	Iceland	3219	>99%	1) missing phenotypes 2) mismatch previous genotypes	Measured	NA	NA	17351290
ARIC	Atherosclerosis Risk in Communities	Population-based	European	USA-North America	9713	>90%	1) first-degree relatives 2) ancestry outliers 3) gender mismatch 4) identity issues 5) excessive heterozygosity 6) missing height or weight	Measured	Measured	Yes	2646917
ARIC	Atherosclerosis Risk in Communities	Population-based	African American	USA-North America	3207	>90%	1) first-degree relatives 2) ancestry outliers 3) gender mismatch 4) identity issues 5) excessive heterozygosity 6) missing height or weight	Measured	Measured	Yes	2646917
AUSTWIN	Australian Twin-Family Studies	Population-based	European	Australia	2166	95%	1) mendelian errors 2) HWE $p < 10^{-6}$ 3) sample call rate 96%	Self-reported	NA	NA	21529783
BHS	Busselton Health Study	Population-based	European	Australia	1468	97%	1) duplicates 2) sex check 3) ethnic outliers	Measured	Measured	Yes	15486340, 19643935
BioMe (MSSM)	The Charles Bronfman Institute for Personalized Medicine; BioMe Program	EHR-linked clinical care cohort	European American	USA (New York City)	2026	≥98%	1) sex mismatch 2) ancestry Outliers 3) related Individuals (inbreeding coefficient $< -0.1$ or $> 0.3$ for common variants (MAF>1%) 4) inbreeding coefficient $< 0.4$ or $> 0.9$ for rare variants (MAF<1%)	Self-reported	NA	NA	25673413
BioMe (MSSM)	The Charles Bronfman Institute for Personalized Medicine; BioMe Program	EHR-linked clinical care cohort	African American	USA (New York City)	3495	≥98%	1) sex mismatch 2) ancestry Outliers 3) related Individuals (inbreeding coefficient $< -0.1$ or $> 0.3$ for common variants (MAF>1%) 4) inbreeding coefficient $< 0.4$ or $> 0.9$ for rare variants (MAF<1%)	Self-reported	NA	NA	25673413

BioMe (MSSM)	The Charles Bronfman Institute for Personalized Medicine; BioMe Program	EHR-linked clinical care cohort	Hispanic / Latinos	USA (New York City)	4711	≥98%	1) sex mismatch 2) ancestry Outliers 3) related individuals (inbreeding coefficient < -0.1 or > 0.3 for common variants (MAF>1%) 4) inbreeding coefficient < 0.4 or > 0.9 for rare variants (MAF<1%)	Self-reported	NA	NA	25673413
BLSA	Baltimore Longitudinal Study of Aging	Population-based	European	Italy	1230	98%	1) Missing Phenotype 2) sex mismatch 3) ethnic outliers	measured	measured	Yes	NA
British 1958 birth cohort (B58C)	British 1958 birth cohort	Population-based	European	UK	6481	≥ 97%	1) Contamination 2) non-European identity 3) missing height or weight	Measured	Measured	Yes	17255346
CHS	The Cardiovascular Health Study	Population-based cohort	European	USA-North America	3271	>95%	1) baseline CHD, CHF, PAD, valvular heart disease, stroke, TIA 2) lack of available DNA 3) genotype discordant with known sex or prior genotyping	Measured	Measured	Yes	1669507
CLHNS	Cebu Longitudinal Health and Nutrition Survey (Offspring)	Population-based	East Asian (Filipino)	Philippines	1895	≥97%	1) 1st-degree relatives 2) missing phenotypes (age, weight, height, smoking)	Measured	Measured	Yes	20507864
COLAUS	Cohorte Lausannoise	Population-based	European	Switzerland	5435	90%	1) PCA outliers	Measured	Measured	Yes	22415877, 18366642
CROATIA-Korcula	The CROATIA study, Korcula Island cohort	Population-based	European	Croatia	898	>97%	1) duplicates 2) gender mismatch 3) identity issues 4) excess heterozygosity	Measured	Measured	Yes	18952825 19798445
CROATIA-Vis	The CROATIA study, Vis Island cohort	Population-based	European	Croatia	924	>97%	1) duplicates 2) gender mismatch 3) identity issues 4) excess heterozygosity	Measured	Measured	Yes	18952825, 19798445
DESIR	Data from an Epidemiological Study on the Insulin Resistance syndrome	Case-control	European	France	731	≥90%	1) low call rate (none) 2) ethnic outliers (n=15 dropped using STRUCTURE)	Measured	Measured	Yes	8927780
EGCUT	Estonian Genome Center, University of Tartu	Population-based	European	Estonia	2059	≥98%	1) call-rate < 95% 2) related smaller than 2nd degree 3) duplicated samples 4) gender mismatch	Measured	Measured	Yes	24518929
EPIC-Norfolk	EPIC (European Prospective Investigation into Cancer) Norfolk	Population-based	European	England	2417	≥94%	1) relatedness 2) ethnic outlier 3) missing height	Measured	Measured	Yes	10466767
ERF	Erasmus Rucphen Family Study	Family-based	European	Netherlands	3,485	95%	1) gender mismatch 2) ethnic outliers 3) sex mismatch 4) excess heterozygosity 5) duplicates	Measured	Measured	Yes	15845033

FamHS	Family Heart Study	Family-based	European	USA - North America	3869	98%	1) To assess Mendelian errors, we ran LOKI on our family data and removed 5,035 SNPs with enough Mendelian errors to be considered outlier SNPs. We also removed 2 individuals who had an unacceptable number (greater than 600) of Mendelian errors, making them outliers as compared to the rest of	Measured	Measured	Yes	8651220
Fenland	Fenland Study	Population-based	European	UK	1500	95%	1) sex-check 2) relatedness check 3) ethnic ancestry outlying 4) heterozygosity check	Measured	Measured	Yes	20519560
FramHS	Framingham Heart Study	Population-based	European	USA	8481	>97%	1) Heterozygosity $\pm$ 5 SD from the mean 2) Call rate < 97% 3) Excessive Mendelian errors	Measured	Measured	Yes	14025561 1208363 17372189
FUSION	Finland-United States Investigation of NIDDM Genetics	Case-control	European	Finland	2333	>99%	1) Missing phenotypes or age<18 2) Gender discrepancy or anomaly 3) Unexplained duplicate sample 4) Relateds	Measured	Measured	Yes	17463248
Gendian	Genetics of Diabetic Nephropathy	Cohort study of type 2 diabetes complications	European	Germany	1026	95%	1) call-rate < 95% 2) related smaller than 2nd degree 3) duplicated samples 4) gender mismatch 5) non-european ethnicity	Measured	Measured	Yes	16961167 21980298
GS	Generation Scotland	Population-based	European	Scotland	9860	>97%	1) duplicates 2) gender mismatch 3) identity issues 4) excess heterozygosity	Measured	Measured	Yes	22786799
GENOA	Genetic Epidemiology Network of Arteriopathy	Cohort of sibships enriched for hypertension	European-American	USA- Rochester, MN	1509	$\geq$ 95%	1) Identical twins 2) sex mismatch 3) outliers ( $\pm$ 6 SDs) on first 10 PCs from EIGENSTRAT	Measured	Measured	Yes	11799070, 15121494
GOOD	Gothenburg Osteoporosis and Obesity Determinants Study	Population-based	European	Sweden	941	>97%	1) heterozygosity > 33% 2) ethnic outliers 3) related individuals 4) duplicates	Measured	Measured	Yes	22247082
GOYA cases	Genetics of Overweight Young Adults	Population-based (case-cohort)	European	Denmark	671 cases,	95%	1) heterozygosity 2) duplicates 3) sex mismatch 4) non-caucasians	Measured	Measured	Yes	18445669, 21935397
GOYA controls	Genetics of Overweight Young Adults	Population-based (case-cohort)	European	Denmark	790 controls	95%	1) heterozygosity 2) duplicates 3) sex mismatch 4) non-caucasians	Measured	Measured	Yes	18445669, 21935397
HERITAGE Family Study	Health, Risk Factors, Training and Genetics (HERITAGE) Family Study	Baseline measurements of an exercise intervention	European	USA -North America	499	>99%	None	Measured	Measured	Yes	21183627



HRS	Health and Retirement Study	Population-based	European-American	USA-North America	8652	>98%	1) duplicates 2) gender discrepancy 3) relatedness 4) ethnic outliers	Measured	NA	NA	24671021
HRS	Health and Retirement Study	Population-based	African American	USA-North America	1519	>98%	1) duplicates 2) gender discrepancy 3) relatedness 4) ethnic outliers	Measured	NA	NA	24671021
HYPERGENES	HYPERGENES	Case-Control	European	Europe	3916	>95%	1) first-degree and second-degree relatives 2) ancestry outliers 3) gender mismatch 4) identity issues 5) excessive heterozygosity 6) missing height or weight	Measured	Measured	Yes	22184326
InCHIANTI	Invecchiare in Chianti	Population-based	European	Italy	1231	97%	1) missing Phenotype 2) sex mismatch 3) Heterozygosity > 0.3	Measured	Measured	Yes	11129752
KORA3	Cooperative Health Research in the Region of Augsburg	Population-based	European	Germany	1,644	93%	1) german passport 2) missing height	Measured	Measured	Yes	16032513, 16032514
KORA4	Cooperative Health Research in the Region of Augsburg	Population-based	European	Germany	1,814	93%	1) german passport 2) missing height	Measured	Measured	Yes	16032513, 16032514
Lifelines	Lifelines Cohort study	Population-based	European	The Netherlands	9,388	95%	1) heterozygosity > 4SD from mean 2) duplicate and MZ samples 3) first-degree relatives 4) sex mismatch 5) non-caucasians	Measured	Measured	Yes	18075776, 25502107, 26333164
LOLIPOP_EW610	London Life Sciences Prospective Population Study	Population-based	European	UK - Lodon	945	95%	1) duplicates 2) gender discrepancy 3) contaminated samples 4) relatedness	Measured	Measured	Yes	21909110
LOLIPOP_IA317	London Life Sciences Prospective Population Study	Population-based with some enrichment	Indian Asian	UK - Lodon	2694	95%	1) duplicates 2) gender discrepancy 3) ethnic outliers 4) contaminated samples 5) relatedness 6) samples already in IA610	Measured	Measured	Yes	18454146
LOLIPOP_IA610	London Life Sciences Prospective Population Study	CHD case-control study	Indian Asian	UK - Lodon	7032	95%	1) duplicates 2) gender discrepancy 3) ethnic outliers 4) contaminated samples 5) relatedness	Measured	Measured	Yes	19820698
LURIC	Ludwigshafen Risk and Cardiovascular Health Study	Case-control	European	Ludwigshafen, Germany	2984	≥95%	1) related individuals 2) ambiguous sex	Measured	Measured	Yes	11258203
MESA	Multi-Ethnic Study of Atherosclerosis	Population-based	European	USA-North America	2399	>95%	1) first-degree relatives 2) ancestry outliers 3) gender mismatch, 4) excessive heterozygosity 5) missing height or weight	Measured	Measured	Yes	19075250

MrOS Sweden	Osteoporotic Fractures in Men (MrOS) Sweden	Population-based	European	Sweden	962	>97%	1) exclusion based on IBD clustering 2) checked for duplicates 3) identical twins	Measured	NA	NA	16598372
NTR	Netherlands Twin Register	Population-based	European	Netherlands	3331	>90%	1) duplicates 2) gender discrepancy 3) contaminated samples 4) relatedness	Measured	Measured	Yes	18763692, 18197199
NFBC66	Northern Finland Birth Cohorts 1966	Population-based	European	Finland	5402	≥95%	(1) duplicates (2) contaminated samples (3) excess heterozygosity (4) cryptic relatedness (5) withdrew consent gender mismatch (7) MDS outliers (6)	Measured	Measured	Yes	4911003
NHS	The Nurses' Health Study	Population-based	European	USA	2368	95%	1) duplicate 2) samples with misidentified sex, 3) related samples (siblings or possible first cousins) 4) samples with evidence of contamination 5) samples with highly variable intensity data, and	Measured	Measured	Yes	7860180
ORCADES	Orkney Complex Disease Study	Population-based	European	Scotland	889	>97%	1) duplicates 2) gender mismatch 3) identity issues 4) excess heterozygosity	Measured	Measured	Yes	18760389
PIVUS	The Prospective Investigation of the Vasculature in Uppsala Seniors	Prospective cohort	European	Sweden	949	>95%	1) gender mismatch 2) excess heterozygosity 3) duplicates	Measured	Measured	Yes	16141402
Prevend	Prevention of renal and vascular end-stage disease	Population-based	European	The Netherlands	3,649	≥95%	1) ethnic outliers 2) related individuals and duplicates 3) missing phenotype	Measured	Measured	Yes	12356629
PROSPER	The PROspective study of Pravastatin in the Elderly at Risk for vascular disease	Population-based	European	Europe	5244	≥95%	1) sex mismatch 2) ethnic outliers 3) heterozygosity (3 SD)	Measured	NA	NA	10569329
QFS	Quebec Family Study	Population-based	European	Quebec-Canada	929	95%	None	Measured	Measured	Yes	24533236
Rotterdam Study I	Rotterdam Study - I	Population-based	European	Netherlands	5974	≥ 98%	1) sex mismatch 2) excess autosomal heterozygosity >0.336 3) outliers identified by IBS clustering analysis	Measured	Measured	Yes	26386597
Rotterdam Study II	Rotterdam Study - II	Population-based	European	Netherlands	2157	≥98%	1) sex mismatch 2) excess autosomal heterozygosity >0.336 3) outliers identified by IBS clustering analysis	Measured	Measured	Yes	26386597
Rotterdam Study III	Rotterdam Study - III	Population-based	European	Netherlands	2078	≥ 98%	1) sex mismatch 2) excess autosomal heterozygosity >0.336 3) outliers identified by IBS clustering analysis	Measured	Measured	Yes	26386597

SARDINIA	SARDINIA Study on Aging	Population-based	European	Ogliastra Region in Sardinia (Italy)	4694	95%	1) gender discrepancy with genetic data from X-linked marker; 2) discrepancy between genetically inferred relationship with other samples and reported pedigree	Measured	Measured	Yes	16934002, 22291609
SHIP	Study of Health in Pomerania	Population-based	European	Germany - West Pomerania	4081	>92%	1) duplicates 2) gender discrepancy	Measured	Measured	Yes	20167617
THISEAS	The Hellenic study of Interactions between Snps and Eating in Atherosclerosis Susceptibility	CAD case-control	European	Greece	1000	≥95%	1) sex mismatch 2) ethnic outliers 3) heterozygosity (3 SD)	Measured	Measured	Yes	20167083
TRAILS	Tracking Adolescents' Individual Lives Survey	Population-based	European	The Netherlands	1354	95%	1) heterozygosity 2) duplicate and MZ samples 3) sex mismatch 4) non-caucasians	Measured	Measured	Yes	18263649, 23021478, 25431468
TwinsUK	TwinsUK	Population-based	European	UK	5654	>98%	1) call rate < 98% 2) heterozygosity across all SNPs ≥2 s.d. from the sample mean 3) duplicated samples 4) gender mismatch 5) evidence of non-European ancestry as assessed by PCA comparison with HanMap2	Measured	Measured	Yes	23088889
WGHS	Women's Genome Health Study	Population-based	European	USA	23294	98%	None	Self-reported	Self-reported	No, waist and WHR assessed 6 years after BMI	18070814
YFS	The Cardiovascular Risk in Young Finns Study	Population-based	European	Finland	2442	95%	1) gender mismatch 2) excess heterozygosity 3) duplicates 4) cryptic relatedness 5) ethnic outliers	Measured	Measured	Yes	18263651

**METABOCHIP DATA**

Study		Study design	Ancestry	Region	Total sample size (N)	Sample QC		Anthropometric assessment method			Study References (PMID)
Short name	Full name					Call rate*	sample exclusion criteria	BMI	WHR	WHR and BMI were assessed at the same time?	
DESIR	Data from an Epidemiological Study on the Insulin Resistance syndrome	Population based	European	France	4993	≥ 90%	1) missing data 2) ethnic outliers (n=66 dropped using PCA)	Measured	Measured	Yes	8927780
DR's EXTRA	DR's EXTRA	Population-based	European	Finland	1250	>99%	1) missing phenotypes or age<18 2) gender discrepancy or anomaly 3) unexplained duplicate sample 4) relateds across DR's EXTRA, FUSION, and METSIM	Measured	Measured	Yes	8177243
EGCUT Metabochip	Estonian Genome Center, University of Tartu	Population-based	European	Estonia	2510	≥ 98%	1) call-rate < 95% 2) related smaller than 2nd degree 3) duplicated samples 4) gender mismatch	Measured	Measured	Yes	24518929
Ely	MRC Ely Study	Population-based	European	UK	1602	95%	1) sex-check 2) relatedness check 3) ethnic ancestry outlying 4) hetezygosity check	Measured	Measured	Yes	17257284

EPIC	European Prospective Investigation into Cancer and Nutrition - Obesity Study	Case-cohort design	European	UK	1700	95%	1) sex-check 2) relatedness check 3) ethnic ancestry outlying 4) heterozygosity check	Measured	Measured	Yes	10466767 12795830
Fenland	Fenland Study	Population-based	European	UK	3217	95%	1) sex-check 2) relatedness check 3) ethnic ancestry outlying 4) heterozygosity check	Measured	Measured	Yes	20519560
FUSION2	Finland-United States Investigation of NIDDM Genetics	Case-control	European	Finland	2014	>99%	1) missing phenotypes or age<18 2) gender discrepancy or anomaly 3) unexplained duplicate sample 4) relateds across DR's EXTRA, FUSION, and METSIM	Measured	Measured	Yes	17463248
GLACIER	Gene x Lifestyle Interactions and Complex Traits Involved in Elevated Disease Risk	Population-based	European	Sweden	6064	≥95%	1) call-rate < 95% 2) sex mismatch	Measured	Waist, but not hip circumference	Yes	25396097
GXE	Gene By Environment	Population-based	Jamaican	Caribbean	613	≥95%	1) missing phenotype data 2) heterozygosity 3) PCA outliers 4) IBD cryptic relateds	Measured	Measured	Yes	9103091, 9098179, 20400458
Health2006	Health2006	Population-based	European	Capital region of Denmark	3207	>99%	1) individuals with 1st or 2nd degree familial relationship 2) extreme inbreeding coefficient 3) low call rate 4) mislabelled sex and 5) high discordance to previous genotypings	Measured	Measured	Yes	23615486
HUNT	The Nord-Trøndelag Health Study	Population-based with enrichment for T2D cases	European	Norway	1567	>99%	1) missing phenotypes or age<18 2) gender discrepancy or anomaly 3) unexplained duplicate sample 4) relateds	Measured	Measured	Yes	[No PMID] Holmen J, Midthjell K, et al. The Nord-Trøndelag Health Study 1995-97 (HUNT 2): Objectives, contents, methods and participation.
IMPROVE	Carotid Intima Media Thickness (IMT) and IMT-Progression as Predictors of Vascular Events in a High-Risk European Population	Population-based (high CVD-risk)	European	Europe (Italy, France, Netherlands, Sweden, Finland)	3426	≥ 95%	1) ambiguous sex 2) cryptic relatedness 3) non-european descent	Measured	Measured	Yes	22999719
Inter99 (I99)	Inter99	Population-based	European	Capital region of Denmark	6127	>99%	1) individuals with 1st or 2nd degree familial relationship 2) extreme inbreeding coefficient 3) low call rate 4) mislabelled sex and 5) high discordance to previous genotypings	Measured	Measured	Yes	14663300 12882858 19898830
KORA S3	Cooperative Health Research in the Region of Augsburg	Population-based	European	Germany	3,113	93%	none	Measured	Measured	Yes	16032513 16032514
KORA S4	Cooperative Health Research in the Region of Augsburg	Population-based	European	Germany	3,028	93%	none	Measured	Measured	Yes	

MEC	The Multiethnic Cohort Study	Population-based	African	USA-North America	≥ 95%	>95%	1) first-degree relatives 2) ancestry outliers 3) gender mismatch 4) identity issues	Self-reported	Self-measured	Yes	10695593
METSIM	Metabolic Syndrome In Men	Population-based with enrichment for T2D cases	European	Finland	2162	>99%	1) missing phenotypes or age<18 2) gender discrepancy or anomaly 3) unexplained duplicate sample 4) relateds across DR's EXTRA, FUSION, and METSIM	Measured	Measured	Yes	19223598
NSHD	MRC National Survey of Health & Development	Birth cohort	European	UK	2476	95%	1) sex-check 2) relatedness check 3) ethnic ancestry outlying 4) hetezygosity check	Measured	Measured	Yes	15814867 16204333
SCARFSHEEP	Stockholm Coronary Atherosclerosis Risk Factor-Stockholm Heart Epidemiology Program	MI case-control	European	Europe (Stockholm, Sweden)	2899	≥95%	1) ambiguous sex 2) cryptic relatedness 3) non-european descent	Measured	Measured	Yes	16238676 10447785
SPT	Spanish Town	Population-based	Jamaican	Caribbean	476	≥95%	1) missing phenotype data 2) heterozygosity 3) PCA outliers 4) IBD cryptic relateds	Measured	Measured	Yes	9103091, 9098179, 20400458
WHI	Women's Health Initiative Study	Population-based	African	USA-North America	YR3/YR4 (3508) ; Pilot (2203)	>95%	1) first-degree relatives 2) ancestry outliers 3) gender mismatch 4) identity issues 5) excessive heterozygosity 6) missing height or weight	Measured	Measured	Yes	14575938
Whitehall	The Whitehall II study	Cohort of London-based civil servants	European	UK	2413	95%	1) missing phenotype data 2) gender check 3) duplicates check 4) relatedness check 5) ethnic check	Measured	Measured	Yes	15576467 21441441
<b>VALIDATION DATA</b>											
UKBB	UK Biobank	Population study	White British	UK	120,286	NA, See UKB document on QC <a href="http://biobank.ctsu.ox.ac.uk/showcase/reference.cgi?id=155580">http://biobank.ctsu.ox.ac.uk/showcase/reference.cgi?id=155580</a>	1) Sex mismatch 2) HWE P<1x10-6 3) non British ancestry	Measured	Measured	Yes	DOI: 10.1371/journal.pmed.1001779

**Supplementary Table 2.** Information on genotyping methods, quality control of SNPs, imputation, and statistical analysis for GWAS and Metabochip study cohorts. Abbreviations: MAF- minor allele frequency, HWE- Hardy-Weinberg Equilibrium, QC- quality control, SNP- single nucleotide polymorphism, GWAS- genome-wide association study.

GWAS DATA											
Study	Ancestry	Genotyping				Imputation					Statistical Analysis Software
		Genotyping array	Genotype calling software	SNP QC		No. of SNPs after QC	No. of SNPs used for imputation	Imputation Software	Imputation reference panel (NCBI build)	Imputed X chromosome data available? (software, reference)	
				Call rate*	p for HWE						
AE	European	Affymetrix SNP 5.0	BRLMM-P	≥ 97%	> 10 <sup>-6</sup>	403,789	403,789	BEAGLE v3.3.2	HapMap r 22 CEU	No	PLINKv1.07
AGES	European	Illumina Hu370CNV	BeadStudio	>97%	> 10 <sup>-6</sup>	325,094	308,340	Mach + MiniMac	HapMap r 22 CEU	Yes, (IMPUTE2)	ProbABEL
ARIC	European	Affymetrix 6.0	Birdseed	≥ 90%	> 10 <sup>-6</sup>	685,812	685,812	MACH v1.0.16	HapMap CEU, release 22, build 36	No	ProbABEL
ARIC	African American	Affymetrix 6.0	Birdseed	≥ 90%	> 10 <sup>-6</sup>	685,812	685,812	MACH v1.0.16	HapMap YRI, release 22, build 36	No	ProbABEL
AUSTWIN	European	Illumina370, Illumina610	Beadstudio-gencall v3.0	95%	> 10 <sup>-6</sup>	269,840	269,840	MACH v1.0.15	HapMap r22 (build 36)	No	ProbABEL,R
BHS	European	Illumina 610 Quad	BeadStudio	>95%	> 10 <sup>-6</sup>	529,526	529,526	MaCH	HapMap r 22 CEU	No	ProbABEL, mach2qtl
BioMe (MSSM)	European American	Illumina HumanOmniExpressExome-8 v1.0	zCall (GenomeStudio)	≥ 90%	> 10 <sup>-6</sup>	906,917	768,517	IMPUTE2	I000G v3 (March 2012)	Yes	SAS, Quicktest
BioMe (MSSM)	African American	Illumina HumanOmniExpressExome-8 v1.0	zCall (GenomeStudio)	≥ 90%	> 10 <sup>-6</sup>	906,917	768,517	IMPUTE2	I000G v3 (March 2012)	Yes	SAS, Quicktest
BioMe (MSSM)	Hispanic / Latinos	Illumina HumanOmniExpressExome-8 v1.0	zCall (GenomeStudio)	≥ 90%	> 10 <sup>-6</sup>	906,917	768,517	IMPUTE2	I000G v3 (March 2012)	Yes	SAS, Quicktest
BLSA	European	Illumina 450K	BeadStudio	≥ 99%	> 10 <sup>-6</sup>	514,027	514,027	MACH	HapMap release22, build 36	No	ProbABEL
British 1958 birth cohort (BS8C)	European	Illumina 550k_v1, 550k_v3, 610k (3 non-overlapping subsets)	BeadStudio	≥ 95%	> 10 <sup>-4</sup>	500,521	500,521	MACH/Minimac	HapMap r 21 CEU	Yes, (MACH/Minimac)	ProbABEL
CHS	European	Illumina 370CNV BeadChip	Illumina BeadStudio	≥ 97%	> 10 <sup>-5</sup>	306,655	306,655	BIMBAM v0.99	HapMap release22, build 36	Yes, (build 36, release 24)	R
CLHNS	East Asian (Filipino)	Affymetrix Genome-Wide Human SNP Array 5.0	Birdseed (version 2)	≥ 90%	> 10 <sup>-6</sup>	352,264	352,264	MACH v.1.0	HapMap r22 CHB+JPT+CEU	No	ProbABEL, mach2qtl
COLAUS	European	Affymetrix 500k	APT	90%	> 10 <sup>-7</sup>	390,631	390,631	IMPUTE	HapMap r 21 CEU	No	Matlab
CROATIA-Korcula	European	Illumina HumanHap370 CNV	BeadStudio	>98%	> 10 <sup>-6</sup>	316,730	316,730	MACH	HapMap r 22 CEU	No	ProbABEL
CROATIA-Vis	European	Illumina HumanHap300	BeadStudio	>98%	> 10 <sup>-6</sup>	308,996	308,996	MACH	HapMap r 22 CEU	No	ProbABEL
DESIR	European	Illumina Human CNV370-Duo Array and Illumina HAP300 array	BeadStudio	≥ 95%	> 10 <sup>-4</sup>	291,609	291,609	IMPUTE2	HapMap r 22 CEU	No	SNPtest
EGCUT GWAS	European	Illumina OmniExpress	Illumina BeadStudio	95%	> 10 <sup>-6</sup>	611,549	611,549	IMPUTE2	HapMap r 22 CEU	No	R, Quicktest
EPIC-Norfolk	European	Affymetrix 500K	BRLMM	≥ 90%	> 10 <sup>-6</sup>	382,036	382,036	IMPUTE	HapMAP 21 CEU	Yes	Quicktest
ERF	European	Illumina 318K, 370K, 610K, Affymetrix 250K	Genome Studio & Beadstudio, BRLMM	95%	> 10 <sup>-6</sup>	649,956	635,956	MACH 1.0.16	HapMap release22, build 36	Yes, (build 36, rel 22 (IMPUTE))	GenABEL, ProbABEL
FamHS	European	Illumina HumMap 550k, Human610-Quadv1, Human 1M-Duov3	BeadStudio	98%	> 10 <sup>-6</sup>	2,543,887	499,558	MaCH	HapMap r 22 CEU	Yes	SAS, R
Fenland	European	Affymetrix SNPs 5.0	BRLMM	95%	> 10 <sup>-6</sup>	360,602	360,602	IMPUTE2	1000GP Phase1 v3	Yes	SNPtest, Quicktest
FramHS	European	Affymetrix 500K	BRLMM	>97%	> 10 <sup>-6</sup>	378,163	378,163	MACH v1.0.15	HapMap r 22 CEU	Yes	R
FUSION	European	Affymetrix 50K supplemental	BeadStudio	>98%	> 10 <sup>-6</sup>	315,635	315,635	MaCH	HapMap r 22 CEU	No	ProbABEL
Gendian	European	Genome-Wide Human SNP Array 6.0	Affymetrix - birdseed, (algorithm: BRLMM)	MAF>.1 & callrate<.9 MAF>.09 & MAF ≤.1 & callrate <.91	> 10 <sup>-6</sup>	747,402	747,402	Mach 1.0.18.c MiniMac 2012-10-09	GIANT ALL 1000G v3 ref panel GRCh build 37	Yes, (MaCH/ minimac, GIANT ALL 1000G v3 ref panel GRCh build 37)	ProbABEL, R, Plink
Generation Scotland	European	Illumina HumanOmniPlusExome	BeadStudio	>98%	> 10 <sup>-6</sup>	706,980	706,980	Shapeit2 + IMPUTE2	1000G (ALL)	Yes, (IMPUTE2)	ProbABEL
GENOA	European American	Affymetrix 6.0 & Illumina 1M-Duo Bead Chip	Birdseed and Genome Studio	≥ 95%	NA	Affymetrix: 596,941; Illumina: 804,154	Affymetrix: 596,941; Illumina: 804,154	MACH 1.0.16	HapMap (release 22) CEU	No	MMAP
GOOD	European	Illumina 610	Beadstudio	>98%	> 10 <sup>-6</sup>	553,191	521,160	MaCH	HapMap CEU, release 22, build 36	Yes	PLINK, R
GOYA cases	European	Illumina 610K Quad	GenomeStudio	≥ 95%	> 10 <sup>-7</sup>	545,349	545,349	Mach 1.0	HapMap r22 (build 36)	No	Quicktest
GOYA controls	European	Illumina 610K Quad	GenomeStudio	≥ 95%	> 10 <sup>-7</sup>	545,349	545,349	Mach 1.0	HapMap r22 (build 36)	No	Quicktest
HERITAGE Family Study	European	Illumina 370CNV	GenomeStudio	≥ 98%	> 10 <sup>-6</sup>	324,607	324,607	MaCH	HapMap r 22 CEU	No	ProbABEL
HRS	European American	Illumina Omni2.5 Beadchip	BeadStudio	98%	> 10 <sup>-4</sup>	1,681,327	551,936	MaCH	HapMap r 22 CEU	Yes, (MaCH)	PLINK, ProbABEL
HRS	African American	Illumina Omni2.5 Beadchip	BeadStudio	98%	> 10 <sup>-4</sup>	1,681,327	909,595	MaCH	HapMap r 22 CEU+YRI	No	PLINK, ProbABEL
HYPERGENES	European	Illumina 1M-Duo	Genome-Studio	≥ 99%	> 10 <sup>-8</sup>	882,854	882,854	Minimac	HapMap r 22 CEU	No	PLINK
InCHIANTI	European	Illumina 450K	BeadStudio	≥ 99%	10 <sup>-4</sup>	498,838	498,838	MACH	HapMap release22, build 36	No	ProbABEL
KORA3	European	Affymetrix 500K	BRLMM	none	none	490,032	490,032	MACH v1.0.9	HapMap r 22 CEU	No	ProbABEL, R
KORA4	European	Affymetrix 6.0	Birdseed	none	none	909,622	909,622	IMPUTE v0.4.2	HapMap r 22 CEU	No	ProbABEL, R
Lifelines	European	Illumina Cyto SNP12 v2	GenomeStudio	>95%	> 10 <sup>-4</sup>	257,581	257,581	BEAGLE v3.3.2	HapMap r24 CEU (build 36)	No	PLINKv1.07
LOLIPOP_EW610	European	Illumina Human610	BeadStudio	95%	> 10 <sup>-6</sup>	544,620	544,620	IMPUTE2	HapMap r 22 CEU	No	Quicktest
LOLIPOP_IA317	Indian Asian	Illumina HumanHap300	BeadStudio	95%	> 10 <sup>-6</sup>	307,303	307,303	IMPUTE2	HapMap r 22 population combined	No	Quicktest











TWINSUK	EU	men	532	19.19	0.54	22.61	3.77	416	78.20	65	12.20	30	5.60	81.73	9.70	0.82	0.05	205	38.50	326	61.50
WGHS	EU	women	2,888	47.34	12.70	25.18	4.68	1,639	56.75	858	29.77	391	13.54	79.15	10.54	0.78	0.06	1,263	43.73	1,625	56.27
WHI Pilot	AF	women	1,998	61.00	6.88	31.36	6.81	323	16.17	660	33.03	1,015	50.80	91.82	14.00	0.82	0.07	220	11.01	1,778	88.99
WHIYR3/YR4	AF	women	3,180	61.20	7.30	31.50	6.75	484	15.22	993	31.23	1,703	53.55	92.59	14.37	0.83	0.09	372	11.70	2,808	88.30
YFS	EU	women	1,067	37.79	4.97	25.29	4.96	588	55.10	299	28.00	169	15.80	83.50	12.48	0.83	0.07	160	15.00	907	85.00
		men	900	37.69	5.04	26.75	4.29	327	36.30	405	45.00	166	18.40	94.44	12.01	0.94	0.07	206	22.90	694	77.10

METBOCHIP Data																					
Study	Ancestry	Groups	N	Age		BMI (kg/m <sup>2</sup> )		BMI Categories*						Waist (cm)		WHR (ratio)		Current Smoking Status			
				mean	sd	mean	sd	Normal weight		Overweight		Obese		mean	sd	mean	sd	Smoker		Non-Smoker	
								n	%	n	%	n	%					n	%	n	%
DESIR	EU	Overall	4,263	46.26	10.21	25.23	3.86	2,182	51.22	1,611	37.82	467	10.96	84.91	11.62	0.87	0.09	1,035	24.28	3,228	75.72
		women	1,968	46.38	10.32	24.79	4.29	1,160	59.00	565	28.74	241	12.26	78.87	10.72	0.80	0.07	362	18.39	1,606	81.61
		men	2,295	46.15	10.12	25.61	3.40	1,022	44.55	1,046	45.60	226	9.85	90.08	9.70	0.92	0.06	673	29.32	1,622	70.68
DR's EXTRA	EU	women	621	66.47	5.25	27.57	5.04	215	34.60	246	39.60	160	25.80	88.71	13.10	0.87	0.07	44	7.10	577	92.90
		men	546	66.50	5.44	27.37	3.74	147	26.90	289	52.90	110	20.20	98.17	10.69	0.99	0.05	78	14.30	466	85.70
EGCUT	EU	women	1490	59.45	12.58	28.27	6.91	573	39.19	319	21.82	570	38.99	87.78	17.69	0.84	0.09	387	36.48	1103	76.44
		men	1014	60.25	11.64	28.02	5.70	362	35.7	288	28.40	364	35.9	97.95	15.03	0.95	0.10	674	63.52	340	23.56
ELY	EU	women	366	57.27	7.57	26.20	4.44	169	46.20	133	36.30	64	17.50	81.89	10.96	0.80	0.08	59	16.10	307	83.90
		men	262	58.07	7.82	26.82	3.09	79	30.20	142	54.20	41	15.60	95.60	9.36	0.96	0.07	47	17.90	215	82.10
EPIC-non-subcohort	EU	women	216	62.68	8.50	28.95	4.61	41	19.00	100	46.30	75	34.70	90.47	11.63	0.84	0.06	31	14.40	185	85.60
		men	321	61.92	8.39	28.38	3.57	35	10.90	218	67.90	68	21.20	101.92	9.72	0.97	0.05	36	11.20	285	88.80
EPIC-subcohort	EU	women	474	58.92	9.59	25.64	3.78	227	47.90	195	41.10	52	11.00	81.00	10.10	0.79	0.06	67	14.10	407	85.90
		men	339	59.45	9.07	25.99	2.96	131	38.60	182	53.70	26	7.70	93.93	9.12	0.92	0.06	39	11.50	300	88.50
FENLAND	EU	women	1,542	47.01	7.01	26.47	5.54	740	48.00	485	31.50	317	20.60	85.18	12.87	0.82	0.07	194	12.60	1,348	87.40
		men	1,368	46.98	7.17	27.04	4.08	453	33.10	642	46.90	273	20.00	96.50	11.20	0.93	0.07	197	14.40	1,171	85.60
FUSION2-controls	EU	women	47	39.09	9.24	26.56	5.99	23	48.90	12	25.50	12	25.50	84.72	15.24	0.81	0.08	30	63.80	17	36.20
		men	43	41.29	13.98	26.47	4.03	14	32.60	24	55.80	5	11.60	95.21	11.11	0.92	0.07	29	67.40	14	32.60
FUSION2-T2D cases	EU	women	43	57.12	10.45	30.96	6.82	8	18.60	13	30.20	22	51.20	99.62	16.00	0.90	0.06	20	46.50	23	53.50
		men	109	58.63	8.04	31.29	5.60	14	12.80	35	32.10	60	55.10	107.91	14.50	1.00	0.07	43	39.40	66	60.60
GLACIER	EU	women	3,619	49.27	8.82	25.56	4.38	1,869	51.80	1,219	33.80	517	14.30	86.56	11.73	NA	NA	861	23.80	2,758	76.20
		men	2,341	50.07	8.33	26.09	3.42	927	39.60	1,146	49.00	265	11.30	96.83	10.07	NA	NA	496	21.20	1,845	78.80
GXE	JAMAICA	women	469	40.02	8.13	32.33	7.47	101	21.54	0	0.00	368	78.47	88.78	15.31	0.80	0.07	20	0.04	449	95.73
		men	140	38.67	8.90	27.69	6.94	66	47.14	0	0.00	74	52.86	87.72	17.91	0.85	0.08	31	22.14	109	77.85
HEALTH2006	EU	women	1,580	48.83	12.97	25.32	5.02	860	54.40	454	28.70	236	14.90	83.23	12.58	0.82	0.07	378	23.90	1,202	76.10
		men	1,304	50.43	12.76	26.60	4.16	496	38.00	581	44.60	225	17.30	95.29	12.06	0.94	0.07	281	21.50	1,023	78.50
HUNT-controls	EU	women	319	68.03	13.56	27.65	4.56	92	28.80	130	40.80	97	30.40	86.72	11.11	0.83	0.06	84	26.30	235	73.70
		men	368	63.58	14.58	26.53	3.30	120	32.60	202	54.90	46	12.50	93.38	8.69	0.92	0.06	106	28.80	262	71.20
HUNT-T2D cases	EU	women	238	70.42	11.92	30.11	5.15	37	15.50	83	34.90	118	49.60	93.94	11.97	0.86	0.06	24	10.10	214	89.90
		men	277	66.90	11.08	28.12	3.79	61	22.00	133	48.00	83	30.00	98.60	9.61	0.95	0.06	58	20.90	219	79.10
IMPROVE	EU	women	1,777	64.38	5.45	27.10	4.76	651	36.60	702	39.50	424	23.90	89.61	12.44	0.87	0.07	238	13.40	1,539	86.60
		men	1,653	64.04	5.35	27.39	3.64	420	25.40	900	54.50	332	20.00	98.70	10.81	0.97	0.07	274	16.60	1,379	83.40
INTER99	EU	women	3,036	45.94	7.90	25.76	5.07	1,582	52.10	919	30.30	505	16.60	80.30	12.33	0.80	0.06	1,075	35.40	1,961	64.60
		men	2,907	46.66	7.72	26.82	4.02	996	34.30	1,403	48.20	503	17.30	93.26	11.04	0.92	0.06	1,070	36.80	1,837	63.20
KORAS3	EU	women	659	40.89	12.66	25.18	4.72	387	58.70	173	26.30	98	14.90	79.12	11.24	0.78	0.06	473	71.80	186	28.20
		men	599	40.58	13.14	26.54	3.43	207	34.60	305	50.90	87	14.50	92.80	9.33	0.90	0.06	392	65.40	207	34.60
KORAS4	EU	women	624	41.35	14.82	25.94	5.09	294	47.10	223	35.70	107	17.10	82.16	12.00	0.79	0.06	476	76.30	148	23.70
		men	582	42.49	15.74	26.64	3.59	197	33.80	295	50.70	90	15.50	94.34	10.00	0.90	0.06	389	66.80	193	33.20
MEC-Diabetes cases	AF	Overall	384	68.72	8.27	31.53	6.63	48	12.50	135	35.16	200	52.08	103.58	15.09	0.91	0.10	70	18.23	314	81.77
		women	278	68.03	8.22	32.18	6.94	35	12.59	88	31.65	154	55.40	102.94	15.55	0.89	0.10	51	18.35	227	81.65

		men	106	70.52	8.15	29.80	5.41	13	12.26	47	44.34	46	43.40	105.26	13.72	0.96	0.08	19	17.92	87	82.08
MEC-controls	AF	Overall	1,284	69.37	8.6	28.59	6.36	367	28.58	492	38.32	414	32.24	95.03	14.86	0.87	0.11	158	12.31	1,126	87.69
		women	1,026	68.90	8.68	29.01	6.61	280	27.29	376	36.65	362	35.28	94.42	15.29	0.86	0.11	116	11.31	910	88.69
		men	258	71.26	7.97	26.91	4.90	87	33.72	116	44.96	52	20.16	97.37	12.82	0.94	0.09	42	16.28	216	83.72
METSIM-controls	EU	men	899	53.94	4.99	26.40	3.39	313	34.80	468	52.10	118	13.10	95.83	9.70	0.95	0.06	145	16.10	754	83.90
METSIM-T2D cases		men	1,143	60.53	6.63	30.17	5.15	150	13.10	480	42.00	513	44.90	107.14	13.33	1.02	0.07	181	15.80	962	84.20
NSHD	EU	women	1,213	53.00	0.00	27.35	5.23	454	37.40	459	37.80	300	24.70	85.59	12.53	0.81	0.07	295	24.30	918	75.70
		men	1,216	53.00	0.00	27.36	3.93	340	28.00	612	50.30	264	21.70	97.66	10.44	0.94	0.06	298	24.50	918	75.50
SCARSHEEP cases	EU	women	402	60.03	7.35	27.02	4.97	148	36.90	149	37.20	104	25.90	90.30	13.52	0.87	0.08	142	35.30	260	64.70
		men	1,120	56.76	7.13	26.92	3.63	341	30.70	569	51.30	199	17.90	99.00	9.92	0.97	0.06	442	39.50	678	60.50
SCARSHEEP controls	EU	women	554	60.72	7.07	25.57	4.06	275	50.20	199	36.30	74	13.50	86.32	11.86	0.85	0.09	176	31.80	378	68.20
		men	1,334	57.55	7.05	25.86	3.48	567	42.60	612	46.00	151	11.40	95.98	9.77	0.96	0.07	371	27.80	963	72.20
SPT	JAMAICA	women	553	45.59	13.06	28.41	6.06	157	28.39	193	34.90	203	36.70	84.24	12.47	1.00	0.00	66	11.93	487	88.07
		men	351	47.95	14.81	24.29	4.34	251	71.50	103	29.34	33	9.40	82.77	12.53	0.85	0.88	116	33.05	235	66.95
WHITEHALL	EU	women	708	61.01	6.12	27.12	5.63	277	39.10	255	36.00	176	24.90	83.69	13.22	0.81	0.07	69	9.70	639	90.30
		men	2,345	60.64	5.91	26.62	3.67	793	33.80	1,179	50.30	373	15.90	94.35	10.49	0.94	0.07	152	6.50	2,193	93.50
<b>VALIDATION Data</b>																					
<b>UKBB</b>	<b>EU</b>	<b>combined</b>	118,634	56.93	7.93	27.5362	4.8278	37,551	31.7	50,468	42.5	29,680	25	90.81	13.6	0.8750	0.0906	13,416	11.3	105,218	88.69

\* BMI categories will not add up to the total sample size (N) in studies that excluded underweight (BMI<18.5) individuals.







KORAS4	EU	men	207	36.28	9.10	26.27	3.54	77	37.20	105	50.70	25	12.10	91.42	9.21	0.90	0.06	392	42.85	14.33	26.68	3.36	130	33.20	200	51.00	62	15.80	93.53	9.32	0.90	0.06
		women	148	35.32	8.77	24.33	4.78	88	59.50	43	29.10	17	11.50	78.78	11.53	0.78	0.06	476	43.23	15.79	26.45	5.08	206	43.30	180	37.80	90	18.90	83.21	11.96	0.79	0.06
		men	193	36.96	10.90	26.21	3.31	72	37.30	101	52.30	20	10.40	93.07	9.49	0.90	0.06	389	45.23	17.01	26.86	3.70	125	32.10	194	49.90	70	18.00	94.98	10.19	0.91	0.06
MEC-Diabetes cases	AF	Overall	70	66.83	8.02	31.21	6.17	10	14.29	26	37.14	34	48.57	102.81	15.61	0.91	0.09	314	69.14	8.27	31.60	6.73	35	11.15	109	34.71	166	52.87	103.75	14.98	0.91	0.11
		women	51	64.77	7.03	31.39	5.66	7	13.73	18	35.29	26	50.98	102.00	15.19	0.90	0.09	227	68.77	8.30	32.36	7.19	28	12.33	70	30.84	128	56.39	103.16	15.66	0.89	0.11
		men	19	72.37	8.04	30.73	7.50	3	15.79	8	42.11	8	42.11	105.13	17.99	0.93	0.06	87	70.11	8.17	29.60	4.86	7	8.05	39	44.83	38	43.68	105.29	13.02	0.97	0.08
MEC-controls	AF	Overall	158	67.93	8.47	27.46	6.56	65	41.14	51	32.28	41	25.95	93.98	15.69	0.89	0.12	1,126	69.58	8.60	28.75	6.32	302	26.82	441	39.17	373	33.13	95.18	14.74	0.87	0.11
		women	116	66.79	8.23	28.09	18.33	43	37.07	38	32.76	35	30.17	94.00	16.08	0.87	0.09	910	69.17	8.71	29.13	6.61	237	26.04	338	37.14	327	35.93	94.48	15.20	0.86	0.11
		men	42	71.07	8.42	25.71	6.20	22	52.38	13	30.95	6	14.29	93.92	14.79	0.95	0.15	216	71.29	7.90	27.15	4.58	65	30.09	103	47.69	46	21.30	98.03	12.34	0.94	0.08
METSIM-controls	EU	men	145	53.84	4.84	26.30	3.48	55	37.90	67	46.20	23	15.90	96.25	9.69	0.97	0.06	754	53.96	5.02	26.43	3.37	258	34.20	401	53.20	95	12.60	95.75	9.71	0.95	0.059
METSIM-T2D cases		men	181	57.56	6.12	30.05	4.89	28	15.50	68	37.60	85	47.00	108.34	11.92	1.04	0.06	962	61.09	6.58	30.19	5.20	122	12.70	412	42.80	428	44.50	106.92	13.58	1.02	0.07
NSHD	EU	women	295	53.00	0.00	26.54	4.73	124	42.00	109	36.90	62	21.00	85.11	12.12	0.82	0.07	918	53.00	0.00	27.60	5.35	330	35.90	350	38.10	238	25.90	85.74	12.66	0.80	0.07
		men	298	53.00	0.00	26.56	3.97	107	35.90	138	46.30	53	17.80	96.39	10.28	0.94	0.06	918	53.00	0.00	27.62	3.88	233	25.40	474	51.60	211	23.00	98.07	10.46	0.94	0.06
SCARSHEEP cases	EU	women	176	58.94	7.24	27.27	5.05	57	32.60	72	41.10	46	26.30	91.26	13.66	0.87	0.08	212	60.81	7.37	26.97	4.98	81	38.20	71	33.50	57	26.90	89.77	13.52	0.87	0.09
		men	442	55.76	6.76	26.76	3.51	135	30.80	230	52.50	73	16.70	99.47	9.42	0.97	0.06	653	57.43	7.34	27.02	3.72	200	30.60	324	49.60	122	18.70	98.61	10.20	0.97	0.06
SCARSHEEP controls	EU	women	142	59.56	7.16	24.91	3.96	77	54.60	49	34.80	15	10.60	85.52	12.21	0.86	0.09	404	61.13	7.02	25.75	4.03	193	47.80	149	36.90	56	13.90	86.52	11.67	0.85	0.09
		men	371	57.09	7.16	25.33	3.56	181	48.90	153	41.40	36	9.70	94.94	10.15	0.96	0.08	947	57.78	7.00	26.06	3.41	376	39.70	454	47.90	112	11.80	96.39	9.58	0.96	0.07
SPT	JAMAICA	women	66	43.355	12.02	28.41	6.06	20	30.30	20	30.30	20	30.30	82.64	13.53	0.89	0.06	487	45.9	13.19	28.58	5.90	126	25.87	173	35.52	183	35.58	84.50	12.31	0.81	0.11
		men	116	49.88	13.53	24.30	4.34	85	73.28	19	16.37	4	0.03	101.6	5.16	0.85	0.11	235	47	15.34	20.24	4.43	117	49.79	84	35.74	29	12.34	84.95	13.02	0.85	0.07
WHITEHALL	EU	women	69	60.19	6.36	27.06	5.88	22	31.90	35	50.70	12	17.40	85.22	14.00	0.84	0.08	639	61.10	6.09	27.13	5.61	255	39.90	220	34.40	164	25.70	83.52	13.14	0.81	0.07
		men	152	58.77	5.42	26.14	3.53	55	36.20	76	50.00	21	13.80	93.86	9.89	0.95	0.06	2,193	60.77	5.92	26.66	3.67	738	33.70	1,103	50.30	352	16.10	94.39	10.53	0.94	0.07

VALIDATION Data

SMOKERS																NON-SMOKERS																
Study	Ancestry	Groups	N	Age		BMI		BMI Categories*						Waist (cm)		WHR (ratio)		N	Age		BMI		BMI Categories*						Waist (cm)		WHR (ratio)	
								Normal weight		Overweight		Obese											Normal weight		Overweight		Obese					
				mean	sd	mean	sd	n	%	n	%	n	%	mean	sd	mean	sd		n	%	n	%	n	%	mean	sd	mean	sd	mean	sd	mean	sd
UKBB	EU	combined	13,416	54.914	8.0029	26.9962	4.8998	4,800	35.78	5,384	40.13	3,007	22.42	90.866	13.590	0.890	0.088	105,218	57.188	7.889	27.605	4.814	32,751	31.100	45,084	42.850	26,673	25.350	90.8008	13.61	0.8732	0.09071



**Supplementary Table 5.** Results for approximate conditional analyses to identify secondary signals and to determine independence from previously-identified anthropometric-associated SNPs for novel loci identified in Approach 1 (SNPadJSMK). \*The top variant after conditioning differed between ARIC and FHS for rs6012558.

Chr	Tag SNP (TS)			Condition on	Most Significant after conditioning			Before Conditioning			ARIC reference panel			FHS reference panel				
	Marker	$\beta$	SE		TS Marker	Marker	Distance	$r^2$	$\beta$	SE	P	$\beta$	SE	P	$\beta$	SE	P	
<b>BMI</b>																		
3	rs6794880	0.028	0.005	<b>4.3E-08</b>	rs6794880	rs7627971	962779	0.006	0.017	0.004	7.95E-05	0.016	0.004	1.62E-04	0.015	0.004	3.44E-04	
6	rs4498364	-0.023	0.004	<b>7.2E-09</b>	rs4498364	rs13213457	945919	0.001	-0.020	0.005	3.03E-05	-0.020	0.005	2.98E-05	-0.020	0.005	5.15E-05	
<b>WHRadjBMI</b>																		
6	rs1049281	-0.025	0.004	2.16E-09	rs1049281	rs2261033	367024	0.129	-0.0193	0.0034	1.92E-08	-0.013	0.003	4.44E-05	-0.014	0.003	1.33E-05	
<b>WCadjBMI</b>																		
3	rs4378999	0.036	0.007	<b>4.12E-08</b>	rs4378999	rs4256170	16520	0.064	0.093	0.019	1.37E-06	0.080	0.019	2.63E-05	0.086	0.019	7.67E-06	
9	rs9409082	0.027	0.005	<b>1.49E-08</b>	rs9409082	rs902143	280862	0.005	0.016	0.004	6.49E-06	0.015	0.004	2.08E-05	0.016	0.004	8.22E-06	
20	rs6012558	0.020	0.004	<b>1.91E-08</b>	rs6012558	rs4810880/ rs237724*	100357 406146	0.125 0.094	0.216 0.024	0.004 0.006	2.96E-07 1.17E-05	0.143 -	0.004 -	3.33E-04 -	-	0.020	0.005	2.83E-04
Chr	Tag SNP (TS) Before Conditioning			Condition On	Known SNP			Known SNP			ARIC reference panel			FHS reference panel				
	Marker	$\beta$	SE		P	Known Marker	Trait	Distance	$r^2$	$\beta$	SE	P	TS After Conditioning	TS After Conditioning	TS After Conditioning	TS After Conditioning		
<b>BMI</b>																		
2	rs10929925	-0.020	0.003	<b>1.1E-09</b>	rs10495537	Visceral fat	538962	3.32E-07	0.002	0.004	6.59E-01	-0.020	0.003	<b>1.42E-09</b>	-0.020	0.003	<b>1.36E-09</b>	
					rs7586540	coronary artery calcification	102806	0.02039	0.002	0.007	7.79E-01	-0.020	0.003	<b>1.20E-09</b>	-0.020	0.003	<b>1.36E-09</b>	
<b>WHRadjBMI</b>																		
					rs6457374	height	35694	0.713	0.023	4.40E-03	1.37E-07	-0.007	0.003	5.08E-03	-0.008	0.003	3.41E-03	
					rs2247056	height/triglycerides	28923	0.714	-0.021	4.00E-03	1.41E-07	-0.008	0.003	3.03E-03	-0.009	0.003	1.95E-03	
					rs2844479	height	336389	0.090	-0.016	3.90E-03	2.94E-05	-0.020	0.004	7.72E-07	-0.021	0.004	4.47E-07	
					rs2857693	height	351817	0.112	0.015	3.70E-03	3.76E-05	-0.020	0.004	1.05E-06	-0.020	0.004	6.39E-07	
					rs2256183	height	143962	0.223	-0.011	4.00E-03	0.006	-0.019	0.004	2.01E-07	-0.020	0.004	1.92E-07	
					rs7741091	HIPadjBMI	116064	0.149	-0.010	3.70E-03	0.007	-0.021	0.004	1.10E-07	-0.021	0.004	1.11E-07	
					rs13437082	height	117993	0.102	0.010	4.20E-03	0.022	-0.022	0.004	<b>4.50E-08</b>	-0.022	0.004	<b>4.67E-08</b>	
					rs1265097	height	130108	0.056	0.012	7.30E-03	0.098	-0.023	0.004	<b>1.27E-08</b>	-0.023	0.004	<b>1.29E-08</b>	
					rs12175489	VATadjBMI	141020	0.010	0.008	5.80E-03	0.167	-0.024	0.004	<b>6.72E-09</b>	-0.024	0.004	<b>5.36E-09</b>	
					rs879882	height	97115	0.093	-0.002	3.90E-03	0.593	-0.024	0.004	<b>2.07E-09</b>	-0.024	0.004	<b>1.83E-09</b>	
<b>WCadjBMI</b>																		
					rs4344931	Height	418445	0.043	-0.008	0.004	6.91E-02	-0.022	0.004	<b>1.40E-10</b>	-0.023	0.003	<b>1.22E-10</b>	
					rs6739772	HIPadjBMI	396261	0.043	-0.007	0.004	1.05E-01	-0.022	0.004	<b>1.49E-10</b>	-0.023	0.003	<b>1.25E-10</b>	
					rs11687941	Height	45562	0.341	0.019	0.005	6.74E-05	-0.006	0.004	1.21E-01	-	-	-	
					rs12694997	Height	26014	0.375	-0.017	0.004	6.96E-05	-0.015	0.003	5.58E-07	-0.014	0.003	5.84E-07	
					rs13088462	Height	136933	0.432	-0.035	0.008	2.58E-05	-0.023	0.006	7.06E-05	-0.012	0.012	3.20E-01	
					rs4256170	Height	16520	0.010	0.093	0.019	1.37E-06	-0.032	0.006	6.91E-07	-0.034	0.006	2.04E-07	
					rs9993613	HipadjBMI, Height	39299	1	0.021	0.004	3.04E-07	-	-	-	0.006	0.002	3.41E-03	
					rs2076529	WHRadjBMI	210216	0.174	-0.013	0.004	2.03E-04	-0.017	0.004	9.56E-06	-0.017	0.004	9.50E-06	
					rs7759742	WHRadjBMI	192435	0.124	0.013	0.004	2.26E-04	-0.017	0.004	8.17E-06	-0.016	0.004	1.12E-05	
					rs6457620	Height	89828	0.039	0.004	0.004	2.91E-01	-0.023	0.004	<b>3.86E-08</b>	-0.023	0.004	<b>3.40E-08</b>	
					rs13196329	Visceral fat	248800	0.002	0.022	0.017	1.89E-01	-0.023	0.004	<b>2.20E-08</b>	-0.024	0.004	<b>1.91E-08</b>	
					rs2888877	Height	25572	0.514	0.020	0.005	6.18E-05	0.013	0.003	7.40E-05	0.013	0.003	7.04E-05	
					rs42039	Height	9550	0.663	0.025	0.005	1.01E-07	0.007	0.003	9.34E-03	0.008	0.003	8.07E-03	
					rs42235	HipadjBMI, Height	5896	0.857	0.016	0.004	1.38E-04	0.009	0.002	5.60E-06	0.009	0.002	4.48E-06	
					rs2040494	Height	2933	0.557	0.016	0.004	3.27E-05	0.012	0.003	1.47E-04	0.012	0.003	1.54E-04	
					rs2282978	Height	10438	1	-0.018	0.004	2.44E-06	-	-	-	-	-	-	
					rs2188177	Height	405188	0.035	0.008	0.004	5.51E-02	0.023	0.004	<b>2.50E-08</b>	0.023	0.004	<b>2.58E-08</b>	
					rs9408815	Lead SNP for Pjoint	10528	0.834	0.026	0.005	<b>2.28E-08</b>	-	-	-	-0.005	0.003	5.65E-02	
					rs902143	Height SNP	280862	0.005	0.016	0.004	6.49E-06	-0.026	0.005	<b>4.61E-08</b>	-0.026	0.005	<b>1.85E-08</b>	
					rs10120372	Visceral adipose tissue/subcutaneous adipose tissue	460507	0.161	0.014	0.009	1.02E-01	-0.026	0.005	<b>2.54E-08</b>	-	-	-	
														-0.026	0.005	<b>3.17E-08</b>		
20	rs6012558	0.020	0.004	<b>1.91E-08</b>	rs17450430	Height SNP	240978	0.555	-0.021	0.005	4.30E-06	0.011	0.003	1.73E-04	0.011	0.003	1.59E-04	
					rs237743	Height SNP	371733	0.441	0.024	0.005	5.76E-07	0.011	0.003	2.27E-04	0.011	0.003	2.39E-04	

† -  $r^2$  calculated in HapMap r22

**Supplementary Table 6.** Results for approximate conditional analyses to identify secondary signals and to determine independence from previously-identified anthropometric-associated SNPs for novel loci identified in Approach 2 (SNPjoint). \*IndexSNP is also a previously identified height SNP.

Secondary Signals	Chr	Marker	Tag SNP (TS)				Condition on Lead SNP	Most Significant Marker After Conditioning	Distance	$r^2$	ARIC reference panel												FHS reference panel															
			SMOKERS		NON-SMOKERS						$P_{joint}$	Before Conditioning				After Conditioning				After Conditioning (FHS)																		
			$\beta$	SE	P	$\beta$						SE	P	$\beta$	SE	P	$P_{joint}$	$\beta$	SE	P	$\beta$	SE	P	$P_{joint}$														
			BMI								WHRadjBMI												WCadjBMI															
	3	rs13069244	0.061	0.014	1.8E-05	0.031	0.008	6.6E-05	<b>3.5E-08</b>	rs13069244	rs6443750	888510	0.00011	-0.006	0.010	5.48E-01	-0.018	0.005	<b>8.11E-04</b>	4.64E-02	-	-	-	-	-	-	-	-	-	-	-	-0.006	0.010	5.69E-01	-0.018	0.005	8.66E-04	3.32E-03
	6	rs1049281	-0.022	0.009	1.27E-02	-0.027	0.005	1.98E-08	<b>5.3E-09</b>	rs1049281	rs9262169	508863	0.004	0.014	0.0298	0.6384	0.057	0.0159	3.38E-04	1.45E-03	0.012186	0.02979	6.82E-01	0.05437	0.015896	6.25E-04	2.65E-03	-0.008	0.004	4.30E-02	-0.010	0.003	3.83E-04	2.35E-04				
	9	rs9408815	0.012	0.010	2.28E-01	0.030	0.005	4.22E-09	<b>1.7E-08</b>	rs9408815	rs902143	10528	0.834	0.0156	0.0074	0.03654	0.0178	0.0041	1.16E-05	8.75E-06	0.015137	0.00739	0.040537	0.016394	0.004094	6.21E-05	4.04E-05	0.015	0.0074	0.039463	0.017	0.004	4.73E-05	3.05E-05				
Independence of known loci	Chr	Marker	Tag SNP (TS)				Condition on Marker	Trait	Distance	$r^2$	Known SNP						Tag SNP After Conditioning						Tag SNP After Conditioning															
			SMOKERS		NON-SMOKERS						$P_{joint}$	SMOKERS		NON-SMOKERS		$P_{joint}$	SMOKERS		NON-SMOKERS		$P_{joint}$	SMOKERS		NON-SMOKERS		$P_{joint}$	SMOKERS		NON-SMOKERS		$P_{joint}$							
			$\beta$	SE	P	$\beta$						SE	P	$\beta$	SE		P	$\beta$	SE	P		$\beta$	SE	P	$\beta$		SE	P	$\beta$	SE		P	$\beta$	SE	P	$P_{joint}$		
			BMI							WHRadjBMI						WCadjBMI						WHRadjBMI																
	15	rs12902602	0.047	0.007	<b>1.77E-11</b>	-0.002	0.004	0.547	<b>1.12E-10</b>	rs16969968 rs6495309 rs899997 rs3825807	smoking smoking stroke CHD	84476 52156 52177 121710	0.40772 0.08937 0.20719 0.56435	-0.039 0.035 -0.023 0.038	0.008 0.009 0.008 0.008	3.28E-07 4.01E-05 4.47E-03 5.66E-07	0.001 -0.008 0.002 0.001	0.004 0.005 0.004 0.004	7.67E-01 8.05E-02 6.11E-01 7.97E-01	2.1E-06 4.84E-05 1.50E-02 3.16E-06	0.026 0.040 0.038 0.023	0.006 0.007 0.006 0.005	3.80E-06 3.54E-09 9.91E-10 5.89E-06	-0.002 -0.001 -0.001 -0.003	0.003 0.004 0.003 0.003	0.589 0.857 0.682 0.282	6.70E-05 7.87E-08 <b>1.84E-09</b> 1.54E-05	0.027 0.04 0.04 0.024	0.0057 0.0068 0.0065 0.0052	3.42E-06 4.09E-09 9.39E-10 5.60E-06	-0.002 -0.04 -0.002 -0.003	0.003 0.004 0.004 0.003	0.590097 0.869515 0.661175 0.289177	1.80E-05 <b>3.06E-08</b> <b>6.71E-09</b> 1.90E-05				
	2	rs67343226	-0.018	0.007	1.29E-02	-0.023	0.004	<b>2.61E-09</b>	<b>5.81E-10</b>	rs4344931 (rs4311055, rsquare=1.00) rs6739772 (rs3936203,rsquare = 0.9885) rs11687941 rs12694997	Height SNP Hipadj Height SNP Height SNP	418445 396261	0.043 0.043	-0.008 -0.004	0.009 0.010	4.15E-01 6.57E-01	-0.009 -0.009	0.005 0.005	8.44E-02 1.01E-01	1.59E-01 2.36E-01	-0.018 -0.018	0.007 0.007	1.24E-02 1.25E-02	-0.023 -0.023	0.004 0.004	<b>1.50E-09</b> <b>5.18E-10</b>	<b>5.11E-10</b> <b>5.18E-10</b>	-0.018 -0.018	0.007 0.007	1.23E-02 1.14E-02	-	-	-	-	-			
	4	rs7697556*	0.004	0.007	6.26E-01	0.025	0.004	<b>7.30E-11</b>	<b>2.93E-09</b>	rs9993613	HipadjBMI, Height	39299	1	0.003	0.008	7.20E-01	0.025	0.004	<b>7.30E-09</b>	6.21E-08	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	9	rs9408815	0.012	0.010	2.28E-01	0.030	0.005	<b>4.22E-09</b>	<b>7.38E-09</b>	rs9409082 rs9409082 rs902143 rs10120372	lead SNP for PadjSMK Height SNP Height SNP VAT/SAT	10528 10528 291390 449979	0.834 0.834 0.016 0.128	-0.017 -0.017 0.016 -0.004	0.010 0.010 0.007 0.018	8.13E-02 8.13E-02 3.65E-02 8.24E-01	-0.029 -0.029 0.018 0.016	0.005 0.005 0.004 0.010	<b>2.56E-08</b> <b>2.56E-08</b> 1.16E-05 1.05E-01	<b>4.58E-08</b> <b>4.58E-08</b> 8.75E-06 2.60E-01	-	-	0.011 0.012	0.010 0.010	2.73E-01 2.19E-01	0.029 0.029	0.005 0.005	<b>8.39E-09</b> <b>4.14E-09</b>	<b>3.42E-08</b> <b>1.47E-08</b>	0.011 0.012	0.010 0.010	2.64E-01 2.16E-01	0.029 0.029	0.005 0.005	<b>6.44E-09</b> <b>4.86E-09</b>	<b>2.58E-08</b> <b>1.71E-08</b>		
	6	rs1049281	-0.022	0.009	1.27E-02	-0.027	0.005	<b>1.98E-08</b>	<b>5.3E-09</b>	rs1265097 rs879882 rs6457374 rs2247056 rs13437082 rs12343082 rs2256183 rs2857693 rs2844479 rs12175489 rs7741091	Height Height Height Height/triglycerides Height Height Height Height Height VATadjBMI HIPadjBMI	130108 97115 35694 28923 117993 143962 351817 336389 141020 116064	0.056 0.093 0.713 0.714 0.102 0.223 0.112 0.090 0.010 0.149	0.0045 0.0008 0.0048 -0.0039	0.0147 0.004 0.0044 0.0043	0.7595 0.8443 0.0127 0.2693 0.3657 0.5293 0.0058 0.1036 0.0119 0.0029 0.2518 0.001 0.0053	0.0133 0.0029 0.0033 0.0032 0.0058 0.0033 0.0033 0.0058 0.0029 0.0047 -0.0011 0.0029 0.0042 0.0042 0.0009 0.0042	1.21E-01 8.13E-01 1.34E-04 3.35E-04 1.96E-04 7.34E-02 1.75E-01 3.23E-02 5.98E-05 5.98E-05 5.52E-04 9.10E-01 4.77E-02	2.89E-01 9.52E-01 3.55E-04 3.55E-04 1.96E-04 1.75E-01 3.23E-02 5.98E-05 5.98E-05 5.52E-04 9.10E-01 1.19E-01	-0.021 -0.022 -0.018 -0.017	0.008 0.009 0.008 0.008	1.29E-02 1.07E-02 0.024 0.020	-0.026 -0.027 -0.017 -0.025	0.005 0.005 0.004 0.005	<b>5.00E-08</b> <b>7.18E-09</b> 9.35E-06 3.11E-05	<b>1.59E-08</b> <b>2.06E-09</b> 2.11E-05 1.13E-05	-0.021 -0.022 -0.018 -0.019	0.0084 0.0085 0.008 0.008	0.012815 0.010552 0.024072 0.019835	-0.026 -0.027 -0.018 -0.018	0.005 0.005 0.004 0.004	5.06E-08 6.60E-09 1.72E-05 2.44E-05	<b>1.61E-08</b> <b>1.88E-09</b> 7.61E-06 8.99E-06					
	6	rs1049281	-0.022	0.009	1.27E-02	-0.027	0.005	<b>1.98E-08</b>	<b>5.3E-09</b>	rs1265097 rs879882 rs6457374 rs2247056 rs13437082 rs12343082 rs2256183 rs2857693 rs2844479 rs12175489 rs7741091	Height Height Height Height/triglycerides Height Height Height Height Height VATadjBMI HIPadjBMI	130108 97115 35694 28923 117993 143962 351817 336389 141020 116064	0.056 0.093 0.713 0.714 0.102 0.223 0.112 0.090 0.010 0.149	0.0045 0.0008 0.0048 -0.0039	0.0147 0.004 0.0044 0.0043	0.7595 0.8443 0.0127 0.2693 0.3657 0.5293 0.0058 0.1036 0.0119 0.0029 0.2518 0.001 0.0053	0.0133 0.0029 0.0033 0.0032 0.0058 0.0033 0.0033 0.0058 0.0029 0.0047 -0.0011 0.0029 0.0042 0.0042 0.0009 0.0042	1.21E-01 8.13E-01 1.34E-04 3.35E-04 1.96E-04 7.34E-02 1.75E-01 3.23E-02 5.98E-05 5.98E-05 5.52E-04 9.10E-01 4.77E-02	2.89E-01 9.52E-01 3.55E-04 3.55E-04 1.96E-04 1.75E-01 3.23E-02 5.98E-05 5.98E-05 5.52E-04 9.10E-01 1.19E-01	-0.021 -0.022 -0.018 -0.017	0.008 0.009 0.008 0.008	1.29E-02 1.07E-02 0.024 0.020	-0.026 -0.027 -0.017 -0.025	0.005 0.005 0.004 0.005	<b>5.00E-08</b> <b>7.18E-09</b> 9.35E-06 3.11E-05	<b>1.59E-08</b> <b>2.06E-09</b> 2.11E-05 1.13E-05	-0.021 -0.022 -0.018 -0.019	0.0084 0.0085 0.008 0.008	0.012815 0.010552 0.024072 0.019835	-0.026 -0.027 -0.018 -0.018	0.005 0.005 0.004 0.004	5.06E-08 6.60E-09 1.72E-05 2.44E-05	<b>1.61E-08</b> <b>1.88E-09</b> 7.61E-06 8.99E-06					

Supplementary Table 7. Results for approximate conditional analyses to identify secondary signals and to determine independence from previously-identified anthropometric-associated SNPs for novel loci identified in Approach 3 (SNPint).

Secondary Signals	ARIC reference panel																				FHS reference panel													
	Chr	Marker	Tag SNP (TS)						Condition on Lead SNP	Most Significant Marker After Conditioning	Distance	r <sup>2</sup>	Before Conditioning						After Conditioning						Most Significant	After Conditioning (FHS)								
			SMOKERS			NON-SMOKERS							P <sub>int</sub>	SMOKERS			NON-SMOKERS			P <sub>int</sub>	SMOKERS			NON-SMOKERS			P <sub>int</sub>							
BMI																																		
4	rs336396	0.063	0.012	4.8E-08	-0.0059	0.0062	0.343	2.1E-08	rs336396	rs10857395	389724	0.001	0.035	0.013	5.7E-03	0.001	0.007	0.853	1.3E-02	0.036	0.012	0.004	0.0008	0.0070	0.9047	0.009	rs10857395	0.036	0.012	3.87E-03	-	-	-	-
Independence of known SNPs	ARIC reference panel																				FHS reference panel													
	Chr	Marker	Tag SNP (TS)						Condition on Marker	Trait	Distance	r <sup>2</sup>	Known SNP						Tag SNP After Conditioning						Most Significant	Tag SNP After Conditioning								
			SMOKERS			NON-SMOKERS							P <sub>int</sub>	SMOKERS			NON-SMOKERS			P <sub>int</sub>	SMOKERS			NON-SMOKERS			P <sub>int</sub>							
BMI																																		
15	rs12902602	0.047	0.007	1.77E-11	-0.002	0.004	0.547	4.06E-11	rs16969968	smoking	84476	0.408	-0.039	0.008	3.28E-07	0.001	0.004	7.67E-01	9.75E-07	0.026	0.006	3.80E-06	-0.002	0.003	0.589	4.22E-06	smoking	0.027	0.006	3.42E-06	-0.002	0.003	0.590	7.18E-07
									rs6495309	smoking	52156	0.089	0.035	0.009	4.01E-05	-0.008	0.005	8.05E-02	2.43E-06	0.040	0.007	3.54E-09	-0.001	0.004	0.857	1.96E-08	smoking	0.040	0.007	4.09E-09	-0.001	0.004	0.870	9.51E-10
									rs899997	stroke	52177	0.207	-0.023	0.008	4.47E-03	0.002	0.004	6.11E-01	3.33E-03	0.038	0.006	9.91E-10	-0.001	0.003	0.682	3.34E-09	stroke	0.040	0.007	9.39E-10	-0.002	0.004	0.661	1.67E-10
									rs3825807	CHD	121710	0.564	0.038	0.008	5.66E-07	0.001	0.004	7.97E-01	4.57E-06	0.023	0.005	5.89E-06	-0.003	0.003	0.282	2.00E-06	CHD	0.024	0.005	5.60E-06	-0.003	0.003	0.289	3.83E-07

**Supplementary Table 8.** Simulation-based type 1 error rates. Shown are the simulation-based type 1 error rates of Approach 1 (adjusted effect), Approach 2 (joint effect), Approach 3 and 4 (interaction effects). For two different MAFs, the approaches were applied to 10,000 simulated stratum-specific effect sizes that were generated under stratum-specific null hypotheses of “no stratum-specific effects” and under the assumption of 50,000 smokers and 180,000 nonsmokers. The type 1 error rates shown reflect the proportion of nominally significant simulation results for the respective approach.

<b>Approach</b>	<b>MAF</b>	<b>#Variants tested</b>	<b>#Variants with P&lt;0.05</b>	<b>Type 1 Error Rate [%]</b>
<b>Approach 1</b>	0.05	10,000	515	5.15
<b>(adjusted effect)</b>	0.3	10,000	486	4.86
<b>Approach 2</b>	0.05	10,000	492	4.92
<b>(joint effect)</b>	0.3	10,000	487	4.87
<b>Approach 3</b>	0.05	10,000	490	4.9
<b>(Interaction)</b>	0.3	10,000	514	5.14
<b>Approach 4</b>	0.05	515	27	5.24
<b>(Interaction)</b>	0.3	486	22	4.53

**Supplementary Table 9.** Variance explained in smoking strata for significant variants from Approach 1 (SNPadjSMK) at varying thresholds.

Trait	Approach 1		Variance smokers	Variance error Smokers	Variance nonsmokers	Variance error Nonsmokers	Difference in Variance (Smokers-Nonsmokers)	Error for difference in Variance	P <sub>RsqDiff</sub>
	Number of SNPs	P <sub>SNPadjSMK</sub> threshold							
BMI	44	1.00E-08	0.01840	0.00125	0.01279	0.00054	0.00562	0.00136	<b>3.83E-05</b>
BMI	50	3.16E-08	0.01907	0.00128	0.01368	0.00056	0.00539	0.00139	<b>1.11E-04</b>
BMI	65	1.00E-07	0.02034	0.00133	0.01583	0.00060	0.00451	0.00146	<b>1.94E-03</b>
BMI	84	3.16E-07	0.02374	0.00145	0.01809	0.00065	0.00565	0.00158	<b>3.64E-04</b>
BMI	105	1.00E-06	0.02616	0.00153	0.02068	0.00070	0.00549	0.00168	<b>1.12E-03</b>
BMI	132	3.16E-06	0.03011	0.00166	0.02343	0.00075	0.00668	0.00182	<b>2.50E-04</b>
BMI	190	1.00E-05	0.03797	0.00189	0.02885	0.00084	0.00912	0.00207	<b>1.07E-05</b>
BMI	271	3.16E-05	0.04679	0.00214	0.03568	0.00095	0.01111	0.00234	<b>1.99E-06</b>
BMI	436	1.00E-04	0.06237	0.00253	0.04806	0.00112	0.01431	0.00276	<b>2.20E-07</b>
BMI	708	3.16E-04	0.08633	0.00304	0.06589	0.00133	0.02044	0.00332	<b>7.41E-10</b>
BMI	1147	1.00E-03	0.11591	0.00361	0.09037	0.00158	0.02555	0.00394	<b>8.49E-11</b>
BMI	1841	3.16E-03	0.15124	0.00422	0.12235	0.00187	0.02889	0.00462	<b>3.87E-10</b>
BMI	2687	1.00E-02	0.18356	0.00475	0.15244	0.00211	0.03112	0.00519	<b>2.08E-09</b>
BMI	3407	3.16E-02	0.20449	0.00510	0.17062	0.00225	0.03387	0.00557	<b>1.23E-09</b>
BMI	3793	1.00E-01	0.21137	0.00524	0.17642	0.00230	0.03495	0.00571	<b>9.62E-10</b>
WCadjBMI	50	1.00E-08	0.01430	0.00120	0.01330	0.00060	0.00090	0.00140	4.98E-01
WCadjBMI	59	3.16E-08	0.01530	0.00130	0.01510	0.00060	0.00020	0.00140	9.05E-01
WCadjBMI	69	1.00E-07	0.01700	0.00130	0.01670	0.00070	0.00030	0.00150	8.38E-01
WCadjBMI	77	3.16E-07	0.01850	0.00140	0.01770	0.00070	0.00080	0.00160	6.14E-01
WCadjBMI	94	1.00E-06	0.02090	0.00150	0.02010	0.00070	0.00080	0.00170	6.51E-01
WCadjBMI	115	3.16E-06	0.02300	0.00160	0.02300	0.00080	0.00000	0.00180	9.87E-01
WCadjBMI	148	1.00E-05	0.02670	0.00170	0.02680	0.00090	-0.00010	0.00190	9.59E-01
WCadjBMI	206	3.16E-05	0.03020	0.00190	0.03350	0.00100	-0.00330	0.00210	1.17E-01
WCadjBMI	322	1.00E-04	0.03800	0.00220	0.04490	0.00120	-0.00690	0.00250	4.91E-03
WCadjBMI	538	3.16E-04	0.05050	0.00260	0.06340	0.00140	-0.01290	0.00290	<b>1.19E-05</b>
WCadjBMI	926	1.00E-03	0.06490	0.00300	0.09200	0.00170	-0.02710	0.00350	<b>8.51E-15</b>
WCadjBMI	1603	3.16E-03	0.08620	0.00360	0.13170	0.00210	-0.04550	0.00420	<b>3.81E-27</b>
WCadjBMI	2505	1.00E-02	0.10590	0.00420	0.17250	0.00250	-0.06650	0.00490	<b>2.04E-42</b>
WCadjBMI	3303	3.16E-02	0.11290	0.00450	0.19910	0.00270	-0.08620	0.00520	<b>1.40E-60</b>
WCadjBMI	3781	1.00E-01	0.11740	0.00470	0.20790	0.00270	-0.09050	0.00540	<b>4.11E-62</b>
WHRadjBMI	50	1.00E-08	0.00154	0.00049	0.00282	0.00030	-0.00128	0.00057	2.55E-02
WHRadjBMI	59	3.16E-08	0.00213	0.00056	0.00356	0.00034	-0.00144	0.00065	2.80E-02
WHRadjBMI	69	1.00E-07	0.00243	0.00060	0.00414	0.00037	-0.00172	0.00070	1.47E-02
WHRadjBMI	77	3.16E-07	0.00266	0.00063	0.00435	0.00038	-0.00169	0.00073	2.13E-02
WHRadjBMI	94	1.00E-06	0.00269	0.00065	0.00500	0.00041	-0.00231	0.00077	<b>2.84E-03</b>
WHRadjBMI	115	3.16E-06	0.00268	0.00069	0.00601	0.00046	-0.00333	0.00083	<b>5.69E-05</b>
WHRadjBMI	148	1.00E-05	0.00294	0.00075	0.00697	0.00050	-0.00404	0.00090	<b>7.68E-06</b>
WHRadjBMI	206	3.16E-05	0.00294	0.00083	0.00948	0.00060	-0.00654	0.00103	<b>1.82E-10</b>
WHRadjBMI	321	1.00E-04	0.00342	0.00101	0.01453	0.00075	-0.01110	0.00125	<b>8.55E-19</b>
WHRadjBMI	537	3.16E-04	0.00444	0.00128	0.02301	0.00096	-0.01858	0.00160	<b>3.18E-31</b>
WHRadjBMI	923	1.00E-03	0.00467	0.00162	0.03627	0.00124	-0.03160	0.00204	<b>3.04E-54</b>
WHRadjBMI	1598	3.16E-03	0.00529	0.00211	0.05407	0.00154	-0.04878	0.00261	<b>8.27E-78</b>
WHRadjBMI	2496	1.00E-02	0.00649	0.00265	0.07207	0.00180	-0.06558	0.00320	<b>3.57E-93</b>
WHRadjBMI	3293	3.16E-02	0.00683	0.00304	0.08359	0.00197	-0.07676	0.00363	<b>1.58E-99</b>
WHRadjBMI	3773	1.00E-01	0.00654	0.00325	0.08819	0.00204	-0.08165	0.00384	<b>1.54E-100</b>

**Supplementary Table 10.** Association of cis-acting expression quantitative trait loci (cis-eQTLs) for novel loci using publicly available databases.

Trait	$r^2$ CEU				Tissue	Transcript	Best E-SNP	Best E-SNP P	$r^2$ CEU	PMID
	IndexSNP	Proxy SNP	IndexSNP vs ProxySNP	P ProxySNP						
BMI	rs12629427	rs9860797	0.905428	2.23E-05	Cerebellum (all samples)	EPHA3	rs9860797	2.23E-05	0.865	23622250
BMI	rs12629427	rs9860797	rs9860797	0.905428	3.71E-05	EPHA3	rs9860797	3.71E-05	0.865	23622250
BMI	rs13069244	rs13069244	IndexSNP	2.09E-05	Peripheral blood mononuclear cells	TTC14	rs1921678	6.46E-109	unavailable	26019233
BMI	rs2481665	rs2481665	IndexSNP	7.31E-06	Prefrontal cortex (Huntington's)	INADL	rs2481665	7.31E-06	SameSNP	23622250
WCadjBMI	rs10269774	rs2282978	0.920627	2.62E-05	Cerebellum (normal samples)	CDK6	rs2282978	2.62E-05	1	23622250
WCadjBMI	rs17396340	rs17396340	IndexSNP	1.85E-15	B-lymphoblastoid cell lines (collected at age 8)	ENSG00000054523	rs17396340	1.85E-15	SameSNP	25010687
WCadjBMI	rs17396340	rs17396340	IndexSNP	8.27E-118	Peripheral blood mononuclear cells	KIF1B	rs17396340	8.27E-118	SameSNP	26019233
WCadjBMI	rs17396340	rs17396340	IndexSNP	1.21E-07	Peripheral blood mononuclear cells	KIF1B	rs17396340	8.27E-118	SameSNP	26019233
WCadjBMI	rs17396340	rs17396340	IndexSNP	3.85E-06	Whole blood (PAX) in individuals without asthma	KIF1B	rs17396340	3.85E-06	SameSNP	25816334
WCadjBMI	rs17396340	rs17396340	IndexSNP	9.81E-198	Whole blood (CHARGE)	KIF1B	rs12139158	9.81E-198	1	24013639
WCadjBMI	rs17396340	rs17396340	IndexSNP	2.64E-11	Whole blood (CHARGE)	KIF1B	rs12139158	9.81E-198	1	24013639
WCadjBMI	rs17396340	rs17396340	IndexSNP	9.01E-29	LCL (MuTHER)	KIF1B	rs6693965	7.66E-29	0.92	22941192
WCadjBMI	rs17396340	rs17397129	1	4.64E-113	Peripheral blood mononuclear cells	KIF1B	rs17396340	8.27E-118	SameSNP	26019233
WCadjBMI	rs17396340	rs17397129	1	3.32E-07	Peripheral blood mononuclear cells	KIF1B	rs17396340	8.27E-118	SameSNP	26019233
WCadjBMI	rs17396340	rs17397129	1	9.81E-198	Whole blood (CHARGE)	KIF1B	rs12139158	9.81E-198	1	24013639
WCadjBMI	rs17396340	rs17397129	1	6.99E-10	Whole blood (CHARGE)	KIF1B	rs12139158	9.81E-198	1	24013639
WCadjBMI	rs17396340	rs17397129	1	1.08E-26	LCL (MuTHER)	KIF1B	rs6693965	7.66E-29	0.92	22941192
WCadjBMI	rs4378999	rs10212250	0.994018	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs10212250	0.994018	5.42E-14	CD14+ monocytes (24h LPS stimulated)	MAPKAPK3	rs7614881	9.39E-18	0.8	24604202
WCadjBMI	rs4378999	rs10212250	0.994018	1.66E-04	CD14+ monocytes (2h LPS stimulated)	MAPKAPK3	rs7614881	7.37E-06	0.8	24604202
WCadjBMI	rs4378999	rs10212250	0.994018	2.26E-04	CD14+ monocytes (2h LPS stimulated)	TEX264	rs1055429	8.02E-07	0.8	24604202
WCadjBMI	rs4378999	rs10212250	0.994018	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs11130274	0.988059	2.39E-06	Liver(Greenawalt)	AKO93691	rs11130274	2.39E-06	1	21602305
WCadjBMI	rs4378999	rs11130274	0.988059	3.18E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs11130274	0.988059	9.28E-08	Prefrontal cortex (all samples)	C3orf18	rs11130274	9.28E-08	1	23622250
WCadjBMI	rs4378999	rs11130274	0.988059	1.13E-25	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs11130274	0.988059	3.69E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs11130282	0.994018	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs11130282	0.994018	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs11919932	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs13324500	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs1383252	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs1383252	0.994018	1.03E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs1480357	0.964819	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs1480357	0.964819	1.29E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs1480358	0.994018	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs1480358	0.994018	8.53E-11	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs1480358	0.994018	1.30E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs1480363	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs1480363	0.994018	1.03E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs1552072	0.994018	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs1552072	0.994018	1.30E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs2061951	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs2061951	0.994018	1.03E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs2355941	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs2355941	0.994018	1.03E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4244696	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4244697	1	9.21E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4244697	1	1.76E-25	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233

WCadjBMI	rs4378999	rs4244704	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4263323	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4286453	0.904684	1.89E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4301044	0.988059	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4301044	0.988059	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4328835	0.988059	7.96E-26	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4328835	0.988059	4.00E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs4367101	0.994018	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4367101	0.994018	1.01E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4373098	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4377512	0.904684	2.54E-11	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs4377512	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4378999	IndexSNP	9.15E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4378999	IndexSNP	1.72E-25	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4446244	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4453876	0.994018	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4453876	0.994018	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4478114	0.904684	4.76E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs4478114	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4505743	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4511933	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4528983	1	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4528983	1	1.01E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4530566	0.904684	6.43E-11	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs4530566	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4532165	0.988059	3.20E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4532165	0.988059	1.05E-25	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4532165	0.988059	3.89E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs4555554	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4568177	0.994018	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4568177	0.994018	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4582086	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4589968	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4615113	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4927978	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4927983	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4974095	0.982324	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4974095	0.982324	1.30E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs4974109	0.976321	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs4974109	0.976321	1.30E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6445455	0.988059	5.42E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs6445455	0.988059	4.79E-26	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6445455	0.988059	4.15E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs6445551	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs6445551	0.994018	1.03E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6445600	0.904684	2.91E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs6445600	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6445717	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6445750	0.904684	4.68E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs6445750	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6445779	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6446011	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6446118	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233

WCadjBMI	rs4378999	rs6446167	0.904684	5.86E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs6446167	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6768601	0.904684	3.84E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs6768601	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6772664	1	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs6772664	1	1.01E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6777719	0.988059	8.54E-06	Lung	TEX264	rs6777719	8.54E-06	1	23209423
WCadjBMI	rs4378999	rs6777719	0.988059	5.46E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs6777719	0.988059	4.84E-26	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6777719	0.988059	4.17E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs6779658	1	1.51E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs6779658	1	4.12E-25	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6793613	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs6809080	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs6809080	0.994018	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7611873	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7614171	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7615291	0.904684	3.19E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs7615291	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7619584	0.994018	1.62E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs7619584	0.994018	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7628533	0.994018	5.42E-14	CD14+ monocytes (24h LPS stimulated)	MAPKAPK3	rs7614881	9.39E-18	0.8	24604202
WCadjBMI	rs4378999	rs7628533	0.994018	1.66E-04	CD14+ monocytes (2h LPS stimulated)	MAPKAPK3	rs7614881	7.37E-06	0.8	24604202
WCadjBMI	rs4378999	rs7628533	0.994018	2.26E-04	CD14+ monocytes (2h LPS stimulated)	TEX264	rs1055429	8.02E-07	0.8	24604202
WCadjBMI	rs4378999	rs7628533	0.994018	1.45E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7630730	0.982324	9.64E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs7630730	0.982324	9.13E-22	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7630730	0.982324	3.88E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs7640263	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7644957	0.988059	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs7644957	0.988059	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7652655	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7652818	0.904684	2.46E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7653451	0.904684	7.37E-16	CD14+ monocytes (24h LPS stimulated)	MAPKAPK3	rs7614881	9.39E-18	0.8	24604202
WCadjBMI	rs4378999	rs7653451	0.904684	2.93E-05	CD14+ monocytes (2h LPS stimulated)	MAPKAPK3	rs7614881	7.37E-06	0.8	24604202
WCadjBMI	rs4378999	rs7653451	0.904684	2.20E-04	CD14+ monocytes (2h LPS stimulated)	TEX264	rs1055429	8.02E-07	0.8	24604202
WCadjBMI	rs4378999	rs7653451	0.904684	3.68E-09	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs7653451	0.904684	2.79E-05	Whole blood (Battle)	ACY1	rs7653451	2.79E-05	0.8	24092820
WCadjBMI	rs4378999	rs922612	0.994018	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs922612	0.994018	1.03E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9682672	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9713241	0.900438	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9758600	0.904684	2.48E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9828200	0.904684	3.90E-12	Monocytes	MAPKAPK3	rs6779819	1.47E-16	0.8	20502693
WCadjBMI	rs4378999	rs9828200	0.904684	2.47E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9855442	0.994018	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs9855442	0.994018	1.30E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9855454	0.988049	1.78E-12	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9858412	0.988059	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs9858412	0.988059	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9869123	0.988059	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs9869123	0.988059	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9871539	0.988059	9.65E-04	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233



WCadjBMI	rs4378999	rs9871539	0.988059	8.85E-22	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9871539	0.988059	3.89E-05	Subc adipose (MuTHER)	ARMET	rs6784455	3.27E-06	0.8	22941192
WCadjBMI	rs4378999	rs9878100	0.994018	1.81E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs9878100	0.994018	1.30E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs4378999	rs9883739	0.98216	1.63E-03	Peripheral blood mononuclear cells	TEX264	rs11130274	3.18E-04	1	26019233
WCadjBMI	rs4378999	rs9883739	0.98216	1.02E-24	Peripheral blood mononuclear cells	GRM2	rs1055429	5.80E-35	0.8	26019233
WCadjBMI	rs6012558	rs6012558	IndexSNP	7.46E-05	CD14+ monocytes (IFNg stimulated)	DDX27	rs6019512	2.56E-05	0.87	24604202
WCadjBMI	rs6743226	rs4675966	0.975484	6.19E-06	Blood	FARP2	rs4675966	6.19E-06	0.87	18344981
WCadjBMI	rs6743226	rs4675966	0.975484	4.02E-07	Lymph	HDLBP	rs4675966	4.02E-07	0.87	17873875
WCadjBMI	rs6743226	rs4675966	0.975484	5.05E-05	Omental adipose	GAL3ST2	rs4675966	5.05E-05	0.87	21602305
WCadjBMI	rs6743226	rs6747036	0.952557	1.37E-06	LCL (GenCord)	ENSG00000115677.12	rs6747036	1.37E-06	0.84	23755361
WCadjBMI	rs6743226	rs6747036	0.952557	3.41E-07	Primary PHA-stimulated T cells (GenCord)	ENSG00000115677.12	rs6747036	3.41E-07	0.84	23755361
WHRadjBMI	rs1049281	rs1049281	IndexSNP	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs2844622	0.907829	1.53E-284	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs7767581	0.935004	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264594	0.912386	2.25E-233	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264594	0.912386	5.92E-05	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264601	0.96172	1.65E-233	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264601	0.96172	6.16E-05	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264602	0.986425	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264602	0.986425	<6.7E-45	Whole blood (Battle)	HLA-L	rs9264602	<6.7E-45	0.967	24092820
WHRadjBMI	rs1049281	rs9264603	0.971449	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264604	0.918434	2.59E-279	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264606	0.974001	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264608	0.986087	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264636	0.971918	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264638	0.915302	2.92E-260	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264638	0.915302	5.12E-12	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1049281	rs9264647	0.935438	2.23E-308	Peripheral blood mononuclear cells	HLA-C	rs1049281	2.23E-308	SameSNP	26019233
WHRadjBMI	rs1856293	rs1856293	1	1.65E-05	Subc adipose (MuTHER)	TAAR6	rs799227	1.32E-05	0.967	22941192
WHRadjBMI	rs589428	rs605203	0.994631	6.33E-20	CD14+ monocytes (IFNg stimulated)	SKIV2L	rs486416	9.84E-21	1	24604202
WHRadjBMI	rs589428	rs589428	IndexSNP	6.33E-20	CD14+ monocytes (IFNg stimulated)	SKIV2L	rs486416	9.84E-21	1	24604202

**Supplementary Table 11.** Association of cis-eQTLs for novel loci in whole blood adjusting for smoking status.

Trait	Transcript	Tag SNP	CHR	POS	Gene	$\beta_{\text{main}}$	$SE_{\text{main}}$	Adj.Pvalue
BMI	2339139	rs2481665	1	62594677	<i>INADL</i>	-0.02494	0.004266	8.980E-08
BMI	2339334	rs2481665	1	62594677	<i>L1TD1</i>	-0.01634	0.005455	1.808E-02
WC	3061319	rs10269774	7	92253972	<i>CDK6</i>	-0.01079	0.003726	2.467E-02
WC	3060994	rs10269774	7	92253972	<i>CYP51A1</i>	-0.0335	0.008983	1.758E-03
WC	3012633	rs10269774	7	92253972	<i>GATAD1</i>	-0.01556	0.003202	1.460E-05
WC	2319661	rs17396340	1	10286176	<i>SLC12A4</i>	0.175292	0.006585	3.520E-154
WC	2675239	rs4378999	3	51208646	<i>C6orf10</i>	-0.01162	0.004206	3.572E-02
WC	2622970	rs4378999	3	51208646	<i>C6orf174</i>	0.011549	0.003284	3.637E-03
WC	2622859	rs4378999	3	51208646	<i>C6orf58</i>	-0.0377	0.004833	1.530E-13
WC	2622912	rs4378999	3	51208646	<i>ECHDC1</i>	-0.06322	0.006041	4.000E-24
WC	2675504	rs4378999	3	51208646	<i>HLA-DOB</i>	0.018156	0.005838	1.334E-02
WC	2623139	rs4378999	3	51208646	<i>PTPRK</i>	-0.03202	0.005981	1.360E-06
WC	2536298	rs6743226	2	242236972	<i>ACD</i>	-0.05566	0.003215	1.630E-65
WC	2536531	rs6743226	2	242236972	<i>ACD</i>	0.015183	0.00276	6.070E-07
WC	2607055	rs6743226	2	242236972	<i>CENPT</i>	0.009859	0.002622	1.586E-03
WC	2607110	rs6743226	2	242236972	<i>CENPT</i>	0.016588	0.005435	1.560E-02
WHR	2902935	rs1049281	6	31236567	<i>AIF1</i>	0.013159	0.003775	3.959E-03
WHR	2949311	rs1049281	6	31236567	<i>C2</i>	0.012404	0.003394	2.244E-03
WHR	2948587	rs1049281	6	31236567	<i>CSNK2B</i>	0.050802	0.004927	1.840E-23
WHR	2949885	rs1049281	6	31236567	<i>CYP21A2</i>	0.014103	0.003826	2.018E-03
WHR	2902178	rs1049281	6	31236567	<i>DPCR1</i>	-0.01876	0.003565	2.050E-06
WHR	2902427	rs1049281	6	31236567	<i>HCG27</i>	0.034784	0.005156	2.980E-10
WHR	2901463	rs1049281	6	31236567	<i>HLA-L</i>	0.013763	0.004762	2.487E-02
WHR	2949132	rs1049281	6	31236567	<i>HSPA1A</i>	0.02243	0.003579	6.750E-09
WHR	2949230	rs1049281	6	31236567	<i>HSPA1B</i>	0.011195	0.003703	1.693E-02
WHR	2902804	rs1049281	6	31236567	<i>LST1</i>	0.009603	0.003193	1.763E-02
WHR	2948630	rs1049281	6	31236567	<i>LY6G5B</i>	0.033662	0.004684	1.510E-11
WHR	2948648	rs1049281	6	31236567	<i>LY6G5B</i>	0.044411	0.007633	1.020E-07
WHR	2902574	rs1049281	6	31236567	<i>MICB</i>	0.028136	0.007337	1.210E-03
WHR	2948887	rs1049281	6	31236567	<i>MSH5</i>	1.877682	0.015225	<1.264E-305
WHR	2948926	rs1049281	6	31236567	<i>MSH5</i>	0.124382	0.005847	9.930E-99
WHR	2902326	rs1049281	6	31236567	<i>MUC21</i>	-0.05582	0.005415	1.840E-23
WHR	2901552	rs1049281	6	31236567	<i>RPP21</i>	0.017709	0.005752	1.465E-02
WHR	2949488	rs1049281	6	31236567	<i>SKIV2L</i>	0.127829	0.005665	6.330E-111
WHR	2949588	rs1049281	6	31236567	<i>STK19</i>	0.019773	0.003975	8.560E-06
WHR	2902416	rs1049281	6	31236567	<i>TCF19</i>	0.0124	0.004302	2.518E-02
WHR	2902725	rs1049281	6	31236567	<i>TNF</i>	0.022217	0.005359	3.638E-04
WHR	3115008	rs2001945	8	126477978	<i>TRIB1</i>	0.012548	0.00379	7.088E-03
WHR	2902884	rs589428	6	31848220	<i>AGER</i>	-0.01319	0.002381	5.060E-07
WHR	2902958	rs589428	6	31848220	<i>AGER</i>	0.010621	0.002251	2.770E-05
WHR	2902935	rs589428	6	31848220	<i>AGER</i>	0.015093	0.003697	4.709E-04
WHR	2902804	rs589428	6	31848220	<i>AGPAT1</i>	0.011354	0.00313	2.456E-03
WHR	2950125	rs589428	6	31848220	<i>CIB2</i>	0.024457	0.006273	9.480E-04
WHR	4048241	rs589428	6	31848220	<i>CTSH</i>	0.69375	0.02946	1.010E-120
WHR	2902427	rs589428	6	31848220	<i>DOM3Z</i>	0.02022	0.005091	7.249E-04
WHR	2902326	rs589428	6	31848220	<i>EHMT2</i>	-0.05188	0.005353	8.920E-21
WHR	2902207	rs589428	6	31848220	<i>EHMT2</i>	0.025565	0.004894	2.460E-06
WHR	2902178	rs589428	6	31848220	<i>EHMT2</i>	-0.01341	0.003505	1.227E-03
WHR	2902574	rs589428	6	31848220	<i>FKBP1</i>	0.03168	0.007208	1.244E-04

WHR	2902609	rs589428	6	31848220	<i>FKBPL</i>	0.015829	0.005918	4.587E-02
WHR	2903258	rs589428	6	31848220	<i>GPSM3</i>	-0.0567	0.007397	4.250E-13
WHR	2903219	rs589428	6	31848220	<i>GPSM3</i>	0.147451	0.028362	2.760E-06
WHR	2949971	rs589428	6	31848220	<i>LINGO1</i>	-0.07492	0.007936	9.780E-20
WHR	2948887	rs589428	6	31848220	<i>MGC34034</i>	0.85956	0.027996	5.680E-205
WHR	2949859	rs589428	6	31848220	<i>MORF4L1</i>	-0.025	0.007999	1.298E-02
WHR	2949488	rs589428	6	31848220	<i>NDUF4F4</i>	0.267428	0.004336	<1.264E-305
WHR	2903189	rs589428	6	31848220	<i>PBX2</i>	-0.03287	0.004706	6.020E-11
WHR	2903075	rs589428	6	31848220	<i>PBX2</i>	0.011404	0.002362	1.680E-05
WHR	2902725	rs589428	6	31848220	<i>PRRT1</i>	0.016694	0.005276	1.170E-02
WHR	4048265	rs589428	6	31848220	<i>RASGRF1</i>	0.488385	0.024768	6.860E-85
WHR	2949885	rs589428	6	31848220	<i>RASGRF1</i>	0.011886	0.003761	1.170E-02
WHR	2949132	rs589428	6	31848220	<i>STX7</i>	0.018885	0.003533	1.370E-06
WHR	2949148	rs589428	6	31848220	<i>TAAR5</i>	-0.02488	0.005096	1.330E-05
WHR	2948926	rs589428	6	31848220	<i>TCF21</i>	0.089165	0.005928	1.430E-49
WHR	2902463	rs589428	6	31848220	<i>TNXB</i>	0.012875	0.003483	1.971E-03
WHR	2949230	rs589428	6	31848220	<i>VNN1</i>	0.01419	0.003638	9.480E-04
WHR	2902348	rs589428	6	31848220	<i>ZBTB12</i>	-0.02464	0.003681	4.130E-10
WHR	2949311	rs589428	6	31848220	<i>DDAH2</i>	0.015901	0.003326	2.090E-05

**Supplementary Table 12.** Association of cis-eQTLs for novel loci in whole blood for joint main + smoking interaction.

Trait	Transcript	Tag SNP	CHR	POS	Gene	$\beta_{\text{main}}$	$SE_{\text{main}}$	$\beta_{\text{int}}$	$SE_{\text{main}}$	$Cov_{\text{main}}$	Adj. Pvalue
BMI	3603436	rs12902602	15	78967401	<i>CHRNA5</i>	-0.03626	0.004127	0.007321	0.0133	-1.67E-05	4.240E-17
BMI	3634811	rs12902602	15	78967401	<i>CTSH</i>	0.03209	0.005488	-0.00724	0.01741	-2.87E-05	2.490E-07
BMI	3603408	rs12902602	15	78967401	<i>PSMA4</i>	-0.03678	0.005925	-0.01281	0.01902	-3.42E-05	2.610E-09
WC	2319661	rs17396340	1	10286176	<i>KIF1B</i>	-0.1778	0.006891	0.02395	0.02162	-4.55E-05	4.810E-154
WC	2536531	rs6743226	2	242236972	<i>FARP2</i>	-0.01581	0.002886	0.005153	0.009423	-8.01E-06	2.770E-06
WC	2607110	rs6743226	2	242236972	<i>HDLBP</i>	0.01823	0.005656	-0.00809	0.01854	-3.10E-05	4.261E-02
WC	2607055	rs6743226	2	242236972	<i>PASK</i>	-0.01045	0.002739	0.005422	0.008806	-6.98E-06	6.528E-03
WC	2536298	rs6743226	2	242236972	<i>SEPT2</i>	0.05532	0.003322	-0.00267	0.0105	-9.89E-06	8.700E-64
WHR	2949311	rs1049281	6	31236567	<i>DDAH2</i>	0.01253	0.003575	-0.00232	0.01127	-1.26E-05	1.362E-02
WHR	2949588	rs1049281	6	31236567	<i>DOM3Z</i>	0.01789	0.004185	0.02139	0.01327	-1.75E-05	1.280E-05
WHR	2948587	rs1049281	6	31236567	<i>FLOT1</i>	-0.04864	0.005155	-0.01361	0.01588	-2.51E-05	6.390E-22
WHR	2949885	rs1049281	6	31236567	<i>GPSM3</i>	0.01243	0.004026	0.01338	0.01269	-1.60E-05	8.922E-03
WHR	2902326	rs1049281	6	31236567	<i>HCP5</i>	-0.05335	0.00569	-0.0261	0.01758	-3.08E-05	7.540E-23
WHR	2948926	rs1049281	6	31236567	<i>HLA-B</i>	-0.1248	0.006133	0.005888	0.01854	-3.43E-05	1.070E-96
WHR	2902725	rs1049281	6	31236567	<i>HSPA1B</i>	0.02119	0.005638	0.008389	0.01761	-3.09E-05	2.192E-03
WHR	2948630	rs1049281	6	31236567	<i>IER3</i>	0.02917	0.004926	0.04421	0.01541	-2.36E-05	2.690E-12
WHR	2902427	rs1049281	6	31236567	<i>LST1</i>	-0.03445	0.005426	-0.00309	0.01694	-2.86E-05	2.830E-09
WHR	2902574	rs1049281	6	31236567	<i>LY6G5B</i>	0.03189	0.007651	-0.02135	0.024	-5.73E-05	1.819E-03
WHR	2949132	rs1049281	6	31236567	<i>NCR3</i>	-0.02313	0.003767	0.00752	0.01176	-1.38E-05	5.170E-08
WHR	2948648	rs1049281	6	31236567	<i>NCRNA00243</i>	0.04079	0.008008	0.04349	0.02457	-6.02E-05	9.640E-08
WHR	2901552	rs1049281	6	31236567	<i>RPP21</i>	0.01873	0.006047	-0.00356	0.01917	-3.65E-05	4.950E-02
WHR	2949488	rs1049281	6	31236567	<i>SLC44A4</i>	-0.1251	0.00593	-0.02214	0.01779	-3.16E-05	4.980E-109
WHR	2902935	rs1049281	6	31236567	<i>STK19</i>	0.01406	0.003975	-0.00735	0.01258	-1.57E-05	1.541E-02
WHR	2902178	rs1049281	6	31236567	<i>TCF19</i>	0.02045	0.003745	-0.02038	0.01172	-1.37E-05	5.420E-06
WHR	2948887	rs1049281	6	31236567	NA*	1.88	0.01597	-0.03048	0.04849	-0.00023	<1.754E-321
WHR	2974671	rs1856293	6	133480940	<i>C6orf192</i>	-0.02827	0.006785	-0.01251	0.021	-4.27E-05	3.215E-04

\*The transcript id is "2948887 " according to the affymetrix exon array annotation. Gene symbol is null, entrze gene id is null.

Supplementary Table 13. GWAS Catalog lookups for novel loci.

Current Study SNP						Previously Identified SNP												
TRAIT	CHR	rsID	POS (hg19)	Distance	rsID	POS	Risk Allele (RA)	RA freq	r <sup>2</sup>	P	OR/Beta	Disease/Trait	PUBMEDID	Discovery Sample Size	Replication Sample Size	Reported Gene	Mapped Gene	Annotation
BMI	15	rs12902602	78967401	73062	rs1051730	78894339	G	0.65	0.52227	3.00E-73	-1.02	Smoking behavior	20418890	74,035	68,988	CHRNA3	CHRNA3	STOP-GAIN
BMI	15	rs12902602	78967401	73062	rs1051730	78894339	G	0.66	0.52227	2.00E-66	-0.08	Smoking behavior	20418889	41,150	120,516	CHRNA5, CHRNA3	CHRNA3	STOP-GAIN
BMI	15	rs12902602	78967401	73062	rs1051730	78894339	T	0.35	0.52227	2.00E-51	1.31	Lung adenocarcinoma	19836008	11,587	21,379	CHRNA5, CHRNA3	CHRNA3	STOP-GAIN
BMI	15	rs12902602	78967401	73062	rs1051730	78894339	T	0.35	0.52227	6.00E-20	0.1	Nicotine dependence	18385739	10,995	4,848	CHRNA5, CHRNA3, CHRNA4	CHRNA3	STOP-GAIN
BMI	15	rs12902602	78967401	73062	rs1051730	78894339	A	0.34	0.52227	2.00E-69	0.8	Smoking behavior	20418888	31,266	54,731	NR	CHRNA3	STOP-GAIN
BMI	15	rs12902602	78967401	73062	rs1051730	78894339	A	NR	0.52227	1.00E-15	1.35	Lung cancer	18978790	6,717	8,472	intergenic	CHRNA3	STOP-GAIN
BMI	15	rs12902602	78967401	112833	rs1994016	79080234	C	0.6	0.559287	5.00E-13	1.19	Coronary artery disease	21239051	2,723	17,053	ADAMTS7	ADAMTS7	intron
BMI	15	rs12902602	78967401	121710	rs3825807	79089111	A	0.57	0.52833	1.00E-12	1.08	Coronary heart disease	21378990	86,995	56,682	ADAMTS7	ADAMTS7	missense
BMI	15	rs12902602	78967401	121710	rs3825807	79089111	A	0.57	0.52833	7.00E-06	0.363	Coronary artery calcification	23561647	2,620	NA	ADAMTS7	ADAMTS7	missense
WCadjBMI	1	rs17396340	10286176	0	rs17396340	10286176	A	NR	1	3.00E-08	0.008	Mean platelet volume	22139419	18,600	18,838	KIF1B	KIF1B, MIR1273D	intron;nearGene-5
WCadjBMI	3	rs4378999	51208646	170628	rs1031925	51379274	NR		0.756449	8.00E-06	1.15	Melanoma	24980573	6,122	18,416	DOCK3	DOCK3	intron
WCadjBMI	4	rs7697556	73515313	39299	rs9993613	73476014	T	0.473	0.986617	5.00E-24	0.03	Height	25282103	253,288	80,067	ADAMTS3	ADAMTS3 - HNRNPA1P67	intergenic
WCadjBMI	4	rs7697556	73515313	0	rs7697556	73515313	T	0.47	1	2.00E-14	0.028	Height	20881960	133,653	50,074	ADAMTS3	ADAMTS3 - HNRNPA1P67	intergenic
WCadjBMI	7	rs10269774	92253972	5896	rs42235	92248076	T	0.31	0.679196	8.00E-47	0.057	Height	20881960	133,653	50,074	CDK6	CDK6	intron
WCadjBMI	7	rs10269774	92253972	5896	rs42235	92248076	T	0.3	0.679196	1.00E-28	1.28	Height	23563607	16,196	9,703	CDK6	CDK6	intron
WCadjBMI	7	rs10269774	92253972	10438	rs2282978	92264410	NR	0.08	0.920627	1.00E-08	-0.06	Height	19343178	12,611	7,187	CDK6	CDK6	intron
WCadjBMI	7	rs10269774	92253972	10438	rs2282978	92264410	C	0.29	0.920627	1.00E-08	5.8	Height	18391951	30,968	8,541	CDK6, ERVWE1, GATAD1, PEX1	CDK6	intron
WCadjBMI	7	rs10269774	92253972	10438	rs2282978	92264410	C	0.33	0.920627	8.00E-23	0.09	Height	18391952	13,665	16,482	CDK6	CDK6	intron
WCadjBMI	8	rs6470765	130736697	12969	rs4733724	130723728	A	0.802	0.920945	1.00E-41	0.05	Height	25282103	253,288	80,067	MLZE	MIR3686 - GSDMC	intergenic
WCadjBMI	8	rs6470765	130736697	11032	rs6470764	130725665	T	0.2	0.911131	2.00E-28	0.05	Height	20881960	133,653	50,074	GSDMC	MIR3686 - GSDMC	intergenic
WCadjBMI	8	rs6470765	130736697	11032	rs6470764	130725665	T	0.203	0.911131	1.00E-06	0.054	Infant length	25281659	28,238	NA	GSDMC	MIR3686 - GSDMC	intergenic
WCadjBMI	8	rs6470765	130736697	2236	rs2062078	130734461	T	0.73	0.992777	1.00E-13	0.032	Height	25429064	36,227	57,699	GSDMC	MIR3686 - GSDMC	intergenic
WHRadjBMI	6	rs1049281	31344546	4456	rs3130542	31340090	A	0.13	0.720397	9.00E-14	1.33	Hepatitis B	24162738	1,888	9,903	HLA-C	TRNAI25	
WHRadjBMI	6	rs1049281	31344546	1751	rs9264638	31346297	A	0.58	0.915302	2.00E-23	-0.04	Beta-2 microglobulin plasma levels	23417110	6,728		HLA-C	HLA-C	intron
WHRadjBMI	6	rs1049281	31344546	15829	rs2524054	31360375	A	0.32	0.79929	2.00E-28	0.37	CD4:CD8 lymphocyte ratio	20045101	3,627	988	HLA-B	TRNAI25	
WHRadjBMI	6	rs1049281	31344546	15829	rs2524054	31360375	A	0.32	0.79929	6.00E-21	-0.31	CD4:CD8 lymphocyte ratio	20045101	3,627	988	HLA-B	TRNAI25	
WHRadjBMI	6	rs1049281	31344546	28923	rs2247056	31373469	T	0.25	0.853347	2.00E-15	-2.99	Triglycerides	20686565	96,598	NA	HLA	TRNAI25	
WHRadjBMI	6	rs1049281	31344546	28923	rs2247056	31373469	T	0.27	0.853347	4.00E-12	1.18	Height	23563607	16,196	9,703	HLA-B, HLA-C	TRNAI25	
WHRadjBMI	6	rs1049281	31344546	35694	rs6457374	31380240	T	0.73	0.857577	8.00E-35	-0.041	Height	25282103	253,288	80,067	HLA-C	WASF5P - HLA-B	intergenic
WHRadjBMI	8	rs2001945	126477978	0	rs2001945	126477978	C	0.42	1	1.00E-20	0.0405	Triglycerides	21909109	12,545	30,395	intergenic	TRIB1 - LINC00861	intergenic
WHRadjBMI	8	rs2001945	126477978	4099	rs2954021	126482077	G	0.5	0.816403	1.00E-07	-0.02	LDL cholesterol	20864672	17,723	47,439	TRIB1	TRIB1 - LINC00861	intergenic
WHRadjBMI	8	rs2001945	126477978	4099	rs2954021	126482077	A	0.5	0.816403	5.00E-09	1.6	Liver enzyme levels (alanine transaminase)	22001757	61,089	NA	TRIB1	TRIB1 - LINC00861	intergenic
WHRadjBMI	8	rs2001945	126477978	4099	rs2954021	126482077	A	0.5	0.816403	2.00E-13	1.4	Liver enzyme levels (alkaline phosphatase)	22001757	61,089	NA	TRIB1	TRIB1 - LINC00861	intergenic
WHRadjBMI	8	rs2001945	126477978	8431	rs17321515	126486409	A	0.47	0.610514	8.00E-07	0.07	Lipid traits	24386095	3,451	8,830	TRIB1	TRIB1 - LINC00861	intergenic
WHRadjBMI	8	rs2001945	126477978	8431	rs17321515	126486409	A	0.56	0.610514	7.00E-13	6.42	Triglycerides	18193043	8,684	9,741	TRIB1	TRIB1 - LINC00861	intergenic
WHRadjBMI	8	rs2001945	126477978	8431	rs17321515	126486409	G	0.49	0.610514	4.00E-17	0.08	Triglycerides	18193044	2,758	18,544	TRIB1	TRIB1 - LINC00861	intergenic
WHRadjBMI	13	rs17065323	44627788	0	rs17065323	44627788	NR	NR	1	4.00E-06	-4.29	Uric acid levels	18759275	868		NR	LINC00284 - SMIM2-AS1	intergenic

**Supplementary Table 14.** Lookups of previously identified smoking loci in current combined ancestries meta-analyses results for BMI, WCadjBMI and WHRadjBMI.

SNPS	CHR	POS(hg19)	DISEASE/TRAIT	REPORTED GENE(S)	PUBMEDID	Effect Allele	Other Allele	EAF	N	SMOKERS			NON-SMOKERS			MAIN and INTERACTION EFFECTS				
										$\beta$	SE	P	$\beta$	SE	P	$\beta_{adj}$	SE <sub>adj</sub>	P <sub>adj</sub>	P <sub>int</sub>	P <sub>joint</sub>
<b>BMI</b>																				
rs1451240	8	42546711	Nicotine dependence	<i>CHRNA3</i>	22524403	A	G	0.263	149,164	-0.011	0.010	2.84E-01	0.000	0.005	9.63E-01	-0.003	0.005	6.04E-01	3.04E-01	5.63E-01
rs6474412	8	42550498	Smoking behavior	<i>CHRNA3, CHRNA6</i>	20418888	T	C	0.740	173,262	0.007	0.010	4.48E-01	-0.003	0.005	5.24E-01	-0.001	0.005	8.90E-01	3.03E-01	6.10E-01
rs3025343	9	136478355	Smoking behavior (cessation)	<i>DBH</i>	20418890	A	G	0.116	168,375	-0.035	0.014	1.14E-02	-0.013	0.008	9.69E-02	-0.019	0.007	<b>4.34E-03</b>	1.28E-01	1.01E-02
rs1329650	10	93348120	Smoking behavior (CPD)	<i>LOC100188947</i>	20418890	T	G	0.300	174,980	0.003	0.009	7.55E-01	-0.008	0.005	9.13E-02	-0.006	0.004	1.51E-01	2.63E-01	2.24E-01
rs6265	11	27679916	Smoking behavior (initiation)	<i>BDNF</i>	20418890	T	C	0.193	217,329	-0.061	0.009	<b>2.49E-11</b>	-0.041	0.005	<b>1.31E-16</b>	-0.043	0.004	<b>8.13E-23</b>	4.24E-02	<b>3.50E-25</b>
rs2036527	15	78851615	Smoking behavior (CPD)	<i>CHRNA5</i>	22832964	A	G	0.331	240,437	-0.039	0.007	<b>1.11E-07</b>	0.002	0.004	6.89E-01	-0.007	0.003	2.98E-02	<b>2.43E-07</b>	<b>7.96E-07</b>
rs1051730	15	78894339	Smoking behavior (CPD, nicotine dependence)	<i>CHRNA3</i>	20418890; 20418888; 20418889; 18385739	A	G	0.329	215,806	-0.041	0.008	<b>8.53E-08</b>	0.002	0.004	6.64E-01	-0.008	0.004	3.09E-02	<b>1.61E-07</b>	<b>5.01E-07</b>
rs3733829	19	41310571	Smoking behavior (CPD)	<i>EGLN2, CYP2A6</i>	20418890	A	G	0.642	183,652	-0.003	0.009	7.29E-01	0.000	0.005	9.59E-01	0.000	0.004	9.55E-01	7.27E-01	9.40E-01
rs4105144	19	41358624	Smoking behavior	<i>CYP2A6, RAB4D</i>	20418888	T	C	0.312	135,367	0.003	0.011	7.66E-01	-0.003	0.006	6.75E-01	-0.002	0.005	7.77E-01	6.22E-01	8.76E-01
rs8102683	19	41363765	Smoking behavior	<i>CYP2A6</i>	23049750	T	C	0.266	157,411	0.006	0.011	5.94E-01	0.000	0.006	9.81E-01	0.002	0.005	7.53E-01	6.12E-01	8.68E-01
<b>WCadjBMI</b>																				
rs1451240	8	42546711	Nicotine dependence	<i>CHRNA3</i>	22524403	A	G	0.246	120,877	-0.007	0.011	5.22E-01	0.008	0.006	1.80E-01	0.007	0.005	1.62E-01	2.03E-01	3.24E-01
rs6474412	8	42550498	Smoking behavior	<i>CHRNA3, CHRNA6</i>	20418888	T	C	0.754	142,297	0.006	0.011	5.76E-01	-0.005	0.005	3.73E-01	-0.005	0.005	3.25E-01	3.45E-01	5.77E-01
rs3025343	9	136478355	Smoking behavior (cessation)	<i>DBH</i>	20418890	A	G	0.116	138,287	0.000	0.015	9.97E-01	0.025	0.008	<b>2.19E-03</b>	0.015	0.007	3.34E-02	1.36E-01	9.19E-03
rs1329650	10	93348120	Smoking behavior (CPD)	<i>LOC100188947</i>	20418890	T	G	0.310	143,896	0.007	0.010	4.66E-01	0.001	0.005	8.20E-01	0.001	0.005	8.96E-01	5.64E-01	7.47E-01
rs6265	11	27679916	Smoking behavior (initiation)	<i>BDNF</i>	20418890	T	C	0.195	185,265	0.005	0.010	6.05E-01	-0.003	0.005	6.10E-01	-0.002	0.005	6.87E-01	4.62E-01	7.65E-01
rs2036527	15	78851615	Smoking behavior (CPD)	<i>CHRNA5</i>	22832964	A	G	0.333	203,471	0.010	0.008	2.20E-01	-0.003	0.004	4.66E-01	-0.001	0.004	7.67E-01	1.32E-01	3.57E-01
rs1051730	15	78894339	Smoking behavior (CPD, nicotine dependence)	<i>CHRNA3</i>	20418890; 20418888; 20418889; 18385739	A	G	0.331	183,565	0.007	0.008	4.06E-01	-0.002	0.004	5.77E-01	0.000	0.004	9.70E-01	3.00E-01	6.13E-01
rs3733829	19	41310571	Smoking behavior (CPD)	<i>EGLN2, CYP2A6</i>	20418890	A	G	0.638	154,278	-0.010	0.009	2.79E-01	-0.005	0.005	3.38E-01	-0.006	0.004	1.83E-01	5.85E-01	3.50E-01
rs4105144	19	41358624	Smoking behavior	<i>CYP2A6, RAB4D</i>	20418888	T	C	0.311	117,256	0.006	0.012	6.14E-01	-0.007	0.007	2.68E-01	-0.003	0.006	5.51E-01	3.06E-01	4.77E-01
rs8102683	19	41363765	Smoking behavior	<i>CYP2A6</i>	23049750	T	C	0.268	130,065	0.008	0.012	5.03E-01	-0.005	0.006	4.62E-01	-0.002	0.006	7.77E-01	3.25E-01	6.07E-01
<b>WHRadjBMI</b>																				
rs1451240	8	42546711	Nicotine dependence	<i>CHRNA3</i>	22524403	A	G	0.240	106,301	-0.011	0.011	3.19E-01	0.007	0.006	2.93E-01	0.004	0.006	4.42E-01	1.52E-01	3.51E-01
rs6474412	8	42550498	Smoking behavior	<i>CHRNA3, CHRNA6</i>	20418888	T	C	0.759	126,252	0.012	0.011	2.77E-01	-0.002	0.006	7.75E-01	-0.001	0.005	8.91E-01	2.63E-01	5.34E-01
rs3025343	9	136478355	Smoking behavior (cessation)	<i>DBH</i>	20418890	A	G	0.117	121,686	-0.008	0.015	5.90E-01	0.011	0.009	2.18E-01	0.004	0.007	6.29E-01	2.65E-01	4.07E-01
rs1329650	10	93348120	Smoking behavior (CPD)	<i>LOC100188947</i>	20418890	T	G	0.312	129,224	0.004	0.010	6.55E-01	-0.005	0.005	3.93E-01	-0.003	0.005	5.83E-01	4.07E-01	6.29E-01
rs6265	11	27679916	Smoking behavior (initiation)	<i>BDNF</i>	20418890	T	C	0.196	166,380	0.000	0.005	9.52E-01	-0.001	0.004	8.30E-01	-0.001	0.005	7.61E-01	9.37E-01	9.78E-01
rs2036527	15	78851615	Smoking behavior (CPD)	<i>CHRNA5</i>	22832964	A	G	0.333	188,062	0.001	0.004	7.16E-01	-0.001	0.003	8.55E-01	0.000	0.004	9.36E-01	6.91E-01	9.27E-01
rs1051730	15	78894339	Smoking behavior (CPD, nicotine dependence)	<i>CHRNA3</i>	20418890; 20418888; 20418889; 18385739	A	G	0.332	166,117	0.001	0.004	7.89E-01	0.000	0.003	9.40E-01	0.001	0.004	8.54E-01	8.52E-01	9.61E-01
rs3733829	19	41310571	Smoking behavior (CPD)	<i>EGLN2, CYP2A6</i>	20418890	A	G	0.637	137,052	-0.004	0.009	6.27E-01	-0.005	0.005	3.33E-01	-0.005	0.004	2.50E-01	9.61E-01	5.61E-01
rs4105144	19	41358624	Smoking behavior	<i>CYP2A6, RAB4D</i>	20418888	T	C	0.314	102,594	0.010	0.012	3.86E-01	-0.010	0.007	1.69E-01	-0.004	0.006	4.80E-01	1.39E-01	2.66E-01
rs8102683	19	41363765	Smoking behavior	<i>CYP2A6</i>	23049750	T	C	0.270	113,338	0.008	0.012	4.81E-01	-0.014	0.007	3.92E-02	-0.008	0.006	1.82E-01	9.25E-02	9.00E-02



GIANT UKBB	1	rs10269774	7	92253972	CDK6	A	G	32,215 0.346 0.024 0.009 6.6E-03 14,687 0.325 0.003 0.012 7.9E-01 46,902 0.339 0.017 0.007 1.8E-02	125,337 0.337 0.023 0.005 1.1E-06 104,926 0.325 0.016 0.005 6.5E-04 230,263 0.331 0.019 0.003 <b>4.6E-09</b>	157,552 0.339 0.023 0.004 <b>2.9E-08</b> 8.8E-01 1.6E-07 119,613 0.325 0.014 0.004 1.0E-03 3.4E-01 3.2E-03 277,165 0.333 0.019 0.003 <b>2.9E-10</b> 7.7E-01 <b>2.1E-09</b>
GIANT + UKBB										
GIANT UKBB	1	rs6470765	8	130736697	GSDMC	A	C	32,162 0.762 0.032 0.010 1.9E-03 14,687 0.798 0.011 0.015 4.7E-01 46,849 0.773 0.025 0.008 3.2E-03	125,288 0.760 0.023 0.005 1.7E-05 104,926 0.798 0.024 0.005 1.2E-05 230,214 0.777 0.023 0.004 <b>8.9E-10</b>	157,450 0.760 0.026 0.005 <b>4.8E-08</b> 4.3E-01 9.5E-07 119,613 0.798 0.022 0.005 1.3E-05 3.9E-01 4.7E-05 277,063 0.777 0.024 0.003 <b>2.5E-12</b> 8.9E-01 <b>9.0E-11</b>
GIANT + UKBB										
GIANT UKBB	2	rs9408815	9	108890521	TMEM38B	C	G	31,918 0.741 0.012 0.010 2.3E-01 14,687 0.755 0.022 0.014 1.2E-01 46,605 0.745 0.015 0.008 5.8E-02	124,509 0.748 0.030 0.005 <b>4.2E-09</b> 104,926 0.755 0.019 0.005 2.9E-04 229,435 0.751 0.024 0.004 <b>1.9E-11</b>	156,427 0.746 0.026 0.005 <b>2.3E-08</b> 8.5E-02 <b>1.7E-08</b> 119,613 0.755 0.019 0.005 8.1E-05 8.4E-01 4.1E-04 276,040 0.750 0.023 0.003 <b>1.2E-11</b> 3.0E-01 <b>2.8E-11</b>
GIANT + UKBB										
GIANT UKBB	1	rs9409082	9	108901049	TMEM38B	C	T	32,248 0.754 0.017 0.010 8.1E-02 14,687 0.758 0.024 0.014 8.2E-02 46,935 0.755 0.020 0.008 1.5E-02	125,537 0.761 0.029 0.005 <b>2.6E-08</b> 104,926 0.758 0.018 0.005 4.0E-04 230,463 0.760 0.024 0.004 <b>1.5E-10</b>	157,785 0.760 0.027 0.005 <b>1.5E-08</b> 2.7E-01 <b>4.6E-08</b> 119,613 0.758 0.019 0.005 8.9E-05 6.9E-01 4.1E-04 277,398 0.759 0.023 0.003 <b>9.5E-12</b> 6.6E-01 <b>6.5E-11</b>
GIANT + UKBB										
GIANT UKBB	3	rs4141488	16	9629067	GRIN2A	T	C	31,839 0.501 0.037 0.009 2.2E-05 14,687 0.501 0.018 0.012 1.3E-01 46,526 0.501 0.030 0.007 1.8E-05	122,053 0.496 -0.015 0.005 9.6E-04 104,926 0.501 0.001 0.004 7.6E-01 226,979 0.498 -0.007 0.003 3.7E-02	153,892 0.497 -0.003 0.004 4.4E-01 <b>2.7E-08</b> 5.0E-07 119,613 0.501 0.003 0.004 4.1E-01 1.9E-01 3.1E-01 273,505 0.499 0.000 0.003 9.5E-01 1.8E-06 1.1E-05
GIANT + UKBB										
GIANT UKBB	1	rs6012558	20	47531286	ARFGF2	A	G	43,171 0.410 0.026 0.007 5.4E-04 14,687 0.420 0.029 0.012 1.7E-02 57,858 0.413 0.026 0.006 2.8E-05	164,833 0.407 0.018 0.004 6.5E-06 104,926 0.420 0.009 0.004 4.4E-02 269,759 0.412 0.014 0.003 3.3E-06	208,004 0.407 0.020 0.004 <b>1.9E-08</b> 3.3E-01 1.3E-07 119,613 0.420 0.011 0.004 6.5E-03 1.3E-01 7.7E-03 327,617 0.412 0.016 0.003 <b>1.5E-09</b> 7.0E-02 <b>3.0E-09</b>
GIANT + UKBB										
GIANT UKBB	2,3:EW	rs6076699	20	4566688	PRNP	A	G	11,858 0.969 0.169 0.039 1.4E-05 7,163 0.978 0.012 0.056 8.3E-01 19,021 0.973 0.117 0.032 2.3E-04	65,072 0.967 -0.070 0.018 1.2E-04 55,848 0.978 -0.016 0.021 4.4E-01 120,920 0.972 -0.047 0.014 6.3E-04	76,930 0.969 -0.034 0.016 3.5E-02 <b>1.4E-08</b> <b>4.8E-08</b> 63,011 0.978 -0.013 0.020 5.2E-01 6.3E-01 7.2E-01 139,941 0.973 -0.025 0.012 4.2E-02 2.3E-06 3.4E-06
GIANT + UKBB										
<b>WHRadjBMI</b>										
GIANT UKBB	4	rs765751	1	219669226	LYPLA1	C	T	40,484 0.647 0.003 0.004 3.9E-01 14,684 0.601 0.038 0.012 1.3E-03 55,168 0.624 0.007 0.004 7.2E-02	148,544 0.639 0.019 0.003 <b>3.1E-11</b> 104,916 0.601 0.034 0.004 <b>3.0E-14</b> 253,460 0.620 0.024 0.002 <b>3.2E-22</b>	186,625 0.621 0.029 0.004 <b>3.1E-16</b> 7.3E-04 <b>2.1E-10</b> 119,600 0.601 0.034 0.004 <b>1.8E-16</b> 7.2E-01 <b>1.7E-15</b> 306,225 0.611 0.031 0.003 <b>9.1E-31</b> <i>1.4E-04</i> <b>7.8E-22</b>
GIANT + UKBB										
GIANT UKBB	1:AW	rs670752	3	107312980	BBX	A	G	20,609 0.319 0.012 0.006 5.5E-02 7,161 0.286 0.058 0.018 1.7E-03 27,770 0.303 0.016 0.006 4.9E-03	86,960 0.303 0.009 0.004 1.5E-02 55,845 0.286 0.015 0.007 2.0E-02 142,805 0.295 0.010 0.003 1.1E-03	106,640 0.305 0.027 0.005 <b>4.9E-08</b> 6.8E-01 7.8E-03 63,006 0.286 0.020 0.006 1.3E-03 3.0E-02 4.8E-04 169,646 0.296 0.024 0.004 <b>3.1E-10</b> 3.8E-01 9.5E-05
GIANT + UKBB										
GIANT UKBB	4:EM	rs30000	5	55803533	MAP3K1	G	A	18,150 0.291 0.002 0.006 7.8E-01 7,523 0.256 -0.008 0.019 6.7E-01 25,673 0.273 0.001 0.005 8.9E-01	53,274 0.266 0.031 0.006 <b>3.7E-08</b> 49,071 0.256 0.045 0.007 <b>5.9E-10</b> 102,345 0.261 0.036 0.004 <b>3.7E-16</b>	71,475 0.263 0.040 0.006 <b>1.7E-10</b> 1.6E-04 2.7E-07 56,594 0.256 0.038 0.007 <b>2.2E-08</b> 9.5E-03 <b>4.2E-09</b> 128,069 0.260 0.039 0.005 <b>2.7E-17</b> <i>3.2E-07</i> <b>3.8E-15</b>
GIANT + UKBB										
GIANT UKBB	4:AM	rs459193	5	55806751	MAP3K1	A	G	19,661 0.286 0.004 0.006 5.0E-01 7,523 0.253 -0.008 0.019 6.6E-01 27,184 0.270 0.003 0.005 6.0E-01	61,191 0.271 0.034 0.005 <b>4.1E-10</b> 49,071 0.253 0.045 0.007 <b>3.6E-10</b> 110,262 0.262 0.038 0.004 <b>1.6E-18</b>	80,920 0.274 0.043 0.006 <b>2.3E-13</b> 6.8E-05 <b>2.2E-09</b> 56,594 0.253 0.038 0.007 <b>1.5E-08</b> 8.6E-03 <b>2.6E-09</b> 137,514 0.264 0.041 0.004 <b>3.5E-20</b> <i>2.5E-07</i> <b>1.6E-17</b>
GIANT + UKBB										
GIANT UKBB	1,2	rs1049281	6	31236567	HLA-C	C	T	32,281 0.664 0.022 0.009 1.3E-02 14,684 0.641 0.033 0.012 6.6E-03 46,965 0.652 0.025 0.007 3.0E-04	117,004 0.664 0.027 0.005 <b>2.0E-08</b> 104,916 0.641 0.027 0.005 <b>2.2E-09</b> 221,920 0.653 0.027 0.005 <b>1.6E-08</b>	149,566 0.663 0.025 0.004 <b>2.2E-09</b> 5.6E-01 <b>5.3E-09</b> 119,600 0.641 0.028 0.004 <b>5.3E-11</b> 6.6E-01 <b>4.3E-10</b> 269,166 0.652 0.026 0.003 <b>1.2E-18</b> 8.3E-01 <b>1.8E-10</b>
GIANT + UKBB										
GIANT UKBB	1:EC	rs589428	6	31848220	EHMT2	G	T	35,979 0.664 0.006 0.004 1.2E-01 14,684 0.632 0.028 0.012 2.2E-02 50,663 0.648 0.008 0.004 2.9E-02	126,939 0.670 0.011 0.003 4.1E-04 104,916 0.632 0.028 0.004 <b>8.4E-10</b> 231,855 0.651 0.016 0.003 <b>2.1E-10</b>	161,392 0.668 0.022 0.004 <b>2.8E-08</b> 3.5E-01 7.0E-04 119,600 0.632 0.027 0.004 <b>6.4E-11</b> 9.9E-01 <b>4.9E-10</b> 280,992 0.650 0.024 0.003 <b>1.1E-17</b> 8.4E-02 <b>1.6E-10</b>
GIANT + UKBB										
GIANT UKBB	4	rs7766106	6	127455138	RSPO3	T	C	39,761 0.479 0.007 0.004 7.9E-02 14,684 0.495 0.032 0.012 6.2E-03 54,445 0.487 0.009 0.004 1.3E-02	148,413 0.484 0.022 0.003 <b>2.2E-15</b> 104,916 0.495 0.044 0.004 <b>1.5E-24</b> 253,329 0.489 0.028 0.002 <b>5.0E-34</b>	186,080 0.477 0.037 0.003 <b>3.7E-27</b> 9.7E-04 <b>3.8E-15</b> 119,600 0.495 0.043 0.004 <b>4.3E-26</b> 3.3E-01 <b>4.5E-25</b> 305,680 0.486 0.039 0.003 <b>4.4E-51</b> <i>1.0E-05</i> <b>3.4E-34</b>
GIANT + UKBB										
GIANT UKBB	2:EC	rs1856293	6	133480940	EYA4	A	C	27,688 0.524 0.006 0.009 5.3E-01 14,684 0.514 -0.011 0.012 3.5E-01 42,372 0.519 0.000 0.007 9.6E-01	99,743 0.518 -0.028 0.005 <b>9.1E-09</b> 104,916 0.514 -0.013 0.004 3.6E-03 204,659 0.516 -0.020 0.003 <b>1.9E-09</b>	127,508 0.519 -0.019 0.004 6.5E-06 5.4E-04 <b>4.7E-08</b> 119,600 0.514 -0.012 0.004 2.3E-03 8.9E-01 9.3E-03 247,108 0.517 -0.016 0.003 9.6E-08 1.3E-02 <b>1.5E-08</b>
GIANT + UKBB										
GIANT UKBB	1:AW	rs2001945	8	126477978	TRIB1	G	C	19,957 0.404 0.009 0.006 1.2E-01 7,161 0.479 -0.003 0.016 8.3E-01 27,118 0.441 0.008 0.006 1.6E-01	83,489 0.442 0.013 0.003 1.0E-04 55,845 0.479 0.019 0.006 1.4E-03 139,334 0.460 0.014 0.003 5.9E-07	102,564 0.488 0.025 0.005 <b>4.7E-08</b> 5.9E-01 1.3E-04 63,006 0.479 0.017 0.006 3.2E-03 2.0E-01 5.9E-03 165,570 0.484 0.022 0.004 <b>1.1E-09</b> 3.0E-01 1.4E-06
GIANT + UKBB										
GIANT UKBB	4:EM	rs754133	12	54418920	HOXC4- HOXC6	A	G	18,192 0.392 0.003 0.005 6.2E-01 7,523 0.362 0.026 0.017 1.3E-01	52,944 0.342 0.026 0.005 8.2E-07 49,071 0.362 0.024 0.007 2.7E-04	71,812 0.360 0.034 0.006 <b>3.0E-09</b> 1.1E-03 4.0E-06 56,594 0.362 0.024 0.006 7.8E-05 9.0E-01 4.1E-04



GIANT + UKBB					<i>HOXC4</i>			25,715	0.377	0.004	0.005	3.7E-01	102,015	0.352	0.025	0.004	<b>7.6E-10</b>	128,406	0.361	0.030	0.004	<b>2.1E-12</b>	9.7E-04	<b>4.0E-09</b>	
GIANT					<i>HOXC4- HOXC6</i>	A	C	18,144	0.402	0.003	0.005	6.0E-01	52,724	0.354	0.026	0.005	1.0E-06	71,571	0.364	0.034	0.006	<b>9.1E-09</b>	1.1E-03	5.7E-06	
UKBB								4:AM	rs2071449	12	54428011	7,523	0.366	0.026	0.017	1.3E-01	49,071	0.366	0.025	0.007	1.3E-04	56,594	0.366	0.025	0.006
GIANT + UKBB								25,667	0.384	0.004	0.005	3.6E-01	101,795	0.360	0.026	0.004	<b>5.4E-10</b>	128,165	0.365	0.006	0.004	<b>2.7E-12</b>	8.0E-04	<b>2.8E-09</b>	
GIANT					<i>SMIM2</i>	T	C	6,602	0.007	0.154	0.116	1.9E-01	63,366	0.008	-0.230	0.036	<b>1.2E-10</b>	86,739	0.007	-0.181	0.032	<b>9.2E-09</b>	1.4E-03	<b>3.9E-10</b>	
UKBB								1:EC	rs17065323	13	44627788	14,684	0.004	0.006	0.107	9.6E-01	104,916	0.004	-0.091	0.040	2.3E-02	119,600	0.004	-0.079	0.037
GIANT + UKBB								21,286	0.006	0.073	0.079	3.5E-01	168,282	0.006	-0.168	0.027	<b>2.5E-10</b>	206,339	0.006	-0.139	0.024	<b>9.6E-09</b>	3.6E-03	<b>1.3E-09</b>	
GIANT					<i>JUND</i>	A	G	19,459	0.389	0.006	0.005	2.6E-01	60,628	0.358	0.025	0.005	5.0E-07	80,912	0.357	0.032	0.005	<b>4.7E-09</b>	5.5E-03	1.8E-06	
UKBB								4:AM	rs12608504	19	18389135	7,523	0.366	0.029	0.017	9.2E-02	49,071	0.366	0.019	0.007	3.1E-03	56,594	0.366	0.021	0.006
GIANT + UKBB								26,982	0.378	0.007	0.005	1.3E-01	109,699	0.362	0.023	0.004	<b>6.9E-09</b>	137,506	0.362	0.027	0.004	<b>2.9E-11</b>	1.3E-02	<b>1.6E-08</b>	

**Supplementary Table 16.** Genetic Risk Score (GRS) calculation in the combined KORA-S3 and KORA-S4 study.

SNPset	Model <sup>a</sup>	Beta <sub>GRS</sub>	Pval <sub>GRS</sub>	Beta <sub>SMK</sub>	Pval <sub>SMK</sub>	Beta <sub>GRSxSMK</sub>	Pval <sub>GRSxSMK</sub>	Multiple R <sup>2</sup>
97 known	BMI~GRS	0.08847	3.13E-13	-	-	-	-	0.01532
	BMI~GRS+SMK	0.08858	2.87E-13	-0.36222	0.0455	-	-	0.01647
	BMI~GRS+SMK+SMK*GRS	0.07959	2.68E-09	-4.85599	0.087	0.04993	0.113	0.01719
97 known + 6 novel	BMI~GRS	0.09259	2.19E-15	-	-	-	-	0.01811
	BMI~GRS+SMK	0.09269	2.00E-15	-0.36242	0.0451	-	-	0.01926
	BMI~GRS+SMK+SMK*GRS	0.08285	1.18E-10	-5.57166	0.0532	0.05482	0.0701	0.02019
97 known + 6 novel + 3 int	BMI~GRS	0.09224	6.39E-16	-	-	-	-	0.01888
	BMI~GRS+SMK	0.09225	6.19E-16	-0.35696	0.0484	-	-	0.01992
	BMI~GRS+SMK+SMK*GRS	0.08158	8.69E-11	-6.13026	0.0338	0.05914	0.0452	0.02106
77 known	WCADJ~GRS	0.14954	<2e-16	-	-	-	-	0.02585
	WCADJ~GRS+SMK	0.1475	<2e-16	0.83181	8.30E-05	-	-	0.03023
	WCADJ~GRS+SMK+SMK*GRS	0.15436	<2e-16	3.58699	0.243	-0.03561	0.369	0.03046
77 known + 11 novel	WCADJ~GRS	0.14768	<2e-16	-	-	-	-	0.02908
	WCADJ~GRS+SMK	0.14571	<2e-16	0.82427	9.38E-05	-	-	0.03338
	WCADJ~GRS+SMK+SMK*GRS	0.1518	<2e-16	3.70027	0.27	-0.03167	0.39	0.03358
77 known + 11 novel + 2 int	WCADJ~GRS	0.14445	<2e-16	-	-	-	-	0.02832
	WCADJ~GRS+SMK	0.1425	<2e-16	0.82549	9.22E-05	-	-	0.03264
	WCADJ~GRS+SMK+SMK*GRS	0.14908	<2e-16	4.04436	0.24	-0.03431	0.349	0.03289
66 known	WHRADJ~GRS	0.0007688	1.11E-07	-	-	-	-	0.008165
	WHRADJ~GRS+SMK	0.0007543	1.61E-07	0.0137037	5.61E-11	-	-	0.02049
	WHRADJ~GRS+SMK+SMK*GRS	0.0008785	3.71E-08	0.0554007	0.0169	-0.0006662	0.0709	0.02142
66 known + 6 novel	WHRADJ~GRS	0.0008429	1.02E-09	-	-	-	-	0.01079
	WHRADJ~GRS+SMK	0.0008294	1.49E-09	0.0136828	5.66E-11	-	-	0.02308
	WHRADJ~GRS+SMK+SMK*GRS	0.0009172	1.81E-09	0.0449584	0.0585	-0.0004602	0.1864	0.02357
66 known + 6 novel + 7 int	WHRADJ~GRS	0.0006968	8.58E-09	-	-	-	-	0.009597
	WHRADJ~GRS+SMK	0.0006777	1.78E-08	0.0135856	8.01E-11	-	-	0.0217
	WHRADJ~GRS+SMK+SMK*GRS	0.0007379	3.05E-08	0.0375582	0.1	-0.0003265	0.292	0.02202

<sup>a</sup> All outcome traits were adjusted for age, age<sup>2</sup> and sex. Waist circumference and waist-hip ratio were additionally adjusted for BMI.

## **SUPPLEMENTARY NOTE 1. Look-up of previously identified loci in our data set**

To fully explore the efficacy of accounting for smoking in GWAS of adiposity traits, we conducted a look-up in our data of recently published SNP associations with BMI, WHRadjBMI, and WCadjBMI identified in well-powered GWAS meta-analyses that did not account for SMK status<sup>1,2</sup>. Although our sample size was as little as one third of previously published GWAS<sup>1,2</sup>, the majority of these loci (92% for BMI, 97% for WCadjBMI, and 92% for WHRadjBMI) reached Bonferroni corrected significant for at least one of the three Approaches in the current study.

All previously identified 97 BMI-associated SNPs were nominally significant ( $P < 0.05$ ) in Approach 1 (SNPadjSMK) for BMI including the sex-specific loci, 95 of the 97 for Approach 2 (SNPjoint), and seven for Approach 3 (SNPint). A total of 86 loci reached Bonferroni-corrected significance ( $P < 5.15 \times 10^{-4}$ ) for Approach 1, 85 for Approach 2, and none for Approach 3. Finally, 41 loci from Approach 1 and 39 of the 97 from Approach 2 reached genome-wide significance (GWS,  $P < 5 \times 10^{-8}$ ) (44 in total, 45%) (**Supplementary Table 11**). Of the 97 previously identified main effects loci for BMI, 3 of these were genome-wide significant GWS for women-only, 3 for men-only and the remaining in the sex-combined analysis in the previous publication. It is also worth noting that we report results for the All Ancestries meta-analysis, as this was our primary meta-analysis data-set; however, Locke et al. (2015) considered their European-descent only meta-analysis their primary data-set.

Of the 77 previously-identified WCadjBMI loci, 3 of these were GWS for women-only, 3 for men-only and the remaining in the sex-combined analysis as reported in Shungin et al.<sup>2</sup>. Of these, 75 were nominally significant for Approach 1 (SNPadjSMK) and Approach 2 (SNPjoint), and 5 for Approach 3 (SNPint). A total of 73 were Bonferroni-corrected significant ( $P < 6.49 \times 10^{-4}$ ) for Approach 1 and 2; with 41 and 40 reaching GWS, respectively (43 non-overlapping, 56%) (**Supplementary Table 12**).

Eleven of the 68 previously published WHRadjBMI SNPs were associated in the women-only analyses in the previous investigation<sup>2</sup>. Of the 68 variants, 64 were nominally significant for Approach 1 (SNPadjSMK), 59 for Approach 2 (SNPjoint), and 10 for Approach 3 (SNPint). A total of 61 were Bonferroni-corrected significant ( $P < 6.49 \times 10^{-4}$ ) for Approach 1 and 38 for Approach 2; with 36 and 8 reaching GWS, respectively (36 in total, 53%) (**Supplementary Table 13**).

In summary, we replicated all previously-identified BMI loci using one or more of our approaches ( $P < 0.05$  and concordant direction of effect), but did not replicate all previously-identified loci for WCadjBMI and WHRadjBMI in our current analyses. It is unclear if the lack of replication of previous findings is due to smaller sample size, patterns of linkage disequilibrium in our all ancestries sample, the adjustment of smoking status in the current discovery analysis, or even a combination of these factors.

## **SUPPLEMENTARY NOTE 2. Summary of literature search on genes nearest to the 21 novel loci and all GxSMK interaction loci.**

We used SNIPPER (<http://csg.sph.umich.edu/boehnke/snipper/>) to identify potential biological functions of genes  $\pm 500$ kb of our novel association signals and those from Approach 3 (SNPint) for further investigation, and present a summary of those findings in this section (**Online Methods**).

### **Body Mass Index (BMI)**

**rs2481665 (*INADL*):** There are seven genes within the 500kb region of the lead SNP rs2481665 on chromosome 1. These genes are *INADL*, *L1TD1*, *KANK4*, *USP1*, *DOCK7*, *TM2D1*, and *ANGPTL3*. The lead SNP is in intron (#15) of the *INADL* (InaD-Like) gene. *INADL* encodes the protein Pals1-Associated Tight Junction (PATJ), which helps regulate the formation of tight junctions, and is involved in the processes of cell polarization and directional migration of epithelial cells<sup>3,4</sup>. A GWAS study (n= 815) designed to identify variants associated with childhood obesity in the Hispanic population, found near genome-wide significant associations between the exonic, non-synonymous SNP rs1056513 in *INADL* (204 kb downstream from our lead SNP) and the following fat distribution traits: weight [kg] (EAF[effect allele frequency]: 0.031, p-value:  $1.18 \times 10^{-07}$ ); BMI [kg/m<sup>2</sup>] (EAF: 0.021, p-value:  $8.34 \times 10^{-06}$ ); fat mass [kg] (EAF: 0.035, p-value:  $1.59 \times 10^{-07}$ ); trunk fat mass [kg] (EAF: 0.035, p-value:  $2.36 \times 10^{-07}$ ); fat free mass [kg] (EAF: 0.034, p-value:  $2.80 \times 10^{-07}$ ) and hip circumference (EAF: 0.022, p-value:  $2.47 \times 10^{-6}$ ).<sup>5</sup> The SNP rs1056513 accounted for 3% of the variance in body weight and body composition<sup>5</sup>. However, this SNP is not in LD with the lead SNP rs2481665 in this study ( $R^2 < 0.2$ ).

Farther away is the *DOCK7* gene, 326 kb downstream from the lead SNP. This gene encodes a guanine nucleotide exchange factor (GEF) protein that is involved in axon formation and neuronal polarization. GWAS studies have reported the association of variants located near the *DOCK7* gene with lipid levels. A GWAS study (n= up to 18,554) conducted with individuals of European ancestry identified the association of rs1213033 with triglycerides (eaf: -0.11,  $2 \times 10^{-8}$ )<sup>6</sup>. Another GWAS meta-analysis found a genome-wide significant association between rs1168013 and triglycerides in individuals of European ancestry (n=17,723; eaf: 0.035 (0.007), p-value:  $6.4 \times 10^{-8}$ )<sup>7</sup>. However, authors could not replicate this finding in other study samples consisting of 37,774 Europeans and 9,665 individuals of Indian Asian ethnicity. A GWAS replication study assessing the association between 15 SNPs and blood lipid and lipoprotein concentrations in individuals of Asian descent (n=4638), found a marginal association between the variant rs10889353, located in the intronic region of *DOCK7*, and triglycerides (eaf: -0.08, p-value:  $6.5 \times 10^{-04}$ )<sup>8</sup>. None of the variants from the different GWAS studies discussed above are in LD with SNP rs2481665 ( $R^2 < 0.2$ ).

*TM2D1* is another gene in the 500kb area that is 404 kb upstream from rs2481665. This gene encodes a beta-amyloid peptide-binding protein (BBP), which is involved in neural death and in the decrease of cognitive skills that occurs in Alzheimer's disease. This protein may be targeted by the beta-amyloid peptide which has been linked to the formation of plaques resulting in neurotoxicity in Alzheimer's disease<sup>9</sup>. The APP, the precursor of beta-amyloid peptide, is expressed in adipose tissue and its expression is up-regulated in obesity<sup>10,11</sup>.

*ANGPTL3* (Angiopoietin-Like 3) is 469 kb upstream from the lead SNP, and upstream of the *DOCK7* gene. *ANGPTL3* encodes a protein that plays a role in angiogenesis. This protein is expressed mostly in the liver. Mutations in this gene lead to the disease familial hypobetalipoproteinemia type 2 (*FHBL2*), which causes low levels of apolipoprotein B (apoB), total cholesterol, low-density lipoprotein (LDL) cholesterol and high density lipoprotein cholesterol<sup>12</sup>. Several genetic association studies suggest that *ANGPTL3* has a role in regulating plasma lipoprotein metabolism<sup>6,8,13,14</sup>. A few single-nucleotide polymorphisms, near the *ANGPTL3* gene, have been associated with lower triglyceride: rs1213033, rs213192, rs12042319<sup>6</sup>. One of these, rs1213033, is also near the *DOCK7* gene<sup>6</sup>.

There are several nearby genes with no documented role in adiposity or related cardiometabolic traits. Including, *L1TD1* (Line-1 type transposase domain containing 1) located 66 kb upstream from the lead SNP. *L1TD1* encodes the protein ES Cell-Associated Protein 11, a RNA-binding protein that plays a role in maintaining the pluripotency of stem cells, and in the proliferation of cancer cells<sup>15,16</sup>. Also, *KANK4* (KN

motif and ankyrin repeat domains 4) is a gene located 107 kb downstream from our SNP of interest. It encodes the protein Ankyrin Repeat Domain 38, a member of the Kank family of proteins, which are involved in the control of cytoskeleton microfilaments by regulating the polymerization of actin. The Kank gene is a tumor suppressor in renal cell carcinoma<sup>17</sup>. *USP1*, 307 kb upstream from rs2481665, encodes a protein that cleaves ubiquitin, a peptide that is added to proteins to signal them for degradation, or modification of their cellular location or enzymatic activity.

The intronic rs2481665 variant does not seem to have a functional role (Score 4 in RegulomeDB<sup>18</sup>). Two eQTLs were found for rs2481665 (Gene: *L1TD1*, p-value:  $2.1 \times 10^{-7}$ , EAF: -0.73, tissue: brain-cerebellum) and (Gene: *INALD*, p-value:  $4.0 \times 10^{-6}$ , EAF: 0.29, tissue: heart-atrial appendage).

**rs10929925 (*LOC400940*):** *LOC400940* and *SOX11* are the two genes on Chr2 that are within 500 kb of the lead SNP rs10929925. SNP rs10929925 is downstream of *LOC400940*, the nearest gene, a non-coding RNA gene that remains uncharacterized. The variant is also 314 kb downstream from *SOX11*, a gene without introns that encodes a transcription factor that is part of the SOX (SRY-related HMG-box) family. This family of transcription factors is involved with processes that regulate embryonic development and cell fate<sup>19</sup>. One study has proposed that *SOX11* has a role in brain development after observing that mutations in the gene may lead to microcephaly, developmental delays and other features found in mild Coffin-Siris Syndrome, a genetic disorder that causes developmental delays<sup>20</sup>. A recent GWAS meta-analysis study of fat distribution, which included 224,459 individuals of European and non-European ancestry, identified a genome wide significant association ( $p=4.5 \times 10^{-8}$ ) between rs10929925 and hip circumference unadjusted for BMI<sup>2</sup>. Based on a literature review, the study identified *SOX11* as the best candidate gene for rs10929925.<sup>2</sup>

There is no available information regarding the potential regulatory role of the lead SNP (RegulomeDB<sup>18</sup>). But there is evidence of an eQTL, although it does not reach 5% FDR (Gene: *SOX11*, P-value:  $8.7 \times 10^{-6}$ , Effect size: 0.39, Tissue: thyroid). In brain tissue, the SNP altered the TATA box motif of the *Dlx3* gene a homeodomain gene (HaploReg<sup>21</sup>).

**rs6794880 (*SRRM1P2*):** The 500kb region around the lead SNP, rs6794880, does not show the presence of any protein coding genes. The nearest genomic feature to rs6794880 is *SRRM1P2*, a pseudogene, named the serine/arginine repetitive matrix 1 pseudogene 2. Upstream rs6794880 is *LINC00971*, a long intergenic non-protein coding RNA gene that remains uncharacterized.

There is no evidence that the lead SNP rs6794880 has a functional/regulatory role (Score 6 in RegulomeDB<sup>18</sup>) in the genome. Additionally, there are no reports of eQTLs for this variant.

**rs12629427 (*EPHA3*):** There is only one gene found within 500kb of the peak signal, rs12629427. *EPHA3* (EPH receptor A3) is 11kb downstream from rs12629427, and is a member of the ephrin receptor subfamily of the protein-tyrosine kinase family. EPH and EPH-related receptors have been implicated in mediating developmental events, particularly in the nervous system. This gene encodes a protein that binds ephrin-A ligands. *EPHA3* has been implicated in the pathogenesis of lung cancer<sup>22-26</sup>. The SNP rs12629427 has a score of 6 in RegulomeDB<sup>18</sup> (minimal binding evidence). No significant eQTLs were found for rs12629427 and no GWAS hits were identified within the 1MB region of the lead SNP.

**rs2173039 (*EPHA3*):** There is only one gene found within 500kb of rs2173039, which is 14.5kb upstream from *EPHA3* (EPH receptor A3). See rs12629427 above.

**rs13069244 (CCDC39):** A total of 4 genes are found within 500kb of the lead marker, rs13069244. *CCDC39* (coiled-coil domain containing 39) is located 43.88kb downstream from the lead marker and encodes a protein involved in the motility of cilia and flagella. Defects in this gene cause primary ciliary dyskinesia type 14. Lung disease was worse in those with IDA/CA/MTD ultrastructural defects, most of whom had biallelic mutations in *CCDC39*<sup>27</sup>. *FXR1* (fragile X mental retardation, autosomal homolog 1) is located 189kb downstream from rs13069244, and codes for an RNA binding protein that shuttles between the nucleus and cytoplasm, and is associated with polyribosomes, predominantly with the 60S ribosomal subunit. Deregulation of FXR protein 1 by the lipodystrophic lamin A p.R482W mutation elicits a myogenic gene expression program in preadipocytes<sup>28</sup>. *DNAJC19* (DnaJ (Hsp40) homolog, subfamily C, member 19), located 260kb upstream from our lead marker, encodes a protein involved in the ATP-dependent transport of transit peptide-containing proteins from the inner cell membrane to the mitochondrial matrix. Defects in this gene are a cause of 3-methylglutaconic aciduria type 5 (MGA5), also known as dilated cardiomyopathy with ataxia (DCMA)<sup>29-31</sup>. The loss of DNAJC19/PHB complexes affects cardiolipin acylation and leads to the accumulation of cardiolipin species with altered acyl chains<sup>32</sup>. There is no evidence that rs13069244 has a functional/regulatory role (RegulomeDB<sup>18</sup> Score 6: minimal binding evidence) in the genome. No GWAS hits were identified within the 1Mb region of rs13069244 and no report of eQTL for the variant.

**rs336396 (INPP4B):** There are two genes found within 500kb of rs336396. The SNP lies within *INPP4B* (inositol polyphosphate-4-phosphatase, type II, 105kDa), which encodes inositol polyphosphate 4-phosphatase type II, one of the enzymes involved in phosphatidylinositol signaling pathways. *INPP4B* has been identified as a tumor suppressor by negatively regulating normal and malignant cell proliferation through regulation of the PI3K/Akt signaling pathway<sup>33,34</sup>. Different residues within the catalytic site of *INPP4B* are responsible for activity with lipid and protein substrates<sup>35</sup>. *IL15* (interleukin 15) is located 407kb upstream of rs336396. *IL15* encodes a cytokine that regulates T and natural killer (NK) cell activation and proliferation. This cytokine may act as an antagonist to IL2, which binds common hematopoietin receptor subunits, and may compete for the same receptor. This cytokine induces the activation of JAK kinases, as well as the phosphorylation and activation of transcription activators STAT3, STAT5, and STAT6. Murine models show that this cytokine may increase expression of apoptosis inhibitor BCL2L1/BCL-x(L), possibly through the transcription activation activity of STAT6, and thus prevent apoptosis. Cigarette smoke compromises IL-15 production – and as a result NK cell function – which could link to the higher incidence of cancers or viral infections observed among smokers<sup>36</sup>. A group of SNPs, upstream from *IL15*, were associated with both smoking status and quantity of cigarette consumption<sup>37</sup>. No data was provided for rs336396 by RegulomeDB<sup>18</sup>. No GWAS hits were identified within the 1Mb region of rs336396 and no report of an eQTL for the variant.

**rs12902602 (CHRNA5-CHRNA3-CHRNA4):** A total of 10 genes are found within 500kb of rs12902602. The SNP is located 33.81kb upstream of *CHRNA4* (cholinergic receptor, nicotinic beta 4). The *CHRNA5-CHRNA3-CHRNA4* gene cluster has consistently been associated with smoking quantity and nicotine dependence<sup>38-40</sup>, COPD, lung cancer and peripheral artery disease<sup>39,41,42</sup>, and increased risk of death<sup>43</sup>. Variants of *CHRNA5-CHRNA3-CHRNA4* have also been associated with lower birth weight from smoking mothers<sup>44</sup>, and with lower BMI in current adult smokers<sup>45,46</sup>, but with lower BMI in never smokers<sup>46</sup>. The *CHRNA5-CHRNA3-CHRNA4* genes encode the nicotinic acetylcholine receptor (nAChR) subunits  $\alpha 3$ ,  $\alpha 5$  and  $\beta 4$  that are expressed in mammalian brain<sup>47,48</sup>. GWASs have also identified loci at *ADAMTS7* (ADAM metalloproteinase with thrombospondin type 1 motif 7), at 84.14 kb downstream from the lead SNP rs12902602, associated with coronary artery disease and its risk factors<sup>49-52</sup>.

**Waist Circumference adjusted for BMI (WCADJBMI):**

**rs17396340 (*KIF1B*).** A total of 10 genes are found within 500kb of the lead marker, rs17396340, which is intronic to *KIF1B*. We highlight four genes in the region here. *KIF1B* is involved in synaptic vesicle and mitochondrial transport, and may play a critical role in the development of hepatocellular carcinoma<sup>53</sup>. *6PGD* codes for an oxidative carboxylase responsible for reduction of 6-phosphogluconate. Cells lacking 6PGD appear to metabolize glucose as an inhibitor to induce senescence<sup>54</sup>. *RBP7* is involved in carotenoid metabolism. In avian model organisms, the *RBP7* promoter is important in regulating expression of several genes in adipose tissue at later developmental stages<sup>55</sup>. Nicotinamide mononucleotide adenylyltransferase (*NMNAT*) reversibly catalyzes the important step in the biosynthesis of NAD from ATP and NMN. NAD and NADP are used reversibly in anabolic and catabolic reactions. NAD is necessary for cell survival in oxidative stress and DNA damage. The top SNP, rs17396340, is associated with the expression levels of ARSA (p-value of 6.0e-05) at LCL tissue in *Homo sapiens*. Human adipocytes express functional DAR (Dopamine receptors) and ARSA, suggesting a regulatory role for peripheral dopamine in adipose functions<sup>56</sup>. It is speculated that the propensity of some DAR-activating antipsychotics to increase weight and alter metabolic homeostasis is due to their direct action on adipose tissue. Our lead SNP is also associated with mean platelet volume<sup>57</sup>. From HaploReg<sup>21</sup>, the lead SNP, rs17396340, is annotated as *KIF1B* in GENCODE, and is functionally annotated as intronic. This lead SNP is associated with enhancer histone marks in 9 tissues; associated with regulatory motifs at GATA and Hoxa5; and with cis-eQTLs from various tissues (cells transformed fibroblasts, muscle skeletal, lymphoblastoid EUR exonlevel, lymphoblastoid EUR genelevel, and whole blood). The RegulomeDB<sup>18</sup> score for the lead SNP is 4.

**rs6743226 (*HDLBP*).** A total of 10 genes are found within 500kb of our lead marker, rs6743226. Three, of biological interest, are mentioned here. Our lead SNP, rs6743226, is intronic to *HDLBP*, which codes for a protein that binds high density lipoprotein (HDL) that functions to regulate excess cholesterol levels in cells.

*STK25* codes for a serine/threonine kinase with important functions in the Golgi apparatus. This gene has been associated with severe hypoxia<sup>58</sup> and pseudohypoparathyroidism, symptoms of which include short stature and obesity<sup>59</sup>. Significantly higher serine/threonine kinase 25 (*STK25*) levels were observed in the skeletal muscle of type 2 diabetic patients, compared with individuals with normal glucose tolerance<sup>60</sup>. The overexpression of *STK25* in conditions of excess dietary fuels associates with a shift in the metabolic balance in peripheral tissues from lipid oxidation to storage, leading to a systemic insulin resistance<sup>61</sup>.

Expression of PAS domain containing serine/threonine kinase (*PASK*) is regulated by glucose and the encoded protein plays a role in the regulation of insulin gene expression. Down regulation of this gene may play a role in type 2 diabetes<sup>62-64</sup>. *Far2* and *Stk25* are candidate genes for the HDL cholesterol locus in mice<sup>65</sup>. The top SNP, rs6743226, is associated with the expression of B-cell CLL/lymphoma 10 (*BCL10*). The protein encoded by the gene *BCL10* contains a caspase recruitment domain (CARD), and induce apoptosis and to activate NF-kappaB MALT1 and this protein are thought to synergize in the activation of NF-kappaB, and the deregulation of either of them may contribute to the same pathogenetic process that leads to the malignancy<sup>66</sup>.

There is no GWAS signal nearby the lead SNP rs6743226. This lead SNP is associated with enhancer histone marks in 4 tissues; associated with regulatory motifs changed at *Goxa* and *TCF12*; and with eQTL from various tissues including adipose subcutaneous, lung, and muscle tissues. The RegulomeDB<sup>18</sup> score for the lead SNP is 6.

**rs4378999 (DOCK3):** A total of 4 genes are found near our lead marker, rs4378999, *DOCK3*, *MANF*, *VPRBP*, and *RBM15B*. Our lead variant is intronic to *DOCK3* (dedicator of cytokinesis 3), which is highly expressed in the central nervous system and like previously identified obesity related genes, is involved in neurite outgrowth downstream of BDNF-TrkB<sup>67</sup>. *MANF* (mesencephalic astrocyte-derived neurotrophic factor) is an endoplasmic reticulum protein that acts to protect ER in response to cellular/organismal stress<sup>68</sup>, for example, expression is increased in skeletal muscle of the leg in rats in response to exercise<sup>69</sup>. Further, recent evidence shows that *MANF* may be an important factor in the protection of pancreatic beta cells and disruption of *MANF* expression can lead to diabetes<sup>68</sup>. There is very little known about *VPRBP*, and *RBM15B*.

Genome-wide association studies have reported the association within 1MB region of lead SNPs for height ( $R^2=0.35$ )<sup>70,71</sup> and melanoma ( $R^2=0.48$ )<sup>72</sup>. Our lead SNP is associated with regulatory motifs changed at Cdx2; and with eQTL from various tissues including adipose subcutaneous, and muscle skeletal. The lead SNP is associated eQTL in esophagus muscularis tissue based on GTEx<sup>73</sup> lookup. GWAS studies have report the association within 1Mb of lead SNP for height ( $R^2=0.38$ )<sup>71</sup>, and fibrinogen ( $R^2=0.41$ )<sup>74</sup>. The RegulomeDB<sup>18</sup> does not have data for lead SNP rs4378999.

**rs7697556 (ADAMTS3):** One gene is found within 500kb of our lead marker, rs7697556. ADAM metalloproteinase with thrombospondin type 1 motif, 3 (*ADAMTS3*) is located 80 kb upstream of our variant, rs7697556. While there is no established role for *ADAMTS3* in obesity-related traits, there are a number of variants within and near this gene associated with relate anthropometric and cardiometabolic traits, including height<sup>70,71</sup>, lipid metabolism<sup>75</sup>, and metabolites<sup>76</sup>. From There is no score assigned for our lead SNP in the RegulomeDB<sup>18</sup>.

**rs10269774 (CDK6):** A total of 10 genes are found within 500 kb of the lead marker, rs10269774. The SNP is located within an intron in cyclin-dependent kinase 6 (*CDK6*). CDK family members are important regulators of cell cycle progression. GWAS have reported associations between *CDK6* variants with height<sup>70,71,77-81</sup>. The *CDK6*-rs2282978 associated with height is in complete LD with our lead marker (rs10269774:  $R^2=1$ ,  $D'=1$ ). Also, GWAS identified associations between *CDK6* variants with white blood cell counts<sup>82</sup> and rheumatoid arthritis<sup>83,84</sup>. *CDK6* rs42041 is associated with juvenile idiopathic arthritis (JIA)<sup>85</sup>, and patients with JIA are significantly shorter and more often overweight or obese than controls<sup>86</sup>. Research suggests that the microRNA-103a-3p controls proliferation and osteogenic differentiation of human adipose tissue-derived stromal cells by binding to specific target sequences in the *CDK6* mRNA 3'-untranslated region<sup>87</sup>. Another study in the human placental transcriptome found that *CDK6* mRNA levels correlated with offspring birth weight and birth weight percentiles<sup>88</sup>.

rs10269774 is located in enhancer regions (H3K4Me1 and H3K27ac) with histone modification enrichment in mammary epithelial tissue and lymphoblastoid cell lines. rs10269774 was suggested to have cis-acting associations with five gamma-glutamyltransferase (GGT) family gene expression in lymphoblastoid of Yoruba population ( $p=6E-05$ )<sup>89</sup>. Elevated serum GGT is associated with waist circumference<sup>90,91</sup>, BMI<sup>91</sup>, visceral fat area<sup>91</sup>, triglyceride levels<sup>91</sup>, metabolic syndrome<sup>90,92</sup>, coronary artery calcification<sup>93</sup> and biomarkers of atherosclerosis<sup>94</sup>, arterial stiffness<sup>95,96</sup>, incident CVD and death<sup>92</sup>. rs10269774 is located near to several transcription factor binding sites (*CTCF*, *EP300*, *JUN*, *POLR2A*, *FOS*, *NFIC*, and *RFX5*, among others).

**rs9409082 and rs9408815 (TMEM38B):** A total of 3 genes are found within 500 kb of the lead markers rs9409082 and rs9408815. At 364 kb downstream of rs9409082 is located *TMEM38B* (transmembrane protein 38B, 9q31.2) gene, which encodes an intracellular monovalent cation channel that functions in



maintenance of intracellular calcium release. Deletions in *TMEM38B* are associated with autosomal recessive osteogenesis imperfecta<sup>97-99</sup>. There is evidence of genome-wide association between rs9409082 with height<sup>70</sup>. Also, GWAS have reported several variants in this region associated with age at menarche<sup>100-102</sup>, which is a risk factor to develop obesity, type 2 diabetes, cardiovascular disease, breast cancer and all-cause mortality<sup>101</sup>. However, the reported variants for age at menarche are in low-to-moderate LD ( $0.005 < R^2 < 0.68$ ) with our lead marker from Approach 1, rs9409082. Variants on 9q31, in low LD with rs9409082, have shown suggestive association with visceral adipose to subcutaneous adipose ratio in men ( $R^2=0.161$ )<sup>103</sup> and with a protein quantitative trait locus modulating cellular response to chemotherapy ( $R^2=0.002$ )<sup>104</sup>.

At 497.6 kb downstream of rs9409082 is the *FKTN* (fukutin, 9q31.2) gene that encodes a putative transmembrane protein of the cis-Golgi compartment. *FKTN* protein may be involved in the glycosylation of alpha-dystroglycan in skeletal muscle. Mutations in *FKTN* have shown association with congenital muscular dystrophy<sup>105,106</sup>. No significant eQTLs were found for SNP rs9409082 (GTEx<sup>73</sup>, SNIPPER, RegulomeDB<sup>18</sup>, and HaploReg<sup>21</sup>).

**rs6012558 (*ARFGEF2*):** A total of 11 genes are found within 500kb +/- of our lead SNP, rs6012558, which is 6,989 bp upstream of *ARFGEF2* (ADP-ribosylation factor guanine nucleotide-exchange factor 2). *ARFGEF2*'s primary function involves intracellular trafficking. Our lead variant is 86,866 bp upstream of *PREX1* (phosphatidylinositol-3,4,5-trisphosphate-dependent Rac exchange factor 1), a gene which encodes a protein involved in intracellular signaling, lipid and protein binding, and regulation of GTPase activity<sup>107-109</sup>. *PREX1* is primarily expressed in the blood leukocytes and brain<sup>107</sup>. Recent mouse models indicate that *PREX1* may be important for the regulation of thermogenic potential of brown adipose tissue and white preadipocytes, making this gene very important for energy expenditure<sup>110</sup>. Additionally, rs6012558 is a significant (<5% FDR) cis-acting expression quantitative trait locus (cis-eQTL) for *ARFGEF2* (subcutaneous adipose and sigmoid colon tissues), *CSE1L* (artery, thyroid, subcutaneous adipose, esophagus mucosa, and skeletal muscle tissues), and *STAU1* (transformed fibroblast cells) (GTEx<sup>73</sup>). Additional evidence that this variant lies in a potentially important regulatory region includes a RegulomeDB<sup>18</sup> score of 4<sup>18</sup>, it is nearby (<500kb +/- and  $R^2 > 0.7$ ) other variants that rest in active enhancers for *ARFGEF2*, other cis-eQTLs for *ARFGEF2* (monocytes, whole blood, cerebellum, and temporal cortex), *DDX27* (monocytes), *C2orf199* (monocytes), *CSE1L* (whole blood), and *PREX1* (Cerebellum and Temporal Cortex) (HaploReg<sup>21</sup> and UCSC Browser<sup>111</sup>). Our lead SNP is within 500kb +/- of several previously identified GWAS SNPs for multiple traits, the nearest of which is rs6012564 associated with tendency toward anger (distance=10kb)<sup>112</sup>; however, all of these are in low LD with rs6012558 ( $R^2 < 0.3$ ).

**rs4141488 (*GRIN2A*):** There are only two genes within 500 kb +/- of our lead SNP, rs4141488, which lies 218 kb downstream of *GRIN2A* (glutamate receptor, ionotropic, N-methyl D-aspartate 2A). The primary function of *GRIN2A* is to assist in controlling long-term memory and learning through regulation and efficiency of synaptic transmission. These receptors are essentially the gateway for calcium into post-synaptic cells<sup>113</sup>. Variants in this gene have been associated with various forms of epilepsy, sleep patterns, delayed psychomotor development, speech difficulties, seizures, mental retardation, and various mental disorders, including heroin addiction<sup>114-120</sup>. The only other gene within 500 kb of rs4141488 is *C16orf72*; little is known about the function of this gene. While GTEx<sup>73</sup> revealed no significant eQTLs nearby our lead variant, there is some evidence that this locus may lie within an important regulatory region. RegulomeDB<sup>18</sup> provided a score of 5 (minimal binding evidence) for rs4141488. Additionally, HaploReg<sup>21</sup> and UCSC browser show that our lead SNP and variants in high LD ( $R^2 > 0.7$ ) are within active enhancer regions for several tissues, including liver, fetal leg muscle, smooth stomach and intestinal muscle, cortex, and several embryonic and pluripotent cell types; and within altered binding motifs for EWSR1-FLI1, Elf3,

STAT, CDP, HNF1, and SOX. Our lead SNP is within 500kb +/- of several previously identified GWAS SNPs for multiple traits, the nearest of which is rs17550532 associated with sudden cardiac arrest<sup>121</sup>. Other associations in this region include behavioral disinhibition<sup>122</sup>, venous thromboembolism<sup>123</sup>, and Transforming Growth Factor- $\beta$ 1<sup>5</sup>; however, all of these are in low LD with rs4141488 ( $R^2 < 0.4$ ).

**rs1545348 (*RAI14*):** Our lead SNP, rs1545348, lies within the intron of *RAI14* (Retinoic Acid Induced 14), although very little is known about the function of this gene in humans. There are four additional genes within 500 kb +/- of rs1545348, including *RAD1* (RAD1 checkpoint DNA exonuclease) 187 kb upstream. *RAD1* encodes a protein involved in stopping the cell cycle in response to DNA damage, as well as recruiting other proteins responsible for DNA repair<sup>124,125</sup>, including in response to stress caused by cigarette smoke<sup>126</sup>. There is strong evidence of a regulatory role within the region surrounding our lead variant (RegulomeDB<sup>18</sup> score 4, minimal binding evidence). One significant (beta=-0.28, P=5.3E-6) eQTL between rs1545348 and *TTC23L* was found in sun exposed skin tissue (lower leg) (GTEx<sup>73</sup>). Additionally, HaploReg<sup>21</sup> and the UCSC browser reveal that the region surrounding our lead variant (+/- 500 kb,  $R^2 > 0.7$ ) harbors marks of open and active chromatin and DNase hypersensitive regions across multiple tissues, including cancer, pluripotent, and normal tissue, brain and adipose tissue among others. Traits with nearby GWAS associations include several metabolite markers and left ventricular mass, although each of these associations are in low LD with rs1545348<sup>127-131</sup>.

**rs6470765 (*GSDMC*):** There are three genes within 500 kb +/- of our lead SNP, rs6470765, which lies within an intron of *GSDMC* (gasdermin C). There is very little known about the function of *GSDMC*. Our lead SNP also lies 80 kb downstream of *FAM49B* (family with sequence similarity 49, member B). Similar to *CDK6*, a gene nearby another one of our novel variants, rs10269774, *FAM49B* is a target of *BACH1* transcription factor, which is involved in cellular response to oxidative stress and management of the cell cycle<sup>132</sup>. Also, *ASAP1* (ArfGAP With SH3 Domain, Ankyrin Repeat And PH Domain 1), a gene located 328 kb upstream of our association signal, may be involved in the differentiation of fibroblasts into adipocytes<sup>133</sup>. There is moderate evidence for the functional role of lead variant in regulation of gene expression (RegulomeDB<sup>18</sup> score of 6: minimal binding evidence). However, the GTEx<sup>73</sup> database indicates that rs6470765 is a significant eQTL for *GSDMC* in skeletal muscle, sun-exposed skin, and mucous in the esophagus. Furthermore, HaploReg<sup>21</sup> and the UCSC Browser highlight moderate evidence for regulatory elements in high LD  $> 0.9$ , including DNase hypersensitive regions, and active enhancer and promoter regions in  $> 20$  tissue types (e.g. lung, adipose, skeletal muscle, epidermal and esophageal tissues, and many stem/pluripotent cell types). Our lead variant is within several altered binding sites for FOX1, FOX2 and SOX. Last, our lead SNP is in high LD with other potential cis-eQTLs for *GSDMC*. Nearby associations with other traits include height, hip circumference adjusted for BMI, and inflammatory bowel disorder<sup>2,70,71,134</sup>.

**rs6076699 (*PRNP*):** There are seven genes within 500 kb +/- of our lead SNP, rs6076699. The lead SNP is 100kb upstream of *PRNP* (prion protein) is likely a signaling transducer involved in multiple biological processes related to nervous system, immune system, and general cellular functions<sup>135-138</sup>. Mutations in the repeat region as well as elsewhere in this gene have been associated with Creutzfeldt-Jakob disease, fatal familial insomnia, Gerstmann-Straussler disease, Huntington disease-like 1, and kuru<sup>139-145</sup>.

Alternate forms of the oligomers have been shown to form in response to oxidative stress caused by copper exposure<sup>146</sup>. Copper is present in cigarette smoke and elevated in serum of smokers, but is not outside of safe ranges according to the U.S. Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, and Office on Smoking and Health<sup>147,148</sup>. Our lead SNP is 136 kb upstream from a related gene, *PRND* (prion protein 2), which is biochemically and structurally similar to *PRNP*<sup>149</sup>. Like PRNP, mutations in this gene may also be involved in neurocognitive disorders, although

there are only weak associations<sup>150,151</sup>. A third prion protein (testes specific, *PRNT*) is found 145 kb away from our lead SNP; however no much is known about the function of this gene. Other nearby genes include *SLC23A2* (Solute Carrier Family 23 [Ascorbic Acid Transporter], Member 2), *ADRA1D* (Adrenoceptor Alpha 1D), *SMOX* (Spermine Oxidase), and *RASSF2* (Ras association [RalGDS/AF-6] domain family member 2). *SLC23A2* is essential for the uptake and transport of Vitamin C, which is an important nutrient for DNA and cellular repair in response to oxidative stress both directly and through supporting the repair of Vitamin E after exposure to oxidative agents<sup>152-155</sup>. Furthermore, this region is associated with success in smoking cessation and is implicated in addictive behaviors in general<sup>156,157</sup>. Nearby GWAS-identified associations include preeclampsia, and height<sup>70,71,158</sup>. There is little evidence that our association signal is involved in regulation of gene expression (RegulomeDB<sup>18</sup> score-5: minimal binding evidence)<sup>18</sup>. While our tag SNP is located within an active enhancer region (open chromatin marks, DNase hypersensitivity, and several transcription factor binding motifs), this activity appears tissue specific (sex-specific tissues and lungs)<sup>21,111</sup>. There are no other significant regulatory elements in high LD with rs6076699<sup>21,73</sup>.

### **Waist-to-Hip Ratio adjusted for BMI (WHRadjBMI)**

**rs670752 (*BBX*):** There are only three genes within 500 kb+/- of our lead SNP, rs670752, which lies within an intron of *BBX* (Bobby Sox Homolog [Drosophila]). While there is little known about the function of *BBX*, another nearby intronic variant, rs6437740, has been associated with smoking behavior in a previous GWAS<sup>159</sup>. Other nearby genes include *CCDC54* (coiled-coil domain containing 54) and *CD47* (CD47 molecule). Much is known about the function of *CD47* due to mouse models. *CD47* encodes a cell surface antigen involved in immune response to bacteria, cell adhesion, inflammatory response, and cell to cell signaling<sup>160-162</sup>. *CD47* expression is significantly decreased in obese individuals and negatively correlated with BMI, WC, and HIP in RBC<sup>163</sup>.

Conversely, in mouse models, *CD47* deficient mice show decreased weight gain on high fat diets, increased energy expenditure, improved glucose profile, and decreased inflammation<sup>164</sup>. Our lead SNP, rs670752, has a score of 6 (very little binding evidence) in RegulomeDB<sup>18</sup> and no significant eQTLs were identified in GTEx<sup>73</sup>. However, our tag SNP was identified as a significant eQTL for *BBX* in brain tissue in HaploReg<sup>21</sup>. Additionally, multiple SNPs in high LD with rs670752 provide several lines of evidence for nearby regulatory elements (e.g. active promoters, transcription factor binding motifs, strong and poised enhancers), mostly in pluripotent and embryonic cell lines, but also blood cell lines and brain tissue<sup>21,111</sup>.

**rs589428 (*EHMT2*):** A total of seventy-seven genes are found near our lead SNP, rs589428, which is intronic within *EHMT2* (Euchromatic Histone-Lysine N-Methyltransferase 2). *EHMT2* encodes a histone methyltransferase, a group of genes involved in repression of transcription through the regulation of chromatin state<sup>165</sup>. The lead SNP is 302kb downstream of *TNF*. In patients with end-stage renal disease (ESRD) on long-term hemodialysis (HD), the SNP in the promoter region of the *IL-6* and *TNF-alpha*, and *IL-10*, show a strong association with indices of comorbidity and function, and biological and nutritional markers<sup>166</sup>. *TNF-alpha* promotes bone loss and inhibits bone formation and has an important role as a mediator of skeletal damage in inflammatory arthritis<sup>167-170</sup>. *TNF* is the master regulator of other inflammatory cytokines and the major cytokine in the pathogenesis of chronic inflammatory disease<sup>171</sup>. *TNF-alpha* exerts an important influence on adipose tissue metabolism and function. It inhibits the expression of two major adipose tissue differentiation regulators: CCAAT and PPAR $\gamma$ -2<sup>172</sup>. *TNF-alpha* promoter methylation levels could be involved in the susceptibility to stroke<sup>173</sup> and correlates with increased risk of coronary artery disease<sup>174</sup>. The risk of early childhood wheeze associated with early maternal smoking may be modified by *TNF*<sup>175</sup>. The lead SNP is also 287kb upstream of *NCR3*, which is associated with pulmonary function<sup>176</sup>.

The top SNP is 17.5kb upstream of *NEU1* (Sialidase 1 (Lysosomal Sialidase)). The activity of *NEU1* is higher in epididymal fat and lower in the livers of two strains of obese and diabetic mice. Fluctuations in *NEU1* activity might be associated with the pathological status of these tissues in obesity<sup>177</sup>. The lead SNP is 50kb downstream of *HSPA1B*. Functional *HSPA1B* variants are associated with lung cancer risk and survival<sup>178</sup>. The top SNP is 65kb upstream of *CFB*. Increased concentrations of circulating binding factors fH and fB in subjects with altered glucose tolerance could reflect increased SVC-induced activation of the alternative pathway of the complement in omental adipose tissue linked to insulin resistance and metabolic disturbances<sup>179</sup>. The top SNP is 91kb upstream of *STK19*, which has been reported to be a pleiotropic gene for metabolic syndrome and inflammation and is associated with TG, BMI, WAIST, SBP and inflammatory markers including plasminogen activator inhibitor 1 (PAI-1) and white blood cell count (WBCC)<sup>180</sup>. Our top snp is 102kb upstream of *C4A*, which was identified as novel potential adipokine candidate regulator of obesity and adipose regions<sup>181</sup> between visceral and subcutaneous adipose tissue. The Top SNP is 102kb upstream of *C4B*. The carriers of C4B\*Q0 (silent allele for the C4B gene) have a substantially increased risk to suffer from myocardial infarction or stroke. Compared to controls, C4B\*Q0 carrier frequency was significantly higher at diagnosis in Icelandic smokers with angina pectoris (AP) or acute myocardial infarction (AMI) and Hungarian smokers with severe coronary artery disease, while no such difference was seen in nonsmokers. These findings indicate that C4B\*Q0 genotype can be considered as a major covariate of smoking in precipitating the risk for AMI and associated mortality<sup>182</sup>. The top SNP is 150kb upstream of *DDAH2* in which SNP rs9267551 may confer increased risk for type 2 diabetes by affecting insulin sensitivity through increased asymmetric dimethylarginine (ADMA) levels<sup>183,184</sup>.

Our top SNP is 222kb downstream of *APOM*. The PCSK9 pathway contributes to plasma apoM regulation in humans and the influence of PCSK9 on circulating apoM appears to be modified by adiposity<sup>185</sup>. In addition, APOM expression is related to FEV1/FVC (forced expiratory volume 1/ forced vital capacity) ratio and per cent emphysema<sup>186</sup>. The top SNP is 261kb downstream of *AGER/RAGE*. The lower level of soluble RAGE/AGER is associated with a number of components of metabolic syndrome (central obesity, hypertension, and hyperglycemia)<sup>187</sup>. Soluble RAGE is inversely associated with pancreatic cancer risk among Finnish male smokers<sup>188</sup>. The RAGE(2) haplotype is associated with diabetic nephropathy (DN) in type 2 diabetics and with earlier DN onset and, thus, can be regarded a marker for DN<sup>189</sup>. RAGE, via its interaction with ligands, serves as a cofactor exacerbating diabetic vascular disease<sup>190</sup>. Serum endogenous secretory RAGE (esRAGE) levels were inversely correlated with BMI and serum HDL-cholesterol<sup>191</sup>. In healthy subjects plasma levels of sRAGE were negatively correlated with BMI and waist/hip ratio supporting a possible protective role for these proteins before any evidence of diabetic or vascular complications<sup>192</sup>.

The top SNP is 263 downstream of *AIF1*. The serum AIF-1 concentrations were positively correlated with levels of fasting plasma glucose, hemoglobin A1c, triglycerides, and uric acid, and with WC and BMI, and were inversely correlated with HDL cholesterol levels<sup>193</sup>. Also, the variants in AIF1 show evidence of association with adult obesity in the Greek population<sup>194</sup>. The top SNP is 306 downstream of *LTA*. SNPs in *LTA* are associated with chronic kidney disease in Type 2 diabetes<sup>195</sup>. The variability of LT-alpha genotypes may have potential implications for individual susceptibility to asthma in atopic or in ever-smoking Chinese adults in Hong Kong<sup>196</sup>.

The genome-wide association studies have reported the associations within 1Mb of region for age at menopause ( $R^2=0.32$ )<sup>197</sup>, telomere length ( $R^2=0.22$ )<sup>198</sup>, idiopathic membranous nephropathy<sup>199</sup> ( $R^2=0.45$ ), chronic hepatitis B infection<sup>200</sup> ( $R^2= 0.45$ ) and phospholipid levels (plasma) ( $R^2=0.23$ )<sup>201</sup>. This lead SNP is associated with regulatory motifs changed at Bcl6b, NF-kappaB, Pou5f1; associated with enhancer histone

marks in stomach mucosa, HSMM cell derived skeletal muscle myotubes cell tissue; and in eQTL in various tissues including subcutaneous adipose, visceral omentum, lung and skeletal muscle tissues. The lead SNP is associated with eQTL in tibial artery and blood tissues from GTEx<sup>73</sup> analysis. The RegulomeDB<sup>18</sup> score for the lead SNP is 1f.

**rs1856293 (EYA4):** A total of nine genes are found near our lead SNP, rs1856293. The lead SNP is 342kb downstream of *RPS12*. *RPS12* is a potential target gene of microRNA-377, which has been consistently upregulated in *in vitro* diabetic nephropathy (DN) models and in *in vivo* DN mouse models<sup>202</sup>. If *RPS12* is also upregulated in the diabetic milieu, it may contribute to the progression of DN. *RPS12* has been reported to be a strong candidate for diabetic nephropathy<sup>203</sup>. In addition, in the study of E3 rats, there were significant positive correlations between TG and the expression of *RPS12* gene<sup>204</sup>. The lead SNP is 83kb upstream of *EYA4*. Serum methylation levels of *EYA4* were significant discriminants between stage I colorectal cancer and healthy controls<sup>205</sup> and high methylation of the *EYA4* gene is associated with ulcerative colitis with colorectal cancer<sup>206</sup>. The lead SNP is 446kb upstream of *VNN1*. Alternative splicing in *VNN1* is associated with colorectal cancer<sup>207</sup>. The combination of *VNN1* and *MMP9* may be used as a blood biomarker panel for the discrimination of pancreatic cancer-associated diabetes from type II diabetes<sup>208</sup>. There is no reported GWAS signal in high LD with the lead SNP. This lead SNP is associated with regulatory motifs changed at *Esr2*, *LRH1*, *Myf\_3*, *Sin3Ak-20\_disc3* and *T3R*; and associated with enhancer histone marks in ESDR, SKIN and brain tissue. The RegulomeDB<sup>18</sup> score for the lead SNP is 6.

**rs2001945 (TRIB1):** There are five protein coding genes within 500 kb+/- of our lead SNP, rs2001945, which lies 27 kb downstream from *TRIB1*. *TRIB1* (tribbles pseudokinase 1) encodes a protein involved in ATP binding and the MAPK/ERK1/2 pathway<sup>209</sup>. Very little is known about the function of the other nearby genes, including *NSMCE2* (non-SMC element 2, *MMS21* homolog), *KIAA0196* (strumpellin), *SQLE* (qualene epoxidase), and *ZNF572* (Zinc Finger Protein 572). GTEx<sup>73</sup> identified no significant eQTLs for our lead SNP; however, RegulomeDB<sup>18</sup> provided a score of 4 (minimal binding evidence [Transcription Factor binding + DNase peak]). Further, HaploReg<sup>21</sup>/UCSC Genome Browser reveal multiple lines of evidence across multiple tissues, including cis-eQTLs between rs2001945 for *TRIB1* and *NSMCE2* in brain tissue, strong DNase hypersensitivity clusters both at the association peak and across SNPs in high LD with our lead SNP, transcription factor binding motifs, and open chromatin marks primarily in Human Umbilical Vein Endothelial Cells (HUVEC). There are several nearby previously-identified GWAS signals for related cardiometabolic and digestion-related traits, including lipids (e.g. triglycerides, LDL, HDL)<sup>6,8,13,14,210-217</sup>, adiponectin<sup>218</sup>, liver enzyme levels<sup>219</sup>, gestational age<sup>5</sup>, inflammatory bowel disease<sup>134</sup>, Crohn's disease<sup>220,221</sup>, and metabolite levels<sup>222</sup>.

**rs17065323 (SMIM2):** A total of 6 genes are found within 500 kb of the lead marker, rs17065323. The SNP rs17065323, which is located 23.19 kb downstream of the long intergenic non-protein coding RNA 284 (*LINC00284*, 13q14.11), showed suggestive association with uric acid levels ( $p=8.7E-6$ ,<sup>223</sup>). Variants of the *LACC1* (laccase (multicopper oxidoreductase) domain containing 1), at 159.72 downstream of rs17065323, were genome-wide associated with Crohn's disease<sup>134,221</sup>, and a *LACC1* mutant showed evidence of association with systemic juvenile idiopathic arthritis<sup>224</sup>. In addition, GWASs have suggested associations between variants on 13q14 with response to tocilizumab in rheumatoid arthritis ( $p=2E-7$ <sup>225</sup>), antineutrophil cytoplasmic antibody-associated vasculitis ( $p=3E-6$ <sup>226</sup>), and myotrophic lateral sclerosis ( $p=4E-6$ ,<sup>227</sup>), as well as *SERP2* genotype-carbohydrate interaction influencing fasting insulin and homeostasis model assessment of insulin resistance ( $p=7E-6$  and  $p=5E-6$ , respectively<sup>228</sup>). The nearest protein-coding gene to our tag SNP is *SMIM2* (Small Integral Membrane Protein 2), located 89.5 kb upstream; however, very little is known about the function of *SMIM2*.

**rs1049281 (HLA-C):** Eighty-six genes are found within 500kb of rs1049281, which lies within the *HLA-C* gene at 6p21.3. *HLA-C* encodes an HLA class I heavy chain paralogue found in nearly all cells and important in the function of the immune system. There is strong evidence that our SNP is in a region likely to affect binding activity and gene expression in adipose tissue (RegulomeDB<sup>18</sup> score 1f). Over 100 alleles of the *HLA-C* gene have been described, and *HLA-C* has been associated with risk of various autoimmune diseases which can influence adiposity, including Type I diabetes, celiac disease, and psoriatic arthritis<sup>229,230</sup>. Our lead SNP is 314569 bp downstream of *DPCR1*, a gene associated with diffuse panbronchiolitis, a chronic inflammatory lung disease<sup>231</sup>. A variant near this gene (rs9368649), has been suggestively associated with smoking status (ever smoker) and pack years ( $P \sim 1.3E-07$ )<sup>232</sup>, but not at GWS. This SNP is not in high LD with our lead SNP ( $R^2=0.152$ ,  $D'=0.902$ ). Our lead SNP is 190789 bp upstream of *HCP5*, a lncRNA. A variant (rs12175489) near this gene was suggestively associated ( $p=2.13E-06$ ) with visceral adipose tissue (VAT) in men<sup>103</sup>, but this variant is also not in high LD with our lead SNP ( $R^2=0.022$ ,  $D'=0.478$ ). Our lead SNP is 336394bp upstream of *AIF1*, 310030bp downstream of *NCR3*, and 341847 bp upstream of *BAT2*. Three variants in this region [rs2260000 ( $R^2=0.122$ ,  $D'=0.526$ ), rs1077393 ( $R^2=0.114$ ,  $D'=0.434$ ), and rs2844479 ( $R^2=0.100$ ,  $D'=0.523$ )] have been previously associated with variation in weight<sup>233</sup>. Another variant near *NCR3* (rs2070600) has been previously associated with ever-smoking and lung function, but is not in high LD with our lead SNP ( $R^2=0.137$ ,  $D'=0.642$ )<sup>176,232</sup>. Our lead SNP is 340905bp downstream of *VARS2*, and a variant near this gene (rs7751505) has been suggestively associated with height change ( $P < 4.05 \times 10^{-6}$ ), though it is not in LD with our top SNP ( $R^2=0.054$ ,  $D'=0.569$ ). Two other variants in the region have been previously associated with extremes of height ( $p < 5E-08$ ), one of which is in strong LD with our lead SNP (rs2247056, 28923bp from rs1049281:  $R^2=0.814$ ,  $D'=1.000$ ; rs7741091:  $R^2=0.093$ ,  $D'=0.652$ )<sup>77</sup>.

### **SUPPLEMENTARY NOTE 3. Detailed summary of eQTL methods and results.**

#### **eQTL Methods**

We used two approaches to systematically explore the role of novel loci in regulating gene expression. First, to gain a general overview of the regulatory role of newly identified GWAS regions, we conducted an eQTL lookup using >50 eQTL studies<sup>234</sup>, with specific citations for >100 datasets included in the current query: 1) Blood cell related eQTL studies included fresh lymphocytes<sup>235</sup>, fresh leukocytes<sup>236</sup>, leukocyte samples in individuals with Celiac disease<sup>237</sup>, whole blood samples<sup>73,238-256</sup>, lymphoblastoid cell lines (LCL) derived from asthmatic children<sup>257,258</sup>, HapMap LCL from 3 populations<sup>259</sup>, a separate study on HapMap CEU LCL<sup>260</sup>, additional LCL population samples<sup>261-267</sup>, neutrophils<sup>268,269</sup>, CD19+ B cells<sup>270</sup>, primary PHA-stimulated T cells<sup>261,264</sup>, CD4+ T cells<sup>271</sup>, peripheral blood monocytes<sup>267,270,272-275</sup>, long non-coding RNAs in monocytes<sup>276</sup> and CD14+ monocytes before and after stimulation with LPS or interferon-gamma<sup>277</sup>, CD11+ dendritic cells before and after *Mycobacterium tuberculosis* infection<sup>278</sup> and a separate study of dendritic cells before or after stimulation with LPS, influenza or interferon-beta<sup>279</sup>. Micro-RNA QTLs<sup>280,281</sup>, DNase-I QTLs<sup>282</sup>, histone acetylation QTLs<sup>283</sup>, and ribosomal occupancy QTLs<sup>284</sup> were also queried for LCL. Splicing QTLs<sup>285</sup> and micro-RNA QTLs<sup>286</sup> were queried in whole blood. 2) Non-blood cell tissue eQTLs searched included omental and subcutaneous adipose tissues<sup>73,238,256,263,287</sup>, visceral adipose tissue<sup>256</sup>, stomach<sup>287</sup>, endometrial carcinomas<sup>288</sup>, ER+ and ER- breast cancer tumor cells<sup>289</sup>, liver<sup>256,287,290-293</sup>, osteoblasts<sup>294</sup>, intestine<sup>295</sup> and normal and cancerous colon<sup>296,297</sup>, skeletal muscle<sup>256,298</sup>, breast tissue (normal and cancer)<sup>299,300</sup>, lung<sup>73,301-304</sup>, skin<sup>73,263,267,305</sup>, primary fibroblasts<sup>261,264,306</sup>, sputum<sup>307</sup>, pancreatic islet cells<sup>308</sup>, prostate<sup>309</sup>, rectal mucosa<sup>310</sup>, arterial wall<sup>256</sup> and heart tissue from left ventricles<sup>73,311</sup> and left and right atria<sup>312</sup>. Micro-RNA QTLs were also queried for gluteal and abdominal adipose<sup>313</sup> and liver<sup>314</sup>. Methylation QTLs were queried in pancreatic islet cells<sup>315</sup>. Further mRNA and micro-RNA QTLs were queried from ER+ invasive breast cancer samples, colon-, kidney renal clear-, lung- and prostate-adenocarcinoma samples<sup>316</sup>; 2 Brain eQTL studies included brain cortex<sup>252,272,317-319</sup>, cerebellar cortex<sup>320</sup>,

cerebellum<sup>289,318,321-323</sup>, frontal cortex<sup>320,321,323</sup>, gliomas<sup>324</sup>, hippocampus<sup>320,323</sup>, inferior olivary nucleus (from medulla)<sup>320</sup>, intralobular white matter<sup>320</sup>, occipital cortex<sup>320</sup>, parietal lobe<sup>322</sup>, pons<sup>321</sup>, pre-frontal cortex<sup>289,323,325,326</sup>, putamen (at the level of anterior commissure)<sup>320</sup>, substantia nigra<sup>320</sup>, temporal cortex<sup>318,320,321,323</sup>, thalamus<sup>323</sup> and visual cortex<sup>289</sup>.

Additional eQTL data was integrated from online sources including ScanDB (<http://www.scandb.org/newinterface/about.html>), the Broad Institute GTEx<sup>73</sup> Portal, and the Pritchard Lab ([eqtl.uchicago.edu](http://eqtl.uchicago.edu)). Cerebellum, parietal lobe and liver eQTL data were downloaded from ScanDB. Cis-eQTLs were limited to those with  $P < 1.0E-6$  and trans-eQTLs with  $P < 5.0E-8$ . Results for GTEx<sup>73</sup> Analysis V4 for 13 tissues were downloaded from the GTEx<sup>73</sup> Portal and then additionally filtered as described below [[www.GTExportal.org](http://www.GTExportal.org): thyroid, leg skin (sun exposed), tibial nerve, aortic artery, tibial artery, skeletal muscle, esophagus mucosa, esophagus muscularis, lung, heart (left ventricle), stomach, whole blood, and subcutaneous adipose tissue<sup>73</sup>]. Splicing QTL (sQTL) results generated with sQTLseeker with false discovery rate  $P \leq 0.05$  were retained. For all gene-level eQTLs, if at least 1 SNP passed the tissue-specific empirical threshold in GTEx<sup>73</sup>, the best SNP for that eQTL was always retained. All gene-level eQTL SNPs with  $P < 1.67E-11$  were also retained, reflecting a global threshold correction of  $P = 0.05 / (30,000 \text{ genes} \times 1,000,000 \text{ tests})$ .

Second, since public databases with eQTL data do not have information available on current smoking status, we also conducted an eQTL association analysis using expression results derived from fasting peripheral whole blood collected. Total RNA was isolated from frozen PAXgene blood tubes (PreAnalytiX, Hombrechtikon, Switzerland) and amplified using the WT-Ovation Pico RNA Amplification System (NuGEN, San Carlos, CA) according to the manufacturers' standard operating procedures. The obtained cDNA was hybridized to the Human Exon 1.0 ST Array (Affymetrix, Inc., Santa Clara, CA). The raw data were quantile-normalized, log<sub>2</sub> transformed, followed by summarization using Robust Multi-array Average<sup>327</sup> and further adjusted for technical covariates, including the first principal component of the expression data, batch effect, and the all-probeset-mean residual. Study specific covariates in the association model included blood cell counts and cohort membership.

We evaluated all transcripts +/- 1MB around each novel variant in the Framingham Heart Study while accounting for current smoking status, using the following four approaches similar to those used in our primary analyses of our traits:

**Model 1 (adjusted main effect of eQTL):** Expression  $\sim \underline{SNP} + SMK + \text{age} + \text{age-squared} + \text{sex} + \text{study specific covariates}$

**Model 2 (main effect of eQTL stratified by smoking status):** Expression  $\sim \underline{SNP} + \text{age} + \text{age-squared} + \text{sex} + \text{study specific covariates}$

**Model 3 (Interaction effect of eQTL):** Expression  $\sim SNP + SMK + \underline{SNP*SMK} + \text{age} + \text{age-squared} + \text{sex} + \text{study specific covariates}$

**Model 4 (Joint effect of eQTL):** Expression  $\sim \underline{SNP} + SMK + \underline{SNP*SMK} + \text{age} + \text{age-squared} + \text{sex} + \text{study specific covariates}$

Significance level was evaluated by  $FDR < 5\%$  per eQTL analysis and across all loci identified for that model in the primary meta-analysis.

## eQTL Results by Trait

Only significant cis-eQTLs in high LD with our novel lead SNPs ( $r^2 > 0.9$ , calculated in the CEU+YRI+CHB+JPT 1000 Genomes reference panel), or proxy SNPs, were retained for consideration.

For BMI, three of our seven novel SNPs across six loci that had at least one variant in high LD ( $r^2 > 0.9$ ) with the tag SNP that is significantly (**Online Methods**) associated with expression of a gene transcript in the cerebellum and prefrontal cortex, or blood cell types, including *EPHA3*, *TTC14*, and *INADL*. Notably, our lead SNP, rs2481665, is a significant cis-eQTL for *INADL*, in prefrontal cortex tissue, and for *INADL* and *LITD1* in whole blood after adjusting for SMK (false discovery rate,  $FDR < 5\%$ ). For the joint main + interaction effect eQTL analysis, we identified one significant eQTL for a BMI associated variant (rs12902602) for three gene transcripts (*PSMA4*, *CHRNA5*, and *CTSH*).

For WCadjBMI, five of our 12 novel SNPs were in high LD with a cis-eQTL for gene transcripts in the cerebellum, temporal cortex, prefrontal cortex, lymphoblastoid cells, liver, lung, lymph, omental adipose, subcutaneous adipose, Primary PHA-stimulated T cells, skin, and blood cell tissues in publicly available databases. In our cis-eQTL analyses adjusting for SMK, four of our nine novel lead SNPs were significant cis-eQTLs for 14 gene transcripts in 12 genes. Additionally, for the joint main + interaction effect eQTL analysis, we identified that two variants that were associated with the expression of *SEPT2*, *FARP2*, *PASK*, and *HDLBP* (rs6743226) and *KIF1B* (rs17396340).

For WHRadjBMI, three of our six novel SNPs were in high LD with a nearby cis-eQTL for gene transcripts in subcutaneous adipose tissue and blood cell types. We identified five novel WHRadjBMI variants near significant cis-eQTLs for 49 gene transcripts after adjusting for SMK, the most significant of which was between our tag SNP rs1049281 and *MSH5*. Additionally, for the joint main and interaction effect eQTL analysis, we identified two novel WHRadjBMI variants (rs1049281, rs1856293) were associated with 19 gene transcripts.

Across all of our three obesity-related traits, the majority of significant cis-eQTLs from public databases are found in blood cell lines (63% of unique SNP-transcript associations) (**Supplementary Table 16**). However, as in previous eQTL analyses of obesity-associated variants, we identify cis-eQTLs in brain and adipose tissue. Further analyses are needed to determine if these tissue-specific eQTLs remain significant after accounting for SMK, but our de-novo analysis in whole blood samples from the Framingham Heart Study using models to account for SMK indicate that gene expression may underlie our association signals in some instances and smoking exposure may play a role in influencing these associations (**Supplementary Tables 16-18**).

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## SUPPLEMENTARY REFERENCES

1. Locke, A.E. *et al.* Genetic studies of body mass index yield new insights for obesity biology. *Nature* **518**, 197-206 (2015).
2. Shungin, D. *et al.* New genetic loci link adipose and insulin biology to body fat distribution. *Nature* **518**, 187-96 (2015).
3. Pena, J.C., Duhalt, R., Navarrette, R. & Garcia Zozaya, J.L. [Periodic hemodialysis in the treatment of chronic renal insufficiency]. *Gac Med Mex* **98**, 150-67 (1968).
4. Shin, K., Wang, Q. & Margolis, B. PATJ regulates directional migration of mammalian epithelial cells. *EMBO Rep* **8**, 158-64 (2007).
5. Comuzzie, A.G. *et al.* Novel genetic loci identified for the pathophysiology of childhood obesity in the Hispanic population. *PLoS One* **7**, e51954 (2012).
6. Kathiresan, S. *et al.* Six new loci associated with blood low-density lipoprotein cholesterol, high-density lipoprotein cholesterol or triglycerides in humans. *Nat Genet* **40**, 189-97 (2008).

7. Zhang, Z. *et al.* Association of genetic loci with blood lipids in the Chinese population. *PLoS One* **6**, e27305 (2011).
8. Waterworth, D.M. *et al.* Genetic variants influencing circulating lipid levels and risk of coronary artery disease. *Arterioscler Thromb Vasc Biol* **30**, 2264-76 (2010).
9. Murphy, M.P. & LeVine, H., 3rd. Alzheimer's disease and the amyloid-beta peptide. *J Alzheimers Dis* **19**, 311-23 (2010).
10. Lee, Y.H. *et al.* Amyloid precursor protein expression is upregulated in adipocytes in obesity. *Obesity (Silver Spring)* **16**, 1493-500 (2008).
11. Puig, K.L., Floden, A.M., Adhikari, R., Golovko, M.Y. & Combs, C.K. Amyloid precursor protein and proinflammatory changes are regulated in brain and adipose tissue in a murine model of high fat diet-induced obesity. *PLoS One* **7**, e30378 (2012).
12. Martin-Campos, J.M. *et al.* Identification of a novel mutation in the ANGPTL3 gene in two families diagnosed of familial hypobetalipoproteinemia without APOB mutation. *Clin Chim Acta* **413**, 552-5 (2012).
13. Kathiresan, S. *et al.* Common variants at 30 loci contribute to polygenic dyslipidemia. *Nat Genet* **41**, 56-65 (2009).
14. Willer, C.J. *et al.* Newly identified loci that influence lipid concentrations and risk of coronary artery disease. *Nat Genet* **40**, 161-9 (2008).
15. Wong, R.C. *et al.* L1TD1 is a marker for undifferentiated human embryonic stem cells. *PLoS One* **6**, e19355 (2011).
16. Santos, M.C. *et al.* Embryonic Stem Cell-Related Protein L1TD1 Is Required for Cell Viability, Neurosphere Formation, and Chemoresistance in Medulloblastoma. *Stem Cells Dev* **24**, 2700-8 (2015).
17. Zhu, Y., Kakinuma, N., Wang, Y. & Kiyama, R. Kank proteins: a new family of ankyrin-repeat domain-containing proteins. *Biochim Biophys Acta* **1780**, 128-33 (2008).
18. Boyle, A.P. *et al.* Annotation of functional variation in personal genomes using RegulomeDB. *Genome Res* **22**, 1790-7 (2012).
19. de la Rocha, A.M., Sampron, N., Alonso, M.M. & Matheu, A. Role of SOX family of transcription factors in central nervous system tumors. *Am J Cancer Res* **4**, 312-24 (2014).
20. Hempel, A. *et al.* Deletions and de novo mutations of SOX11 are associated with a neurodevelopmental disorder with features of Coffin-Siris syndrome. *J Med Genet* **53**, 152-62 (2016).
21. Ward, L.D. & Kellis, M. HaploReg: a resource for exploring chromatin states, conservation, and regulatory motif alterations within sets of genetically linked variants. *Nucleic Acids Res* **40**, D930-4 (2012).
22. Zhuang, G. *et al.* Effects of cancer-associated EPHA3 mutations on lung cancer. *J Natl Cancer Inst* **104**, 1182-97 (2012).
23. Wood, L.D. *et al.* Somatic mutations of GUCY2F, EPHA3, and NTRK3 in human cancers. *Hum Mutat* **27**, 1060-1 (2006).
24. Lisabeth, E.M., Fernandez, C. & Pasquale, E.B. Cancer somatic mutations disrupt functions of the EphA3 receptor tyrosine kinase through multiple mechanisms. *Biochemistry* **51**, 1464-75 (2012).
25. Lee, D.J. *et al.* Multiple tumor-suppressor genes on chromosome 3p contribute to head and neck squamous cell carcinoma tumorigenesis. *Cancer Biol Ther* **10**, 689-93 (2010).
26. Lahtela, J. *et al.* A high-content cellular senescence screen identifies candidate tumor suppressors, including EPHA3. *Cell Cycle* **12**, 625-34 (2013).
27. Davis, S.D. *et al.* Clinical features of childhood primary ciliary dyskinesia by genotype and ultrastructural phenotype. *Am J Respir Crit Care Med* **191**, 316-24 (2015).

28. Oldenburg, A.R., Delbarre, E., Thiede, B., Vigouroux, C. & Collas, P. Deregulation of Fragile X-related protein 1 by the lipodystrophic lamin A p.R482W mutation elicits a myogenic gene expression program in preadipocytes. *Hum Mol Genet* **23**, 1151-62 (2014).
29. Sparkes, R., Patton, D. & Bernier, F. Cardiac features of a novel autosomal recessive dilated cardiomyopathic syndrome due to defective importation of mitochondrial protein. *Cardiol Young* **17**, 215-7 (2007).
30. Ojala, T. *et al.* New mutation of mitochondrial DNAJC19 causing dilated and noncompaction cardiomyopathy, anemia, ataxia, and male genital anomalies. *Pediatr Res* **72**, 432-7 (2012).
31. Davey, K.M. *et al.* Mutation of DNAJC19, a human homologue of yeast inner mitochondrial membrane co-chaperones, causes DCMA syndrome, a novel autosomal recessive Barth syndrome-like condition. *J Med Genet* **43**, 385-93 (2006).
32. Richter-Dennerlein, R. *et al.* DNAJC19, a mitochondrial cochaperone associated with cardiomyopathy, forms a complex with prohibitins to regulate cardiolipin remodeling. *Cell Metab* **20**, 158-71 (2014).
33. Perez-Lorenzo, R. *et al.* A tumor suppressor function for the lipid phosphatase INPP4B in melanocytic neoplasms. *J Invest Dermatol* **134**, 1359-68 (2014).
34. Fedele, C.G. *et al.* Inositol polyphosphate 4-phosphatase II regulates PI3K/Akt signaling and is lost in human basal-like breast cancers. *Proc Natl Acad Sci U S A* **107**, 22231-6 (2010).
35. Lopez, S.M. *et al.* Determinants of the tumor suppressor INPP4B protein and lipid phosphatase activities. *Biochem Biophys Res Commun* **440**, 277-82 (2013).
36. Mian, M.F., Pek, E.A., Mossman, K.L., Stampfli, M.R. & Ashkar, A.A. Exposure to cigarette smoke suppresses IL-15 generation and its regulatory NK cell functions in poly I:C-augmented human PBMCs. *Mol Immunol* **46**, 3108-16 (2009).
37. Liu, Y.Z. *et al.* Genome-wide association analyses suggested a novel mechanism for smoking behavior regulated by IL15. *Mol Psychiatry* **14**, 668-80 (2009).
38. Thorgeirsson, T.E. *et al.* Sequence variants at CHRN3-CHRNA6 and CYP2A6 affect smoking behavior. *Nat Genet* **42**, 448-53 (2010).
39. Saccone, N.L. *et al.* Multiple independent loci at chromosome 15q25.1 affect smoking quantity: a meta-analysis and comparison with lung cancer and COPD. *PLoS Genet* **6**(2010).
40. Hancock, D.B. *et al.* Genome-wide meta-analysis reveals common splice site acceptor variant in CHRNA4 associated with nicotine dependence. *Transl Psychiatry* **5**, e651 (2015).
41. Thorgeirsson, T.E. *et al.* A variant associated with nicotine dependence, lung cancer and peripheral arterial disease. *Nature* **452**, 638-42 (2008).
42. Chen, L.S. *et al.* CHRNA5 risk variant predicts delayed smoking cessation and earlier lung cancer diagnosis--a meta-analysis. *J Natl Cancer Inst* **107**(2015).
43. Hallden, S. *et al.* Gene variance in the nicotinic receptor cluster (CHRNA5-CHRNA3-CHRN4) predicts death from cardiopulmonary disease and cancer in smokers. *J Intern Med* (2015).
44. Tyrrell, J. *et al.* Genetic variation in the 15q25 nicotinic acetylcholine receptor gene cluster (CHRNA5-CHRNA3-CHRN4) interacts with maternal self-reported smoking status during pregnancy to influence birth weight. *Hum Mol Genet* **21**, 5344-58 (2012).
45. Winslow, U.C., Rode, L. & Nordestgaard, B.G. High tobacco consumption lowers body weight: a Mendelian randomization study of the Copenhagen General Population Study. *Int J Epidemiol* **44**, 540-50 (2015).
46. Taylor, A.E. *et al.* Stratification by smoking status reveals an association of CHRNA5-A3-B4 genotype with body mass index in never smokers. *PLoS Genet* **10**, e1004799 (2014).
47. Morel, C. *et al.* Nicotine consumption is regulated by a human polymorphism in dopamine neurons. *Mol Psychiatry* **19**, 930-6 (2014).

48. Antolin-Fontes, B., Ables, J.L., Gorlich, A. & Ibanez-Tallon, I. The habenulo-interpeduncular pathway in nicotine aversion and withdrawal. *Neuropharmacology* **96**, 213-22 (2015).
49. van Setten, J. *et al.* Genome-wide association study of coronary and aortic calcification implicates risk loci for coronary artery disease and myocardial infarction. *Atherosclerosis* **228**, 400-5 (2013).
50. Schunkert, H. *et al.* Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. *Nat Genet* **43**, 333-8 (2011).
51. Reilly, M.P. *et al.* Identification of ADAMTS7 as a novel locus for coronary atherosclerosis and association of ABO with myocardial infarction in the presence of coronary atherosclerosis: two genome-wide association studies. *Lancet* **377**, 383-92 (2011).
52. Dichgans, M. *et al.* Shared genetic susceptibility to ischemic stroke and coronary artery disease: a genome-wide analysis of common variants. *Stroke* **45**, 24-36 (2014).
53. Wang, Z.C. *et al.* Genetic polymorphism of the kinesin-like protein KIF1B gene and the risk of hepatocellular carcinoma. *PLoS One* **8**, e62571 (2013).
54. Sukhatme, V.P. & Chan, B. Glycolytic cancer cells lacking 6-phosphogluconate dehydrogenase metabolize glucose to induce senescence. *FEBS Lett* **586**, 2389-95 (2012).
55. Ahn, J. *et al.* Identification of the avian RBP7 gene as a new adipose-specific gene and RBP7 promoter-driven GFP expression in adipose tissue of transgenic quail. *PLoS One* **10**, e0124768 (2015).
56. Borcharding, D.C. *et al.* Dopamine receptors in human adipocytes: expression and functions. *PLoS One* **6**, e25537 (2011).
57. Gieger, C. *et al.* New gene functions in megakaryopoiesis and platelet formation. *Nature* **480**, 201-8 (2011).
58. Nogueira, E. *et al.* SOK1 translocates from the Golgi to the nucleus upon chemical anoxia and induces apoptotic cell death. *J Biol Chem* **283**, 16248-58 (2008).
59. Davids, M.S. *et al.* STK25 is a candidate gene for pseudopseudohypoparathyroidism. *Genomics* **77**, 2-4 (2001).
60. Nerstedt, A. *et al.* Serine/threonine protein kinase 25 (STK25): a novel negative regulator of lipid and glucose metabolism in rodent and human skeletal muscle. *Diabetologia* **55**, 1797-807 (2012).
61. Cansby, E. *et al.* Increased expression of STK25 leads to impaired glucose utilization and insulin sensitivity in mice challenged with a high-fat diet. *FASEB J* **27**, 3660-71 (2013).
62. Semplici, F. *et al.* Human mutation within Per-Arnt-Sim (PAS) domain-containing protein kinase (PASK) causes basal insulin hypersecretion. *J Biol Chem* **286**, 44005-14 (2011).
63. Grose, J.H. & Rutter, J. The role of PAS kinase in PASSing the glucose signal. *Sensors (Basel)* **10**, 5668-82 (2010).
64. da Silva Xavier, G., Rutter, J. & Rutter, G.A. Involvement of Per-Arnt-Sim (PAS) kinase in the stimulation of preproinsulin and pancreatic duodenum homeobox 1 gene expression by glucose. *Proc Natl Acad Sci U S A* **101**, 8319-24 (2004).
65. Su, Z., Cox, A., Shen, Y., Stylianou, I.M. & Paigen, B. Farp2 and Stk25 are candidate genes for the HDL cholesterol locus on mouse chromosome 1. *Arterioscler Thromb Vasc Biol* **29**, 107-13 (2009).
66. Li, B.Z. *et al.* [Abnormal expression of bcl-10 protein in extranodal marginal zone B cell lymphoma of mucosa-associated lymphoid tissue lymphoma type]. *Zhonghua Bing Li Xue Za Zhi* **36**, 819-24 (2007).
67. Namekata, K. *et al.* Dock3 regulates BDNF-TrkB signaling for neurite outgrowth by forming a ternary complex with Elmo and RhoG. *Genes Cells* **17**, 688-97 (2012).
68. Liu, H., Tang, X. & Gong, L. Mesencephalic astrocyte-derived neurotrophic factor and cerebral dopamine neurotrophic factor: New endoplasmic reticulum stress response proteins. *Eur J Pharmacol* **750**, 118-22 (2015).

69. Padilla, J. *et al.* Transcriptome-wide RNA sequencing analysis of rat skeletal muscle feed arteries. II. Impact of exercise training in obesity. *J Appl Physiol (1985)* **116**, 1033-47 (2014).
70. Wood, A.R. *et al.* Defining the role of common variation in the genomic and biological architecture of adult human height. *Nat Genet* **46**, 1173-86 (2014).
71. Lango Allen, H. *et al.* Hundreds of variants clustered in genomic loci and biological pathways affect human height. *Nature* **467**, 832-8 (2010).
72. Song, F. *et al.* Identification of a melanoma susceptibility locus and somatic mutation in TET2. *Carcinogenesis* **35**, 2097-101 (2014).
73. Consortium, G.T. The Genotype-Tissue Expression (GTEx) project. *Nat Genet* **45**, 580-5 (2013).
74. Sabater-Lleal, M. *et al.* Multiethnic meta-analysis of genome-wide association studies in >100 000 subjects identifies 23 fibrinogen-associated Loci but no strong evidence of a causal association between circulating fibrinogen and cardiovascular disease. *Circulation* **128**, 1310-24 (2013).
75. Kettunen, J. *et al.* Genome-wide association study identifies multiple loci influencing human serum metabolite levels. *Nat Genet* **44**, 269-76 (2012).
76. Inouye, M. *et al.* Novel Loci for metabolic networks and multi-tissue expression studies reveal genes for atherosclerosis. *PLoS Genet* **8**, e1002907 (2012).
77. Berndt, S.I. *et al.* Genome-wide meta-analysis identifies 11 new loci for anthropometric traits and provides insights into genetic architecture. *Nat Genet* **45**, 501-12 (2013).
78. Weedon, M.N. *et al.* Genome-wide association analysis identifies 20 loci that influence adult height. *Nat Genet* **40**, 575-83 (2008).
79. Soranzo, N. *et al.* Meta-analysis of genome-wide scans for human adult stature identifies novel Loci and associations with measures of skeletal frame size. *PLoS Genet* **5**, e1000445 (2009).
80. Lettre, G. *et al.* Identification of ten loci associated with height highlights new biological pathways in human growth. *Nat Genet* **40**, 584-91 (2008).
81. Gudbjartsson, D.F. *et al.* Many sequence variants affecting diversity of adult human height. *Nat Genet* **40**, 609-15 (2008).
82. Reiner, A.P. *et al.* Genome-wide association study of white blood cell count in 16,388 African Americans: the continental origins and genetic epidemiology network (COGENT). *PLoS Genet* **7**, e1002108 (2011).
83. Okada, Y. *et al.* Genetics of rheumatoid arthritis contributes to biology and drug discovery. *Nature* **506**, 376-81 (2014).
84. Raychaudhuri, S. *et al.* Common variants at CD40 and other loci confer risk of rheumatoid arthritis. *Nat Genet* **40**, 1216-23 (2008).
85. Albers, H.M. *et al.* Genetic variation in VTCN1 (B7-H4) is associated with course of disease in juvenile idiopathic arthritis. *Ann Rheum Dis* **73**, 1198-201 (2014).
86. Markula-Patjas, K.P. *et al.* High adiposity and serum leptin accompanied by altered bone turnover markers in severe juvenile idiopathic arthritis. *J Rheumatol* **41**, 2474-81 (2014).
87. Kim da, S., Lee, S.Y., Lee, J.H., Bae, Y.C. & Jung, J.S. MicroRNA-103a-3p controls proliferation and osteogenic differentiation of human adipose tissue-derived stromal cells. *Exp Mol Med* **47**, e172 (2015).
88. Sedlmeier, E.M. *et al.* Human placental transcriptome shows sexually dimorphic gene expression and responsiveness to maternal dietary n-3 long-chain polyunsaturated fatty acid intervention during pregnancy. *BMC Genomics* **15**, 941 (2014).
89. Gamazon, E.R. *et al.* SCAN: SNP and copy number annotation. *Bioinformatics* **26**, 259-62 (2010).
90. Li, M., Campbell, S. & McDermott, R. gamma-Glutamyltransferase, obesity, physical activity, and the metabolic syndrome in indigenous Australian adults. *Obesity (Silver Spring)* **17**, 809-13 (2009).



91. Iwasaki, T. *et al.* Hepatic fat content-independent association of the serum level of gamma-glutamyltransferase with visceral adiposity, but not subcutaneous adiposity. *Diabetes Res Clin Pract* **79**, e13-4 (2008).
92. Lee, D.S. *et al.* Gamma glutamyl transferase and metabolic syndrome, cardiovascular disease, and mortality risk: the Framingham Heart Study. *Arterioscler Thromb Vasc Biol* **27**, 127-33 (2007).
93. Atar, A.I. *et al.* Association between gamma-glutamyltransferase and coronary artery calcification. *Int J Cardiol* **167**, 1264-7 (2013).
94. Bradley, R.D. *et al.* Associations between gamma-glutamyltransferase (GGT) and biomarkers of atherosclerosis: the Multi-ethnic Study of Atherosclerosis (MESA). *Atherosclerosis* **233**, 387-93 (2014).
95. Zhu, C. *et al.* Association of serum gamma-glutamyltransferase with arterial stiffness in established coronary artery disease. *Angiology* **64**, 15-20 (2013).
96. Park, J.S. *et al.* Association between gamma-glutamyltransferase, adiponectin and arterial stiffness. *J Atheroscler Thromb* **19**, 90-7 (2012).
97. Volodarsky, M. *et al.* A deletion mutation in TMEM38B associated with autosomal recessive osteogenesis imperfecta. *Hum Mutat* **34**, 582-6 (2013).
98. Shaheen, R. *et al.* Study of autosomal recessive osteogenesis imperfecta in Arabia reveals a novel locus defined by TMEM38B mutation. *J Med Genet* **49**, 630-5 (2012).
99. Rubinato, E. *et al.* A novel deletion mutation involving TMEM38B in a patient with autosomal recessive osteogenesis imperfecta. *Gene* **545**, 290-2 (2014).
100. Perry, J.R. *et al.* Meta-analysis of genome-wide association data identifies two loci influencing age at menarche. *Nat Genet* **41**, 648-50 (2009).
101. Perry, J.R. *et al.* Parent-of-origin-specific allelic associations among 106 genomic loci for age at menarche. *Nature* **514**, 92-7 (2014).
102. Elks, C.E. *et al.* Thirty new loci for age at menarche identified by a meta-analysis of genome-wide association studies. *Nat Genet* **42**, 1077-85 (2010).
103. Fox, C.S. *et al.* Genome-wide association for abdominal subcutaneous and visceral adipose reveals a novel locus for visceral fat in women. *PLoS Genet* **8**, e1002695 (2012).
104. Melzer, D. *et al.* A genome-wide association study identifies protein quantitative trait loci (pQTLs). *PLoS Genet* **4**, e1000072 (2008).
105. Ismail, S., Schaffer, A.E., Rosti, R.O., Gleeson, J.G. & Zaki, M.S. Novel mutation in the fukutin gene in an Egyptian family with Fukuyama congenital muscular dystrophy and microcephaly. *Gene* **539**, 279-82 (2014).
106. Costa, C. *et al.* A Portuguese case of Fukuyama congenital muscular dystrophy caused by a multi-exonic duplication in the fukutin gene. *Neuromuscul Disord* **23**, 557-61 (2013).
107. Welch, H.C. *et al.* P-Rex1, a PtdIns(3,4,5)P<sub>3</sub>- and Gbetagamma-regulated guanine-nucleotide exchange factor for Rac. *Cell* **108**, 809-21 (2002).
108. Kimura, S., Sato, K., Banno, Y., Nagase, T. & Ueda, H. The importance of interaction with membrane lipids through the pleckstrin homology domain of the guanine nucleotide exchange factor for rho family small guanosine triphosphatase, FLJ00018. *Biol Pharm Bull* **36**, 1204-7 (2013).
109. Damoulakis, G. *et al.* P-Rex1 directly activates RhoG to regulate GPCR-driven Rac signalling and actin polarity in neutrophils. *J Cell Sci* **127**, 2589-600 (2014).
110. Xue, R. *et al.* Clonal analyses and gene profiling identify genetic biomarkers of the thermogenic potential of human brown and white preadipocytes. *Nat Med* **21**, 760-8 (2015).
111. Kuhn, R.M., Haussler, D. & Kent, W.J. The UCSC genome browser and associated tools. *Brief Bioinform* **14**, 144-61 (2013).
112. Mick, E. *et al.* Genome-wide association study of proneness to anger. *PLoS One* **9**, e87257 (2014).

113. Micu, I. *et al.* NMDA receptors mediate calcium accumulation in myelin during chemical ischaemia. *Nature* **439**, 988-92 (2006).
114. Zhong, H.J. *et al.* Functional polymorphisms of the glutamate receptor N-methyl D-aspartate 2A gene are associated with heroin addiction. *Genet Mol Res* **13**, 8714-21 (2014).
115. Turner, S.J. *et al.* GRIN2A: an aptly named gene for speech dysfunction. *Neurology* **84**, 586-93 (2015).
116. Liu, R. *et al.* Correlation of functional GRIN2A gene promoter polymorphisms with schizophrenia and serum D-serine levels. *Gene* **568**, 25-30 (2015).
117. Leuba, G. *et al.* Pathological reorganization of NMDA receptors subunits and postsynaptic protein PSD-95 distribution in Alzheimer's disease. *Curr Alzheimer Res* **11**, 86-96 (2014).
118. Lemke, J.R. *et al.* Mutations in GRIN2A cause idiopathic focal epilepsy with rolandic spikes. *Nat Genet* **45**, 1067-72 (2013).
119. DeVries, S.P. & Patel, A.D. Two patients with a GRIN2A mutation and childhood-onset epilepsy. *Pediatr Neurol* **49**, 482-5 (2013).
120. Carvill, G.L. *et al.* GRIN2A mutations cause epilepsy-aphasia spectrum disorders. *Nat Genet* **45**, 1073-6 (2013).
121. Aouizerat, B.E. *et al.* GWAS for discovery and replication of genetic loci associated with sudden cardiac arrest in patients with coronary artery disease. *BMC Cardiovasc Disord* **11**, 29 (2011).
122. McGue, M. *et al.* A genome-wide association study of behavioral disinhibition. *Behav Genet* **43**, 363-73 (2013).
123. Greliche, N. *et al.* A genome-wide search for common SNP x SNP interactions on the risk of venous thrombosis. *BMC Med Genet* **14**, 36 (2013).
124. Volkmer, E. & Karnitz, L.M. Human homologs of *Schizosaccharomyces pombe* rad1, hus1, and rad9 form a DNA damage-responsive protein complex. *J Biol Chem* **274**, 567-70 (1999).
125. Marathi, U.K. *et al.* RAD1, a human structural homolog of the *Schizosaccharomyces pombe* RAD1 cell cycle checkpoint gene. *Genomics* **54**, 344-7 (1998).
126. Chaudhuri, S.P. *et al.* Activation of S phase checkpoint by cigarette smoke extract in *Schizosaccharomyces pombe*. *Yeast* **22**, 1223-38 (2005).
127. Suhre, K. *et al.* A genome-wide association study of metabolic traits in human urine. *Nat Genet* **43**, 565-9 (2011).
128. Seppala, I. *et al.* Genome-wide association study on dimethylarginines reveals novel AGXT2 variants associated with heart rate variability but not with overall mortality. *Eur Heart J* **35**, 524-31 (2014).
129. Rueedi, R. *et al.* Genome-wide association study of metabolic traits reveals novel gene-metabolite-disease links. *PLoS Genet* **10**, e1004132 (2014).
130. Nicholson, G. *et al.* A genome-wide metabolic QTL analysis in Europeans implicates two loci shaped by recent positive selection. *PLoS Genet* **7**, e1002270 (2011).
131. Arnett, D.K. *et al.* Genome-wide association study identifies single-nucleotide polymorphism in KCNB1 associated with left ventricular mass in humans: the HyperGEN Study. *BMC Med Genet* **10**, 43 (2009).
132. Warnatz, H.J. *et al.* The BTB and CNC homology 1 (BACH1) target genes are involved in the oxidative stress response and in control of the cell cycle. *J Biol Chem* **286**, 23521-32 (2011).
133. Kim, J. *et al.* Functional genomic screen for modulators of ciliogenesis and cilium length. *Nature* **464**, 1048-51 (2010).
134. Jostins, L. *et al.* Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. *Nature* **491**, 119-24 (2012).
135. Linden, R. *et al.* Physiology of the prion protein. *Physiol Rev* **88**, 673-728 (2008).

136. Vanik, D.L. & Surewicz, W.K. Disease-associated F198S mutation increases the propensity of the recombinant prion protein for conformational conversion to scrapie-like form. *J Biol Chem* **277**, 49065-70 (2002).
137. Steele, A.D., Emsley, J.G., Ozdinler, P.H., Lindquist, S. & Macklis, J.D. Prion protein (PrP<sup>c</sup>) positively regulates neural precursor proliferation during developmental and adult mammalian neurogenesis. *Proc Natl Acad Sci U S A* **103**, 3416-21 (2006).
138. Mouillet-Richard, S. *et al.* Signal transduction through prion protein. *Science* **289**, 1925-8 (2000).
139. Telling, G.C. *et al.* Evidence for the conformation of the pathologic isoform of the prion protein enciphering and propagating prion diversity. *Science* **274**, 2079-82 (1996).
140. Poulter, M. *et al.* Inherited prion disease with 144 base pair gene insertion. 1. Genealogical and molecular studies. *Brain* **115 ( Pt 3)**, 675-85 (1992).
141. Moore, R.C. *et al.* Huntington disease phenocopy is a familial prion disease. *Am J Hum Genet* **69**, 1385-8 (2001).
142. Mead, S. *et al.* A novel protective prion protein variant that colocalizes with kuru exposure. *N Engl J Med* **361**, 2056-65 (2009).
143. Haik, S. *et al.* Striking PrP<sup>Sc</sup> heterogeneity in inherited prion diseases with the D178N mutation. *Ann Neurol* **56**, 909-10; author reply 910-1 (2004).
144. Collinge, J. *et al.* Diagnosis of Gerstmann-Straussler syndrome in familial dementia with prion protein gene analysis. *Lancet* **2**, 15-7 (1989).
145. Basset-Leobon, C. *et al.* Familial Creutzfeldt-Jakob disease with an R208H-129V haplotype and Kuru plaques. *Arch Neurol* **63**, 449-52 (2006).
146. Redecke, L. *et al.* Structural characterization of beta-sheeted oligomers formed on the pathway of oxidative prion protein aggregation in vitro. *J Struct Biol* **157**, 308-20 (2007).
147. United States. Public Health Service. Office of the Surgeon General. *How tobacco smoke causes disease : the biology and behavioral basis for smoking-attributable disease : a report of the Surgeon General*, xv, 704 p (U.S. Dept. of Health and Human Services, Public Health Service, Rockville, MD; Washington, DC, 2010).
148. Bernhard, D., Rossmann, A. & Wick, G. Metals in cigarette smoke. *IUBMB Life* **57**, 805-9 (2005).
149. Moore, R.C. *et al.* Ataxia in prion protein (PrP)-deficient mice is associated with upregulation of the novel PrP-like protein doppel. *J Mol Biol* **292**, 797-817 (1999).
150. Croes, E.A. *et al.* Polymorphisms in the prion protein gene and in the doppel gene increase susceptibility for Creutzfeldt-Jakob disease. *Eur J Hum Genet* **12**, 389-94 (2004).
151. Schroder, B. *et al.* Polymorphisms within the prion-like protein gene (Prnd) and their implications in human prion diseases, Alzheimer's disease and other neurological disorders. *Hum Genet* **109**, 319-25 (2001).
152. Savini, I., Rossi, A., Pierro, C., Avigliano, L. & Catani, M.V. SVCT1 and SVCT2: key proteins for vitamin C uptake. *Amino Acids* **34**, 347-55 (2008).
153. Catania, A.S., Barros, C.R. & Ferreira, S.R. [Vitamins and minerals with antioxidant properties and cardiometabolic risk: controversies and perspectives]. *Arq Bras Endocrinol Metabol* **53**, 550-9 (2009).
154. Babaev, V.R. *et al.* Combined vitamin C and vitamin E deficiency worsens early atherosclerosis in apolipoprotein E-deficient mice. *Arterioscler Thromb Vasc Biol* **30**, 1751-7 (2010).
155. Hediger, M.A. New view at C. *Nat Med* **8**, 445-6 (2002).
156. Uhl, G.R., Drgon, T., Li, C.Y., Johnson, C. & Liu, Q.R. Smoking and smoking cessation in disadvantaged women: assessing genetic contributions. *Drug Alcohol Depend* **104 Suppl 1**, S58-63 (2009).

157. Rose, J.E., Behm, F.M., Drgon, T., Johnson, C. & Uhl, G.R. Personalized smoking cessation: interactions between nicotine dose, dependence and quit-success genotype score. *Mol Med* **16**, 247-53 (2010).
158. Zhao, L., Bracken, M.B. & DeWan, A.T. Genome-wide association study of pre-eclampsia detects novel maternal single nucleotide polymorphisms and copy-number variants in subsets of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study cohort. *Ann Hum Genet* **77**, 277-87 (2013).
159. Caporaso, N. *et al.* Genome-wide and candidate gene association study of cigarette smoking behaviors. *PLoS One* **4**, e4653 (2009).
160. Oldenborg, P.A. *et al.* Role of CD47 as a marker of self on red blood cells. *Science* **288**, 2051-4 (2000).
161. Lindberg, F.P. *et al.* Decreased resistance to bacterial infection and granulocyte defects in IAP-deficient mice. *Science* **274**, 795-8 (1996).
162. Finley, M.J., Clark, K.A., Alferiev, I.S., Levy, R.J. & Stachelek, S.J. Intracellular signaling mechanisms associated with CD47 modified surfaces. *Biomaterials* **34**, 8640-9 (2013).
163. Wiewiora, M., Piecuch, J., Sedek, L., Mazur, B. & Sosada, K. The effects of obesity on CD47 expression in erythrocytes. *Cytometry B Clin Cytom* (2015).
164. Maimaitiyiming, H., Norman, H., Zhou, Q. & Wang, S. CD47 deficiency protects mice from diet-induced obesity and improves whole body glucose tolerance and insulin sensitivity. *Sci Rep* **5**, 8846 (2015).
165. Mozzetta, C., Pontis, J. & Ait-Si-Ali, S. Functional Crosstalk Between Lysine Methyltransferases on Histone Substrates: The Case of G9A/GLP and Polycomb Repressive Complex 2. *Antioxid Redox Signal* **22**, 1365-81 (2015).
166. Balakrishnan, V.S. *et al.* Cytokine gene polymorphisms in hemodialysis patients: association with comorbidity, functionality, and serum albumin. *Kidney Int* **65**, 1449-60 (2004).
167. Simmonds, R.E. & Foxwell, B.M. Signalling, inflammation and arthritis: NF-kappaB and its relevance to arthritis and inflammation. *Rheumatology (Oxford)* **47**, 584-90 (2008).
168. Nanes, M.S. Tumor necrosis factor-alpha: molecular and cellular mechanisms in skeletal pathology. *Gene* **321**, 1-15 (2003).
169. Boyce, B.F., Schwarz, E.M. & Xing, L. Osteoclast precursors: cytokine-stimulated immunomodulators of inflammatory bone disease. *Curr Opin Rheumatol* **18**, 427-32 (2006).
170. Lu, X. *et al.* Identification of the homeobox protein Prx1 (MHox, Prrx-1) as a regulator of osterix expression and mediator of tumor necrosis factor alpha action in osteoblast differentiation. *J Bone Miner Res* **26**, 209-19 (2011).
171. Clark, I.A. How TNF was recognized as a key mechanism of disease. *Cytokine Growth Factor Rev* **18**, 335-43 (2007).
172. Popko, K. *et al.* Proinflammatory cytokines Il-6 and TNF-alpha and the development of inflammation in obese subjects. *Eur J Med Res* **15 Suppl 2**, 120-2 (2010).
173. Gomez-Uriz, A.M. *et al.* Epigenetic patterns of two gene promoters (TNF-alpha and PON) in stroke considering obesity condition and dietary intake. *J Physiol Biochem* **70**, 603-14 (2014).
174. Elahi, M.M., Gilmour, A., Matata, B.M. & Mastana, S.S. A variant of position -308 of the Tumour necrosis factor alpha gene promoter and the risk of coronary heart disease. *Heart Lung Circ* **17**, 14-8 (2008).
175. Panasevich, S. *et al.* Interaction between early maternal smoking and variants in TNF and GSTP1 in childhood wheezing. *Clin Exp Allergy* **40**, 458-67 (2010).
176. Soler Artigas, M. *et al.* Genome-wide association and large-scale follow up identifies 16 new loci influencing lung function. *Nat Genet* **43**, 1082-90 (2011).

177. Natori, Y., Ohkura, N., Nasui, M., Atsumi, G. & Kihara-Negishi, F. Acidic sialidase activity is aberrant in obese and diabetic mice. *Biol Pharm Bull* **36**, 1027-31 (2013).
178. Guo, H. *et al.* Variations in HSPA1B at 6p21.3 are associated with lung cancer risk and prognosis in Chinese populations. *Cancer Res* **71**, 7576-86 (2011).
179. Moreno-Navarrete, J.M. *et al.* Complement factor H is expressed in adipose tissue in association with insulin resistance. *Diabetes* **59**, 200-9 (2010).
180. Kraja, A.T. *et al.* Pleiotropic genes for metabolic syndrome and inflammation. *Mol Genet Metab* **112**, 317-38 (2014).
181. Dahlman, I. *et al.* Functional annotation of the human fat cell secretome. *Arch Physiol Biochem* **118**, 84-91 (2012).
182. Arason, G.J. *et al.* Smoking and a complement gene polymorphism interact in promoting cardiovascular disease morbidity and mortality. *Clin Exp Immunol* **149**, 132-8 (2007).
183. Sesti, G. *et al.* A functional variant of the dimethylarginine dimethylaminohydrolase-2 gene is associated with chronic kidney disease. *Atherosclerosis* **231**, 141-4 (2013).
184. Andreozzi, F. *et al.* A functional variant of the dimethylarginine dimethylaminohydrolase-2 gene is associated with insulin sensitivity. *PLoS One* **7**, e36224 (2012).
185. Kappelle, P.J., Lambert, G., Dahlback, B., Nielsen, L.B. & Dullaart, R.P. Relationship of plasma apolipoprotein M with proprotein convertase subtilisin-kexin type 9 levels in non-diabetic subjects. *Atherosclerosis* **214**, 492-4 (2011).
186. Burkart, K.M. *et al.* APOM and high-density lipoprotein cholesterol are associated with lung function and per cent emphysema. *Eur Respir J* **43**, 1003-17 (2014).
187. Hudson, B.I. *et al.* Serum levels of soluble receptor for advanced glycation end-products and metabolic syndrome: the Northern Manhattan Study. *Metabolism* **63**, 1125-30 (2014).
188. Jiao, L. *et al.* Evidence that serum levels of the soluble receptor for advanced glycation end products are inversely associated with pancreatic cancer risk: a prospective study. *Cancer Res* **71**, 3582-9 (2011).
189. Kankova, K., Stejskalova, A., Hertlova, M. & Znojil, V. Haplotype analysis of the RAGE gene: identification of a haplotype marker for diabetic nephropathy in type 2 diabetes mellitus. *Nephrol Dial Transplant* **20**, 1093-102 (2005).
190. Nawroth, P., Bierhaus, A., Marrero, M., Yamamoto, H. & Stern, D.M. Atherosclerosis and restenosis: is there a role for RAGE? *Curr Diab Rep* **5**, 11-6 (2005).
191. Gohda, T. *et al.* Increased serum endogenous secretory receptor for advanced glycation end-product (esRAGE) levels in type 2 diabetic patients with decreased renal function. *Diabetes Res Clin Pract* **81**, 196-201 (2008).
192. Norata, G.D. *et al.* Circulating soluble receptor for advanced glycation end products is inversely associated with body mass index and waist/hip ratio in the general population. *Nutr Metab Cardiovasc Dis* **19**, 129-34 (2009).
193. Fukui, M. *et al.* The serum concentration of allograft inflammatory factor-1 is correlated with metabolic parameters in healthy subjects. *Metabolism* **61**, 1021-5 (2012).
194. Rouskas, K. *et al.* Common variants in FTO, MC4R, TMEM18, PRL, AIF1, and PCSK1 show evidence of association with adult obesity in the Greek population. *Obesity (Silver Spring)* **20**, 389-95 (2012).
195. Wang, Y. *et al.* Predictive role of multilocus genetic polymorphisms in cardiovascular disease and inflammation-related genes on chronic kidney disease in Type 2 diabetes--an 8-year prospective cohort analysis of 1163 patients. *Nephrol Dial Transplant* **27**, 190-6 (2012).
196. Mak, J.C. *et al.* Polymorphisms in the IL-4, IL-4 receptor alpha chain, TNF-alpha, and lymphotoxin-alpha genes and risk of asthma in Hong Kong Chinese adults. *Int Arch Allergy Immunol* **144**, 114-22 (2007).

197. Stolk, L. *et al.* Loci at chromosomes 13, 19 and 20 influence age at natural menopause. *Nat Genet* **41**, 645-7 (2009).
198. Levy, D. *et al.* Genome-wide association identifies OBFC1 as a locus involved in human leukocyte telomere biology. *Proc Natl Acad Sci U S A* **107**, 9293-8 (2010).
199. Stanescu, H.C. *et al.* Risk HLA-DQA1 and PLA(2)R1 alleles in idiopathic membranous nephropathy. *N Engl J Med* **364**, 616-26 (2011).
200. Kim, Y.J. *et al.* A genome-wide association study identified new variants associated with the risk of chronic hepatitis B. *Hum Mol Genet* **22**, 4233-8 (2013).
201. Walt, A.J., Bouwman, D.L., Weaver, D.W. & Sachs, R.J. The impact of technology on the management of pancreatic pseudocyst. Fifth annual Samuel Jason Mixter Lecture. *Arch Surg* **125**, 759-63 (1990).
202. Wang, Q. *et al.* MicroRNA-377 is up-regulated and can lead to increased fibronectin production in diabetic nephropathy. *FASEB J* **22**, 4126-35 (2008).
203. McDonough, C.W. *et al.* A genome-wide association study for diabetic nephropathy genes in African Americans. *Kidney Int* **79**, 563-72 (2011).
204. Lan, X. *et al.* Identification of differentially expressed genes related to metabolic syndrome induced with high-fat diet in E3 rats. *Exp Biol Med (Maywood)* **240**, 235-41 (2015).
205. Liu, Y. *et al.* Serum methylation levels of TAC1, SEPT9 and EYA4 as diagnostic markers for early colorectal cancers: a pilot study. *Biomarkers* **18**, 399-405 (2013).
206. Kisiel, J.B., Garrity-Park, M.M., Taylor, W.R., Smyrk, T.C. & Ahlquist, D.A. Methylated eyes absent 4 (EYA4) gene promotor in non-neoplastic mucosa of ulcerative colitis patients with colorectal cancer: evidence for a field effect. *Inflamm Bowel Dis* **19**, 2079-83 (2013).
207. Lovf, M. *et al.* A novel transcript, VNN1-AB, as a biomarker for colorectal cancer. *Int J Cancer* **135**, 2077-84 (2014).
208. Huang, H. *et al.* Novel blood biomarkers of pancreatic cancer-associated diabetes mellitus identified by peripheral blood-based gene expression profiles. *Am J Gastroenterol* **105**, 1661-9 (2010).
209. Soubeyrand, S., Naing, T., Martinuk, A. & McPherson, R. ERK1/2 regulates hepatocyte Trib1 in response to mitochondrial dysfunction. *Biochim Biophys Acta* **1833**, 3405-14 (2013).
210. Zhou, L. *et al.* A genome wide association study identifies common variants associated with lipid levels in the Chinese population. *PLoS One* **8**, e82420 (2013).
211. Kim, Y.J. *et al.* Large-scale genome-wide association studies in East Asians identify new genetic loci influencing metabolic traits. *Nat Genet* **43**, 990-5 (2011).
212. Kraja, A.T. *et al.* A bivariate genome-wide approach to metabolic syndrome: STAMPEED consortium. *Diabetes* **60**, 1329-39 (2011).
213. Ko, A. *et al.* Amerindian-specific regions under positive selection harbour new lipid variants in Latinos. *Nat Commun* **5**, 3983 (2014).
214. Kamatani, Y. *et al.* Genome-wide association study of hematological and biochemical traits in a Japanese population. *Nat Genet* **42**, 210-5 (2010).
215. Global Lipids Genetics, C. *et al.* Discovery and refinement of loci associated with lipid levels. *Nat Genet* **45**, 1274-83 (2013).
216. Aulchenko, Y.S. *et al.* Loci influencing lipid levels and coronary heart disease risk in 16 European population cohorts. *Nat Genet* **41**, 47-55 (2009).
217. Teslovich, T.M. *et al.* Biological, clinical and population relevance of 95 loci for blood lipids. *Nature* **466**, 707-13 (2010).
218. Dastani, Z. *et al.* Novel loci for adiponectin levels and their influence on type 2 diabetes and metabolic traits: a multi-ethnic meta-analysis of 45,891 individuals. *PLoS Genet* **8**, e1002607 (2012).

219. Chambers, J.C. *et al.* Genome-wide association study identifies loci influencing concentrations of liver enzymes in plasma. *Nat Genet* **43**, 1131-8 (2011).
220. Barrett, J.C. *et al.* Genome-wide association defines more than 30 distinct susceptibility loci for Crohn's disease. *Nat Genet* **40**, 955-62 (2008).
221. Franke, A. *et al.* Genome-wide meta-analysis increases to 71 the number of confirmed Crohn's disease susceptibility loci. *Nat Genet* **42**, 1118-25 (2010).
222. Yu, B. *et al.* Genome-wide association study of a heart failure related metabolomic profile among African Americans in the Atherosclerosis Risk in Communities (ARIC) study. *Genet Epidemiol* **37**, 840-5 (2013).
223. McArdle, P.F. *et al.* Association of a common nonsynonymous variant in GLUT9 with serum uric acid levels in old order amish. *Arthritis Rheum* **58**, 2874-81 (2008).
224. Wakil, S.M. *et al.* Association of a mutation in LACC1 with a monogenic form of systemic juvenile idiopathic arthritis. *Arthritis Rheumatol* **67**, 288-95 (2015).
225. Wang, J. *et al.* Genome-wide association analysis implicates the involvement of eight loci with response to tocilizumab for the treatment of rheumatoid arthritis. *Pharmacogenomics J* **13**, 235-41 (2013).
226. Lyons, P.A. *et al.* Genetically distinct subsets within ANCA-associated vasculitis. *N Engl J Med* **367**, 214-23 (2012).
227. Ahmeti, K.B. *et al.* Age of onset of amyotrophic lateral sclerosis is modulated by a locus on 1p34.1. *Neurobiol Aging* **34**, 357 e7-19 (2013).
228. Zheng, J.S. *et al.* Genome-wide contribution of genotype by environment interaction to variation of diabetes-related traits. *PLoS One* **8**, e77442 (2013).
229. Sokolik, R. *et al.* Significance of association of HLA-C and HLA-E with psoriatic arthritis. *Hum Immunol* **75**, 1188-91 (2014).
230. Smigoc Schweiger, D. *et al.* Genetic risk for co-occurrence of type 1 diabetes and celiac disease is modified by HLA-C and killer immunoglobulin-like receptors. *Tissue Antigens* **84**, 471-8 (2014).
231. Matsuzaka, Y. *et al.* Identification of novel candidate genes in the diffuse panbronchiolitis critical region of the class I human MHC. *Immunogenetics* **54**, 301-9 (2002).
232. Hancock, D.B. *et al.* Genome-wide joint meta-analysis of SNP and SNP-by-smoking interaction identifies novel loci for pulmonary function. *PLoS Genet* **8**, e1003098 (2012).
233. Thorleifsson, G. *et al.* Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity. *Nat Genet* **41**, 18-24 (2009).
234. Zhang, X. *et al.* Synthesis of 53 tissue and cell line expression QTL datasets reveals master eQTLs. *BMC Genomics* **15**, 532 (2014).
235. Goring, H.H. *et al.* Discovery of expression QTLs using large-scale transcriptional profiling in human lymphocytes. *Nat Genet* **39**, 1208-16 (2007).
236. Idaghdour, Y. *et al.* Geographical genomics of human leukocyte gene expression variation in southern Morocco. *Nat Genet* **42**, 62-7 (2010).
237. Heap, G.A. *et al.* Complex nature of SNP genotype effects on gene expression in primary human leukocytes. *BMC Med Genomics* **2**, 1 (2009).
238. Emilsson, V. *et al.* Genetics of gene expression and its effect on disease. *Nature* **452**, 423-8 (2008).
239. Fehrmann, R.S. *et al.* Trans-eQTLs reveal that independent genetic variants associated with a complex phenotype converge on intermediate genes, with a major role for the HLA. *PLoS Genet* **7**, e1002197 (2011).
240. Mehta, D. *et al.* Impact of common regulatory single-nucleotide variants on gene expression profiles in whole blood. *Eur J Hum Genet* **21**, 48-54 (2013).

241. Zhernakova, D.V. *et al.* DeepSAGE reveals genetic variants associated with alternative polyadenylation and expression of coding and non-coding transcripts. *PLoS Genet* **9**, e1003594 (2013).
242. Sasayama, D. *et al.* Identification of single nucleotide polymorphisms regulating peripheral blood mRNA expression with genome-wide significance: an eQTL study in the Japanese population. *PLoS One* **8**, e54967 (2013).
243. Landmark-Hoyvik, H. *et al.* Genome-wide association study in breast cancer survivors reveals SNPs associated with gene expression of genes belonging to MHC class I and II. *Genomics* **102**, 278-87 (2013).
244. Westra, H.J. *et al.* Systematic identification of trans eQTLs as putative drivers of known disease associations. *Nat Genet* **45**, 1238-43 (2013).
245. van Eijk, K.R. *et al.* Genetic analysis of DNA methylation and gene expression levels in whole blood of healthy human subjects. *BMC Genomics* **13**, 636 (2012).
246. Battle, A. *et al.* Characterizing the genetic basis of transcriptome diversity through RNA-sequencing of 922 individuals. *Genome Res* **24**, 14-24 (2014).
247. Benton, M.C. *et al.* Mapping eQTLs in the Norfolk Island genetic isolate identifies candidate genes for CVD risk traits. *Am J Hum Genet* **93**, 1087-99 (2013).
248. Narahara, M. *et al.* Large-scale East-Asian eQTL mapping reveals novel candidate genes for LD mapping and the genomic landscape of transcriptional effects of sequence variants. *PLoS One* **9**, e100924 (2014).
249. Quinlan, J. *et al.* Genomic architecture of sickle cell disease in West African children. *Front Genet* **5**, 26 (2014).
250. Wright, F.A. *et al.* Heritability and genomics of gene expression in peripheral blood. *Nat Genet* **46**, 430-7 (2014).
251. Schramm, K. *et al.* Mapping the genetic architecture of gene regulation in whole blood. *PLoS One* **9**, e93844 (2014).
252. Lock, E.F. *et al.* Joint eQTL assessment of whole blood and dura mater tissue from individuals with Chiari type I malformation. *BMC Genomics* **16**, 11 (2015).
253. Powell, J.E. *et al.* The Brisbane Systems Genetics Study: genetical genomics meets complex trait genetics. *PLoS One* **7**, e35430 (2012).
254. Pierce, B.L. *et al.* Mediation analysis demonstrates that trans-eQTLs are often explained by cis-mediation: a genome-wide analysis among 1,800 South Asians. *PLoS Genet* **10**, e1004818 (2014).
255. Chen, W. *et al.* Expression quantitative trait loci (eQTL) mapping in Puerto Rican children. *PLoS One* **10**, e0122464 (2015).
256. Foroughi Asl, H. *et al.* Expression quantitative trait Loci acting across multiple tissues are enriched in inherited risk for coronary artery disease. *Circ Cardiovasc Genet* **8**, 305-15 (2015).
257. Dixon, A.L. *et al.* A genome-wide association study of global gene expression. *Nat Genet* **39**, 1202-7 (2007).
258. Liang, L. *et al.* A cross-platform analysis of 14,177 expression quantitative trait loci derived from lymphoblastoid cell lines. *Genome Res* **23**, 716-26 (2013).
259. Stranger, B.E. *et al.* Population genomics of human gene expression. *Nat Genet* **39**, 1217-24 (2007).
260. Kwan, T. *et al.* Genome-wide analysis of transcript isoform variation in humans. *Nat Genet* **40**, 225-31 (2008).
261. Dimas, A.S. *et al.* Common regulatory variation impacts gene expression in a cell type-dependent manner. *Science* **325**, 1246-50 (2009).



262. Cusanovich, D.A. *et al.* The combination of a genome-wide association study of lymphocyte count and analysis of gene expression data reveals novel asthma candidate genes. *Hum Mol Genet* **21**, 2111-23 (2012).
263. Grundberg, E. *et al.* Mapping cis- and trans-regulatory effects across multiple tissues in twins. *Nat Genet* **44**, 1084-9 (2012).
264. Gutierrez-Arcelus, M. *et al.* Passive and active DNA methylation and the interplay with genetic variation in gene regulation. *Elife* **2**, e00523 (2013).
265. Mangravite, L.M. *et al.* A statin-dependent QTL for GATM expression is associated with statin-induced myopathy. *Nature* **502**, 377-80 (2013).
266. Bryois, J. *et al.* Cis and trans effects of human genomic variants on gene expression. *PLoS Genet* **10**, e1004461 (2014).
267. Huang, J. *et al.* eQTL mapping identifies insertion- and deletion-specific eQTLs in multiple tissues. *Nat Commun* **6**, 6821 (2015).
268. Naranbhai, V. *et al.* Genomic modulators of gene expression in human neutrophils. *Nat Commun* **6**, 7545 (2015).
269. Andiappan, A.K. *et al.* Genome-wide analysis of the genetic regulation of gene expression in human neutrophils. *Nat Commun* **6**, 7971 (2015).
270. Fairfax, B.P. *et al.* Genetics of gene expression in primary immune cells identifies cell type-specific master regulators and roles of HLA alleles. *Nat Genet* **44**, 502-10 (2012).
271. Murphy, A. *et al.* Mapping of numerous disease-associated expression polymorphisms in primary peripheral blood CD4+ lymphocytes. *Hum Mol Genet* **19**, 4745-57 (2010).
272. Heinzen, E.L. *et al.* Tissue-specific genetic control of splicing: implications for the study of complex traits. *PLoS Biol* **6**, e1 (2008).
273. Zeller, T. *et al.* Genetics and beyond--the transcriptome of human monocytes and disease susceptibility. *PLoS One* **5**, e10693 (2010).
274. Almlof, J.C. *et al.* Powerful identification of cis-regulatory SNPs in human primary monocytes using allele-specific gene expression. *PLoS One* **7**, e52260 (2012).
275. Kirsten, H. *et al.* Dissecting the genetics of the human transcriptome identifies novel trait-related trans-eQTLs and corroborates the regulatory relevance of non-protein coding locidagger. *Hum Mol Genet* **24**, 4746-63 (2015).
276. Almlof, J.C. *et al.* Single nucleotide polymorphisms with cis-regulatory effects on long non-coding transcripts in human primary monocytes. *PLoS One* **9**, e102612 (2014).
277. Fairfax, B.P. *et al.* Innate immune activity conditions the effect of regulatory variants upon monocyte gene expression. *Science* **343**, 1246949 (2014).
278. Barreiro, L.B. *et al.* Deciphering the genetic architecture of variation in the immune response to Mycobacterium tuberculosis infection. *Proc Natl Acad Sci U S A* **109**, 1204-9 (2012).
279. Lee, M.N. *et al.* Common genetic variants modulate pathogen-sensing responses in human dendritic cells. *Science* **343**, 1246980 (2014).
280. Huang, R.S. *et al.* Population differences in microRNA expression and biological implications. *RNA Biol* **8**, 692-701 (2011).
281. Fischer, D. *et al.* MiRNA Profiles in Lymphoblastoid Cell Lines of Finnish Prostate Cancer Families. *PLoS One* **10**, e0127427 (2015).
282. Degner, J.F. *et al.* DNase I sensitivity QTLs are a major determinant of human expression variation. *Nature* **482**, 390-4 (2012).
283. del Rosario, R.C. *et al.* Sensitive detection of chromatin-altering polymorphisms reveals autoimmune disease mechanisms. *Nat Methods* **12**, 458-64 (2015).
284. Battle, A. *et al.* Genomic variation. Impact of regulatory variation from RNA to protein. *Science* **347**, 664-7 (2015).

285. Zhang, X. *et al.* Identification of common genetic variants controlling transcript isoform variation in human whole blood. *Nat Genet* **47**, 345-52 (2015).
286. Huan, T. *et al.* Genome-wide identification of microRNA expression quantitative trait loci. *Nat Commun* **6**, 6601 (2015).
287. Greenawalt, D.M. *et al.* A survey of the genetics of stomach, liver, and adipose gene expression from a morbidly obese cohort. *Genome Res* **21**, 1008-16 (2011).
288. Kompass, K.S. & Witte, J.S. Co-regulatory expression quantitative trait loci mapping: method and application to endometrial cancer. *BMC Med Genomics* **4**, 6 (2011).
289. Zhang, B. *et al.* Integrated systems approach identifies genetic nodes and networks in late-onset Alzheimer's disease. *Cell* **153**, 707-20 (2013).
290. Schadt, E.E. *et al.* Mapping the genetic architecture of gene expression in human liver. *PLoS Biol* **6**, e107 (2008).
291. Innocenti, F. *et al.* Identification, replication, and functional fine-mapping of expression quantitative trait loci in primary human liver tissue. *PLoS Genet* **7**, e1002078 (2011).
292. Schroder, A. *et al.* Genomics of ADME gene expression: mapping expression quantitative trait loci relevant for absorption, distribution, metabolism and excretion of drugs in human liver. *Pharmacogenomics J* **13**, 12-20 (2013).
293. Wang, X. *et al.* Mapping of hepatic expression quantitative trait loci (eQTLs) in a Han Chinese population. *J Med Genet* **51**, 319-26 (2014).
294. Grundberg, E. *et al.* Population genomics in a disease targeted primary cell model. *Genome Res* **19**, 1942-52 (2009).
295. Kabakchiev, B. & Silverberg, M.S. Expression quantitative trait loci analysis identifies associations between genotype and gene expression in human intestine. *Gastroenterology* **144**, 1488-96, 1496 e1-3 (2013).
296. Ongen, H. *et al.* Putative cis-regulatory drivers in colorectal cancer. *Nature* **512**, 87-90 (2014).
297. Hular, I. *et al.* Enrichment of inflammatory bowel disease and colorectal cancer risk variants in colon expression quantitative trait loci. *BMC Genomics* **16**, 138 (2015).
298. Keildson, S. *et al.* Expression of phosphofructokinase in skeletal muscle is influenced by genetic variation and associated with insulin sensitivity. *Diabetes* **63**, 1154-65 (2014).
299. Quigley, D.A. *et al.* The 5p12 breast cancer susceptibility locus affects MRPS30 expression in estrogen-receptor positive tumors. *Mol Oncol* **8**, 273-84 (2014).
300. Curtis, C. *et al.* The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. *Nature* **486**, 346-52 (2012).
301. Hao, K. *et al.* Lung eQTLs to help reveal the molecular underpinnings of asthma. *PLoS Genet* **8**, e1003029 (2012).
302. Gao, C. *et al.* HEFT: eQTL analysis of many thousands of expressed genes while simultaneously controlling for hidden factors. *Bioinformatics* **30**, 369-76 (2014).
303. Lamontagne, M. *et al.* Refining susceptibility loci of chronic obstructive pulmonary disease with lung eqtls. *PLoS One* **8**, e70220 (2013).
304. Luo, W. *et al.* Airway Epithelial Expression Quantitative Trait Loci Reveal Genes Underlying Asthma and Other Airway Diseases. *Am J Respir Cell Mol Biol* (2015).
305. Ding, J. *et al.* Gene expression in skin and lymphoblastoid cells: Refined statistical method reveals extensive overlap in cis-eQTL signals. *Am J Hum Genet* **87**, 779-89 (2010).
306. Wagner, J.R. *et al.* The relationship between DNA methylation, genetic and expression inter-individual variation in untransformed human fibroblasts. *Genome Biol* **15**, R37 (2014).
307. Qiu, W. *et al.* Genetics of sputum gene expression in chronic obstructive pulmonary disease. *PLoS One* **6**, e24395 (2011).

308. Fadista, J. *et al.* Global genomic and transcriptomic analysis of human pancreatic islets reveals novel genes influencing glucose metabolism. *Proc Natl Acad Sci U S A* **111**, 13924-9 (2014).
309. Larson, N.B. *et al.* Comprehensively evaluating cis-regulatory variation in the human prostate transcriptome by using gene-level allele-specific expression. *Am J Hum Genet* **96**, 869-82 (2015).
310. Singh, T. *et al.* Characterization of expression quantitative trait loci in the human colon. *Inflamm Bowel Dis* **21**, 251-6 (2015).
311. Koopmann, T.T. *et al.* Genome-wide identification of expression quantitative trait loci (eQTLs) in human heart. *PLoS One* **9**, e97380 (2014).
312. Lin, H. *et al.* Gene expression and genetic variation in human atria. *Heart Rhythm* **11**, 266-71 (2014).
313. Rantalainen, M. *et al.* MicroRNA expression in abdominal and gluteal adipose tissue is associated with mRNA expression levels and partly genetically driven. *PLoS One* **6**, e27338 (2011).
314. Gamazon, E.R. *et al.* A genome-wide integrative study of microRNAs in human liver. *BMC Genomics* **14**, 395 (2013).
315. Olsson, A.H. *et al.* Genome-wide associations between genetic and epigenetic variation influence mRNA expression and insulin secretion in human pancreatic islets. *PLoS Genet* **10**, e1004735 (2014).
316. Li, Q. *et al.* Expression QTL-based analyses reveal candidate causal genes and loci across five tumor types. *Hum Mol Genet* **23**, 5294-302 (2014).
317. Webster, J.A. *et al.* Genetic control of human brain transcript expression in Alzheimer disease. *Am J Hum Genet* **84**, 445-58 (2009).
318. Zou, F. *et al.* Brain expression genome-wide association study (eGWAS) identifies human disease-associated variants. *PLoS Genet* **8**, e1002707 (2012).
319. Kim, Y. *et al.* A meta-analysis of gene expression quantitative trait loci in brain. *Transl Psychiatry* **4**, e459 (2014).
320. Ramasamy, A. *et al.* Genetic variability in the regulation of gene expression in ten regions of the human brain. *Nat Neurosci* **17**, 1418-28 (2014).
321. Gibbs, J.R. *et al.* Abundant quantitative trait loci exist for DNA methylation and gene expression in human brain. *PLoS Genet* **6**, e1000952 (2010).
322. Gamazon, E.R. *et al.* Enrichment of cis-regulatory gene expression SNPs and methylation quantitative trait loci among bipolar disorder susceptibility variants. *Mol Psychiatry* **18**, 340-6 (2013).
323. Kim, S., Cho, H., Lee, D. & Webster, M.J. Association between SNPs and gene expression in multiple regions of the human brain. *Transl Psychiatry* **2**, e113 (2012).
324. Shpak, M. *et al.* An eQTL analysis of the human glioblastoma multiforme genome. *Genomics* **103**, 252-63 (2014).
325. Colantuoni, C. *et al.* Temporal dynamics and genetic control of transcription in the human prefrontal cortex. *Nature* **478**, 519-23 (2011).
326. Liu, C. *et al.* Whole-genome association mapping of gene expression in the human prefrontal cortex. *Mol Psychiatry* **15**, 779-84 (2010).
327. Irizarry, R.A. *et al.* Exploration, normalization, and summaries of high density oligonucleotide array probe level data. *Biostatistics* **4**, 249-64 (2003).