

# Refining the accuracy of validated target identification through coding variant fine-mapping in type 2 diabetes

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## SUPPLEMENTARY NOTES

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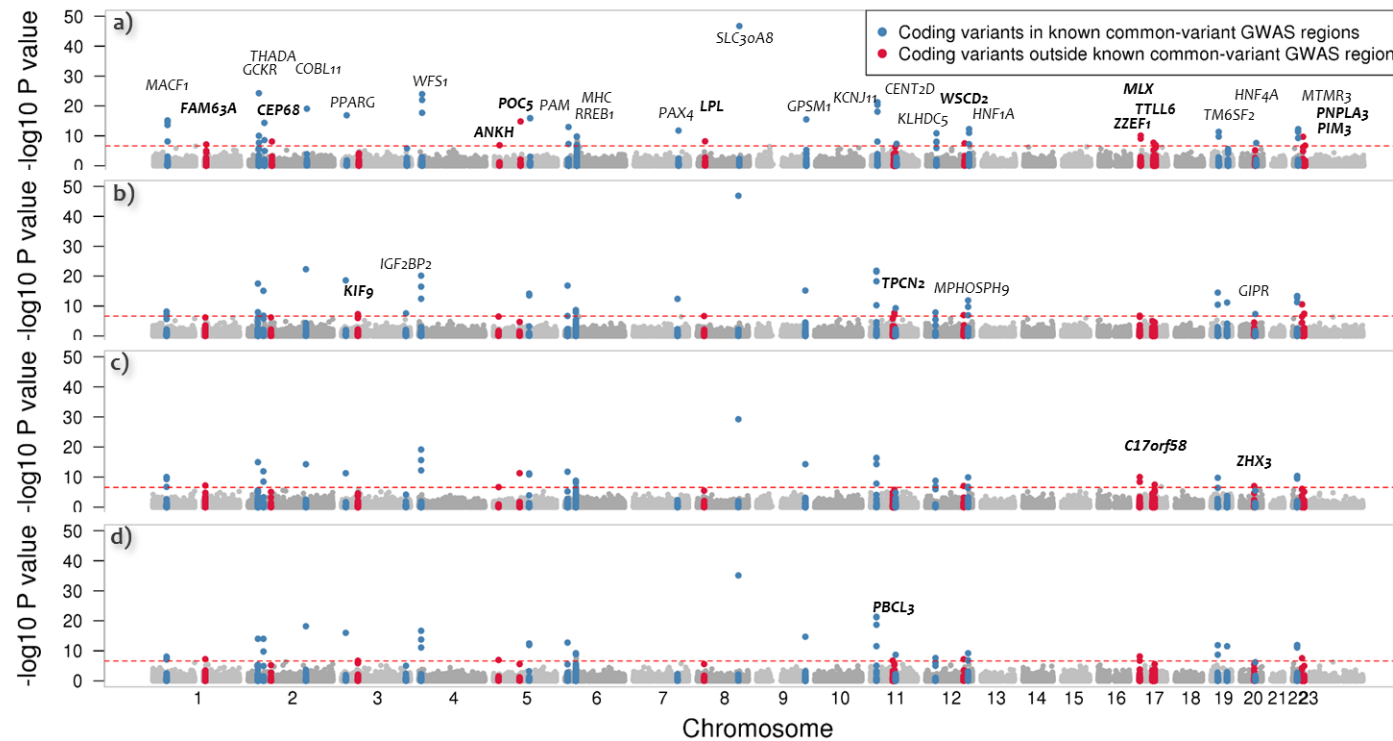
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### iii. Grants, funding support and acknowledgements for individuals and studies

### iv. Consortium membership

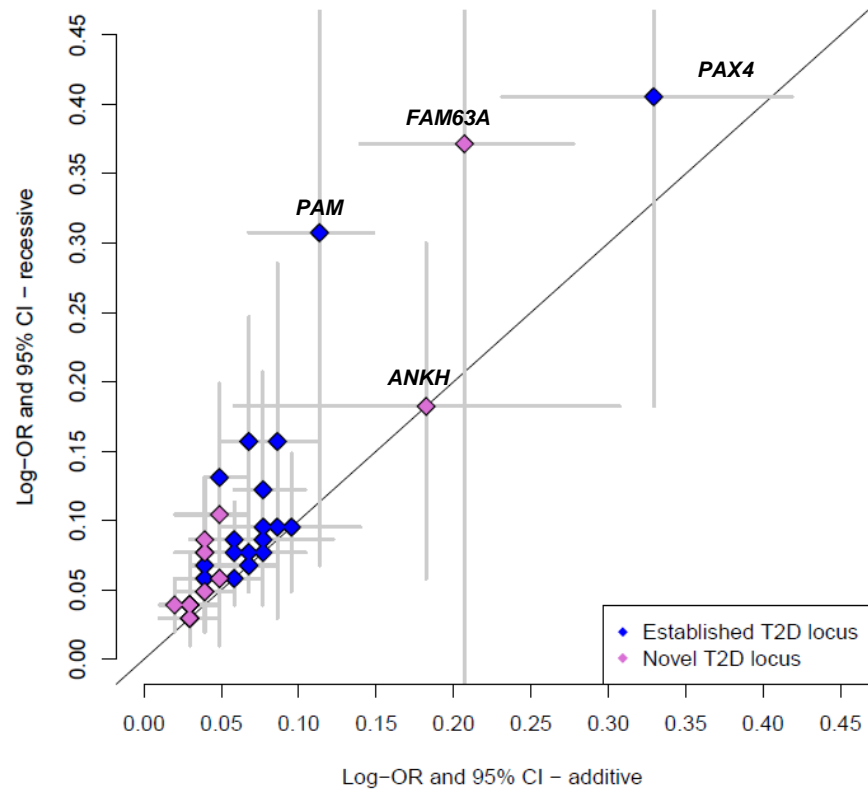
## i. Supplementary Figures

**Supplementary Figure 1 | Manhattan plots of coding variants associated with type 2 diabetes in discovery analysis.** The x-axis represents chromosomal location, and the y-axis represents the  $-\log_{10} p$ -value for tests of association between SNPs and T2D. The dashed line represents exome-wide significance at  $p=2.2 \times 10^{-7}$ . Coding variants in known, common-variant GWAS regions are shown in blue; and variants outside common-variant GWAS regions are shown in red. Coding association signals mapping outside regions previously implicated in T2D susceptibility, defined as >500kb from the reported lead GWAS SNPs are highlighted in bold. Plots are shown by ancestry and with and without BMI adjustment: **a)** trans-ethnic meta-analyses of 81,412 cases and 370,832 controls, **b)** trans-ethnic meta-analyses adjusted for BMI of 68,048 cases and 304,612 controls, **c)** European-specific of 48,286 cases and 250,671 controls, **d)** European-specific adjusted for BMI of 47,181 cases and 249,280 controls.

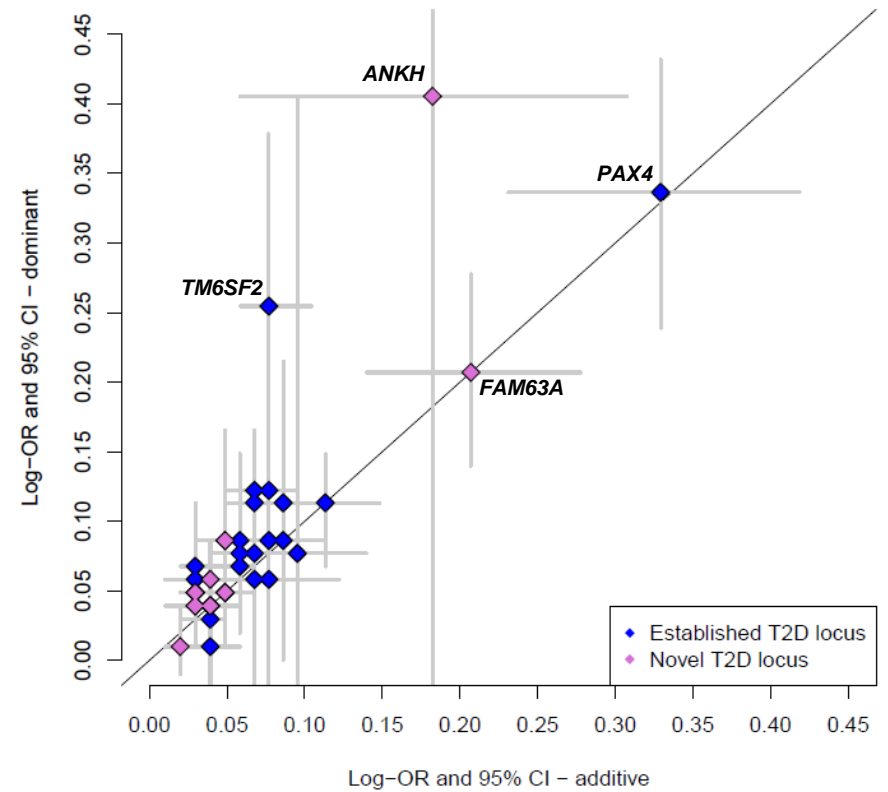


**Supplementary Figure 2 | Plots of allelic effect sizes by mode of inheritance.** Allelic effects sizes from additive model against: **a)** recessive and **b)** dominant models estimated in trans-ethnic meta-analyses of 58,425 cases and 188,032. Each point represents a coding variant with the log-OR and 95% CI from the additive model plotted on the x-axis and the log-OR and 95% CI from recessive or dominant model plotted on the y-axis. Novel coding association signals are coloured pink and coding variant signals within established T2D risk loci are coloured blue. Novel coding association signals are coloured pink and coding variant signals within established T2D risk loci are coloured blue.

a)

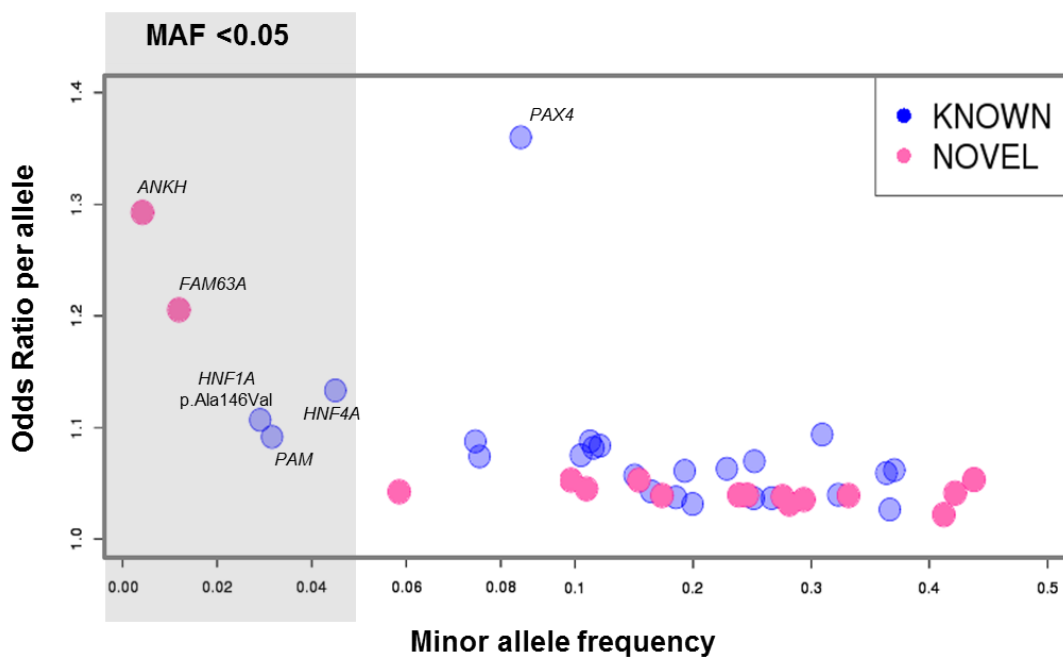


b)

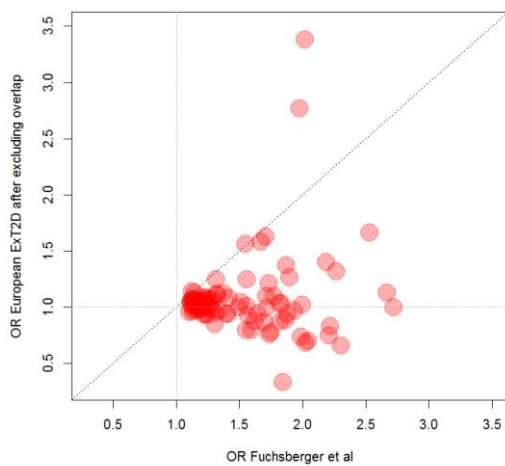


**Supplementary Figure 3 | Contribution of low-frequency and rare coding variation to T2D susceptibility.** a) Allelic effects sizes of the 40 coding association signals from additive models are plotted against minor allele frequency. Known variants are shown in blue; and novel variants are shown in pink. Variants with a minor allele frequency <0.05 are highlighted in grey. (b-c) Fuchsberger *et al.*<sup>1</sup> observed 100 low-frequency coding variants with modest effects (allelic OR 1.10-2.66) for which the association evidence was strong but not genome-wide significant. The European-specific OR of these 100 low-frequency coding variants from Fuchsberger *et al.* was compared to the European-specific ORs from this study (EXT2D): b) ORs from Fuchsberger *et al.* plotted on the x-axis and OR from European EXT2D samples after removing overlapping samples. c) ORs from Fuchsberger *et al.* plotted on the x-axis and OR from all European EXT2D samples. <sup>1</sup> Fuchsberger, C. *et al.* The genetic architecture of type 2 diabetes. *Nature* **536**, 41-7 (2016).

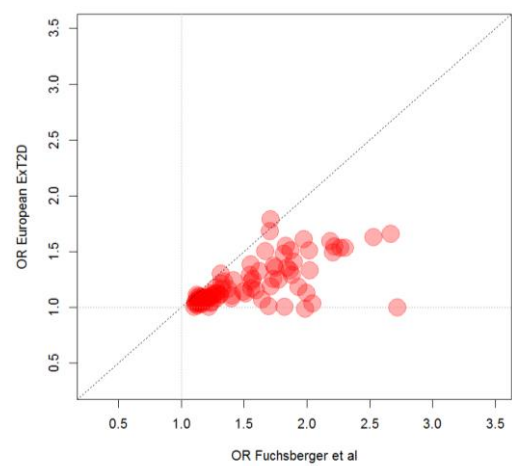
a)



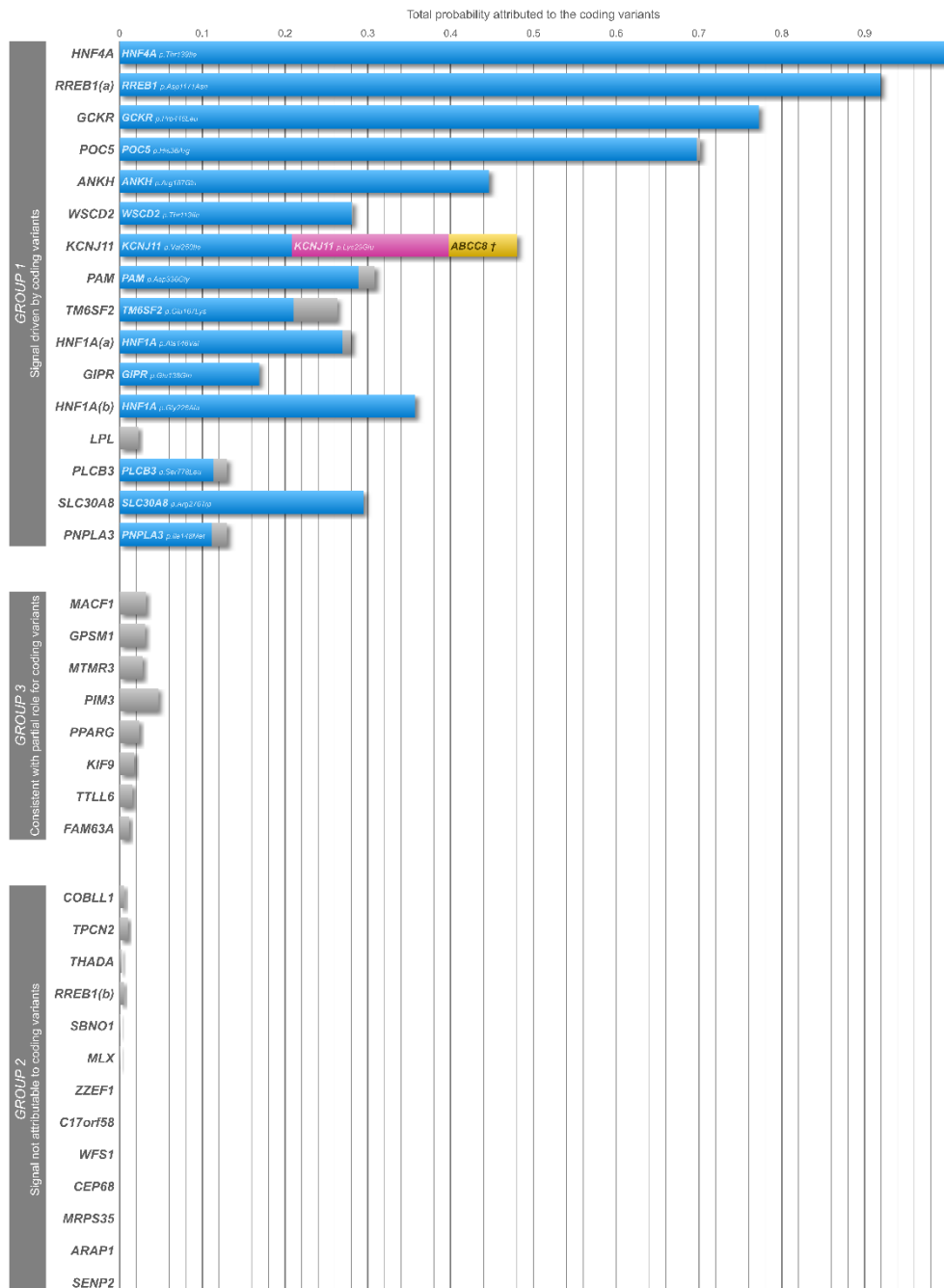
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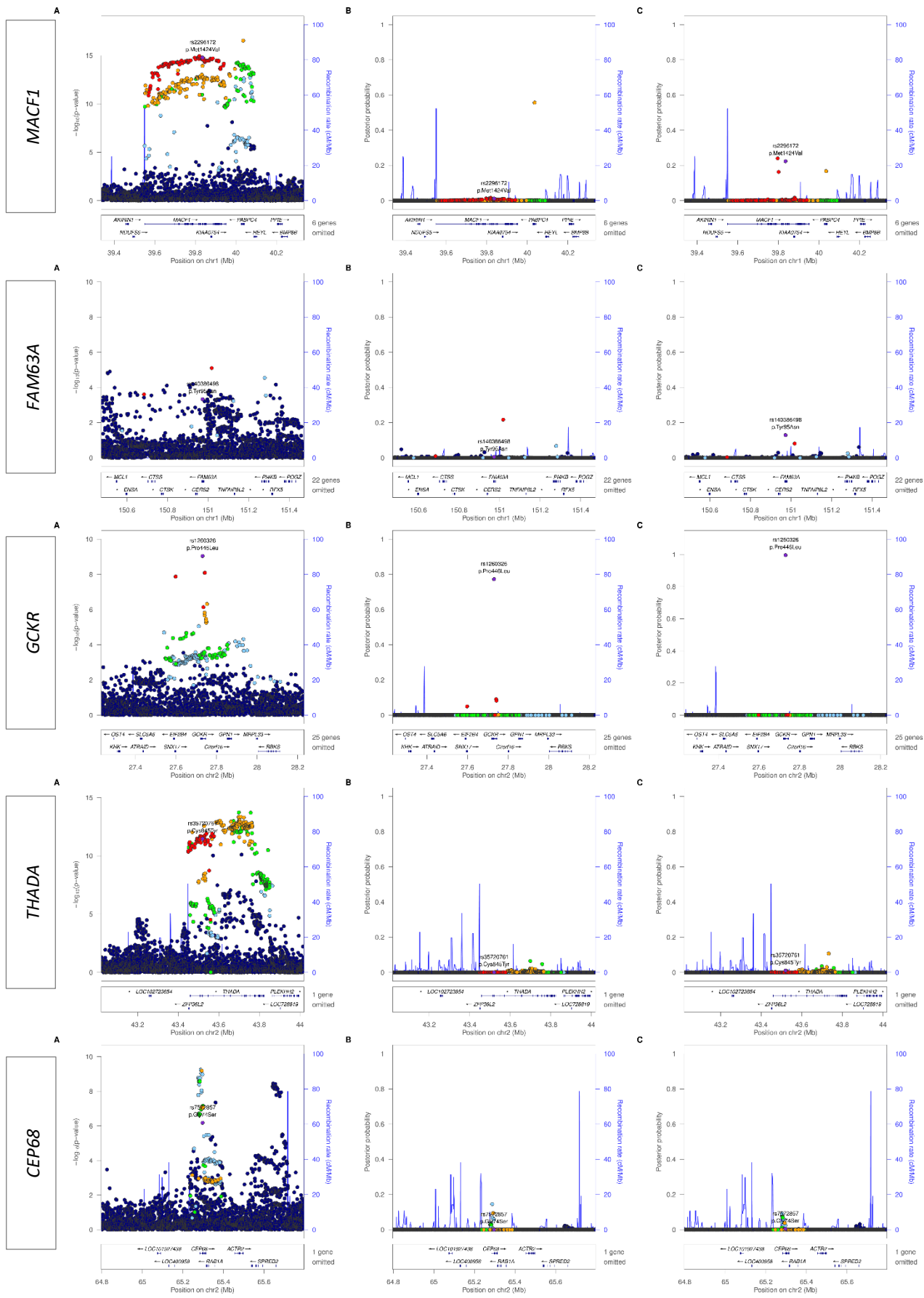
c)



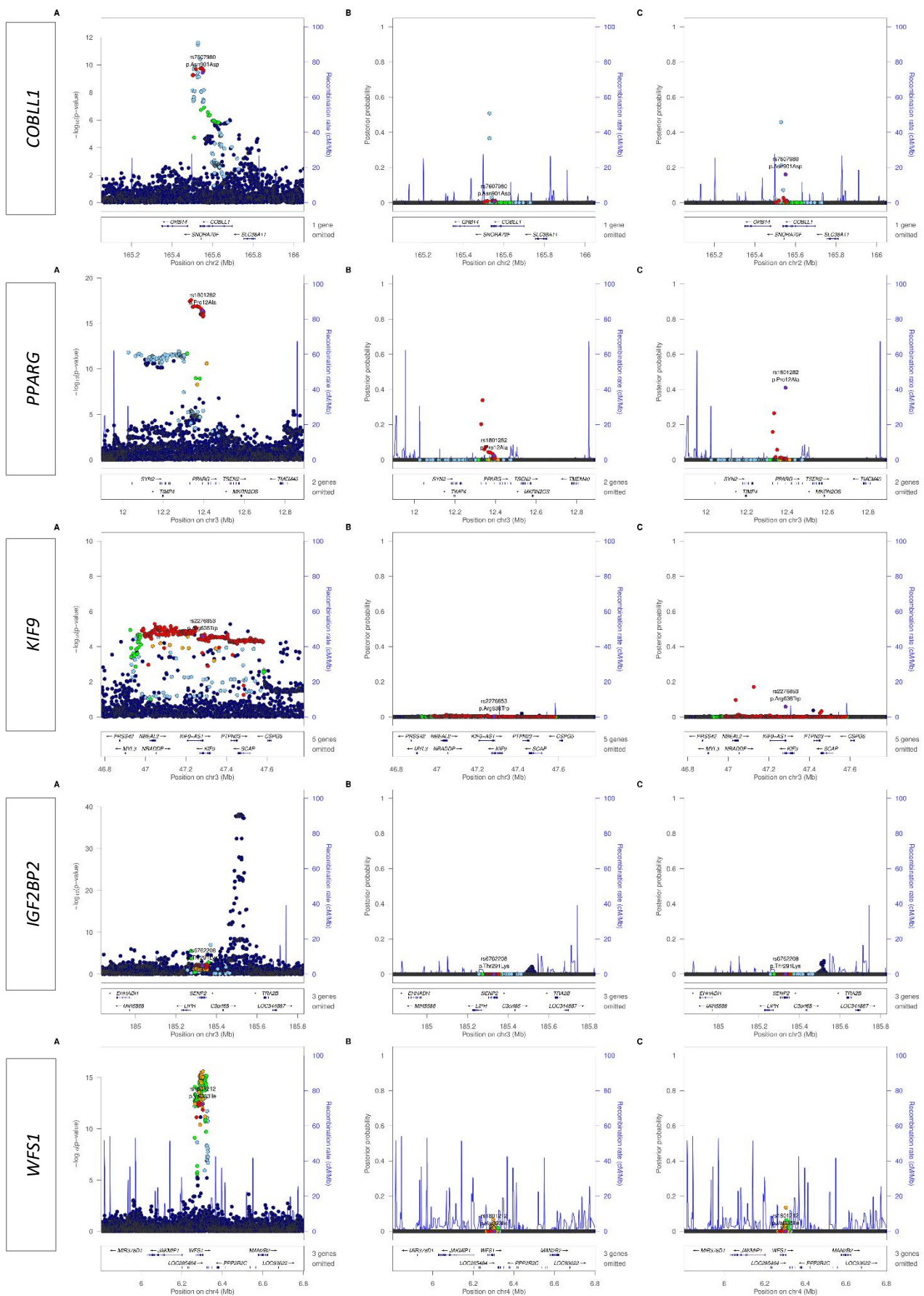
**Supplementary Figure 4 | Posterior probabilities for coding variants across loci with functionally unweighted priors.** Fine-mapping of 37 distinct association signals was performed using European ancestry GWAS meta-analysis including 50,160 T2D cases and 465,272 controls. For each signal, we constructed a credible set of variants accounting for 99% of the posterior probability of driving the association. Each bar here represents a signal with the total probability attributed to the coding variants within the 99% credible set plotted on the y-axis. When the probability (bar) is split across multiple coding variants (at least 0.05 probability attributed to a variant) at a particular locus, these are indicated by blue, pink, and yellow. The combined probability of the remaining coding variants is highlighted in grey. *RREB1(a)*: *RREB1* p.Asp1171Asn; *RREB1(b)*: *RREB1* p.Ser1499Tyr; *HNF1A(a)*: *HNF1A* p.Ala146Val; *HNF1A(b)*: *HNF1A* p.Ile75Leu; *ABCC8*† : *ABCC8* p.Ala1369Ser. Note that the groups are defined based on the annotation-informed priors.

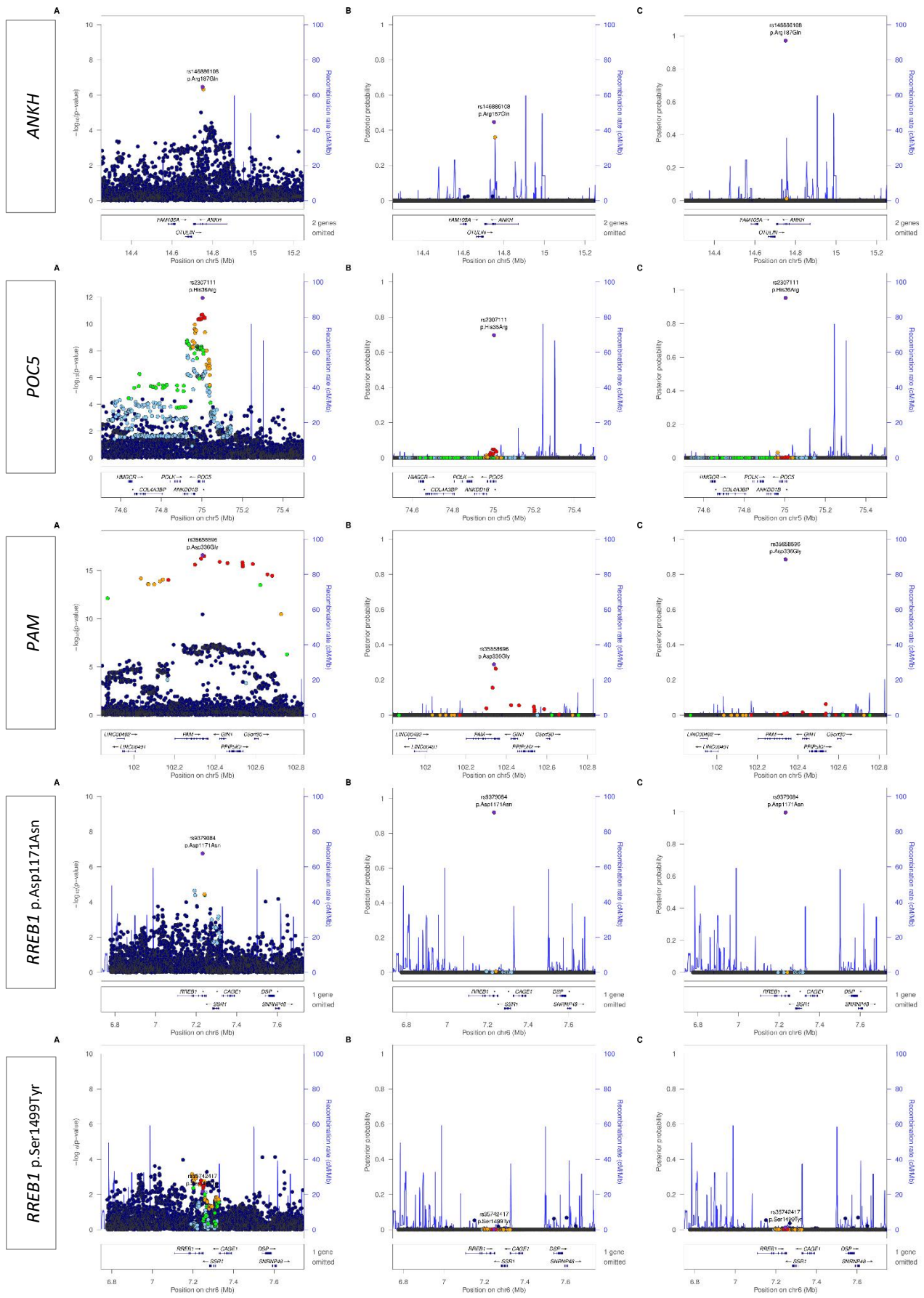


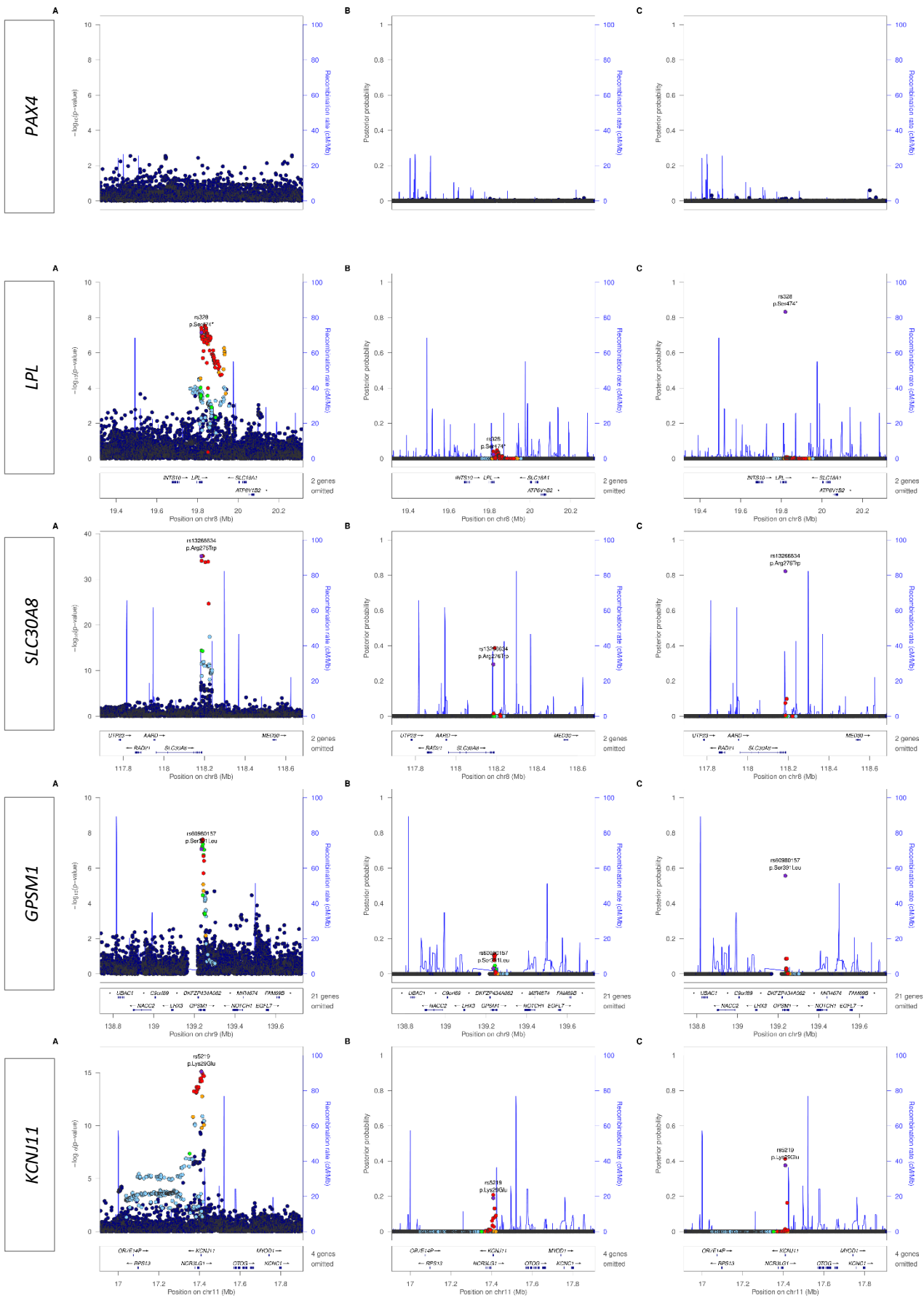
**Supplementary Figure 5 | Locus zoom and posterior probability plots for the distinct association signals from fine-mapping analysis.** For each locus: **a)**  $p$ -values for association from fine-mapping meta-analyses; **b)** posteriors for driving the association under functionally unweighted; and **c)** posteriors for driving the association under annotation informed priors. Each point represents a SNP passing quality control in the meta-analysis, plotted with their  $p$ -value (on a  $-\log_{10}$  scale) or posteriors as a function of genomic position (NCBI build 37). In each plot, the index variant is represented by the purple symbol. The colour coding of all other SNPs indicates LD with the index variant in European ancestry haplotypes from the 1000 Genomes Project reference panel: red  $r^2 \geq 0.8$ ; gold  $0.6 \leq r^2 < 0.8$ ; green  $0.4 \leq r^2 < 0.6$ ; cyan  $0.2 \leq r^2 < 0.4$ ; blue  $r^2 < 0.2$ ; grey  $r^2$  unknown. Fine-mapping was performed using European ancestry GWAS meta-analysis including 50,160 T2D cases and 465,272 controls.

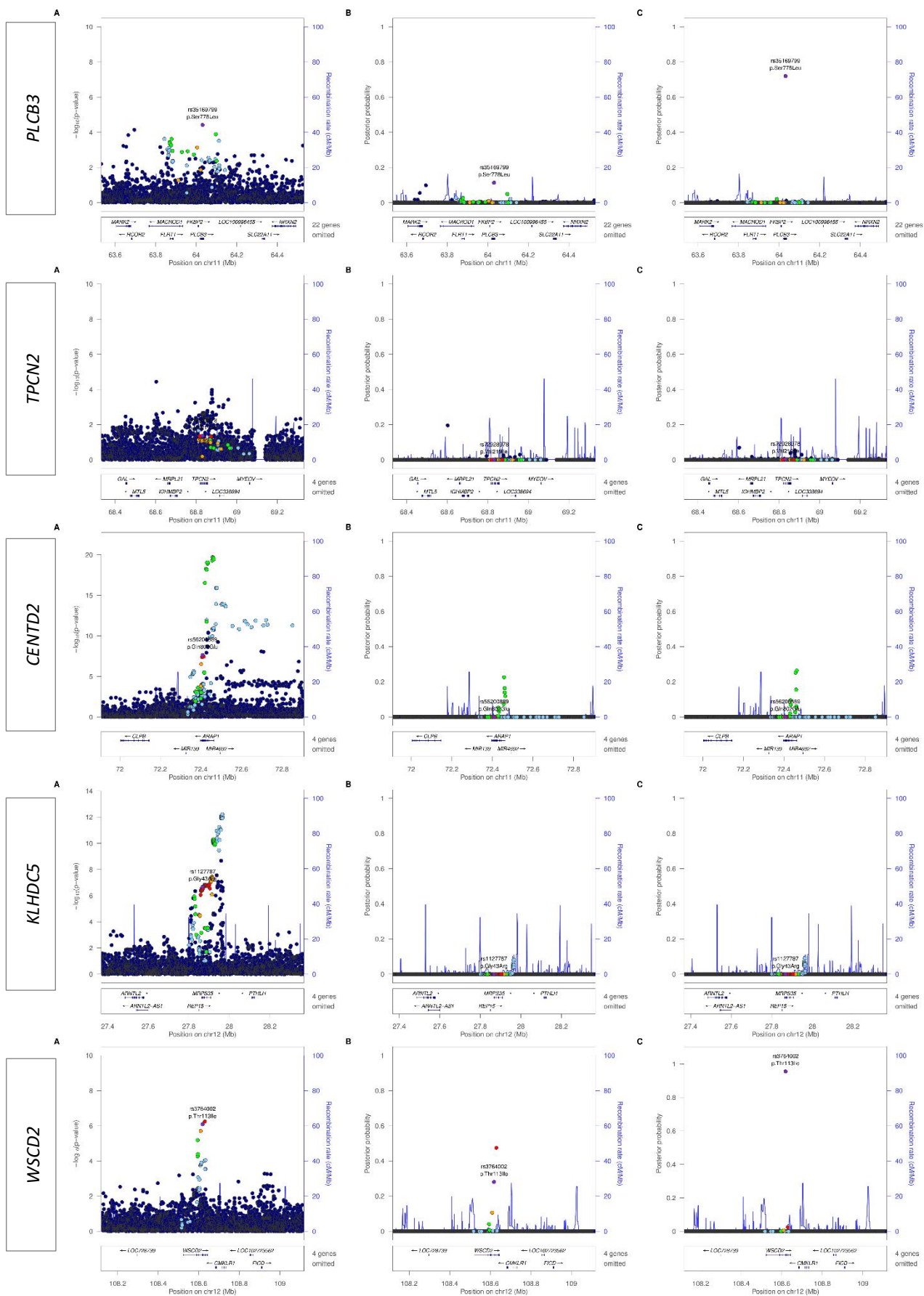




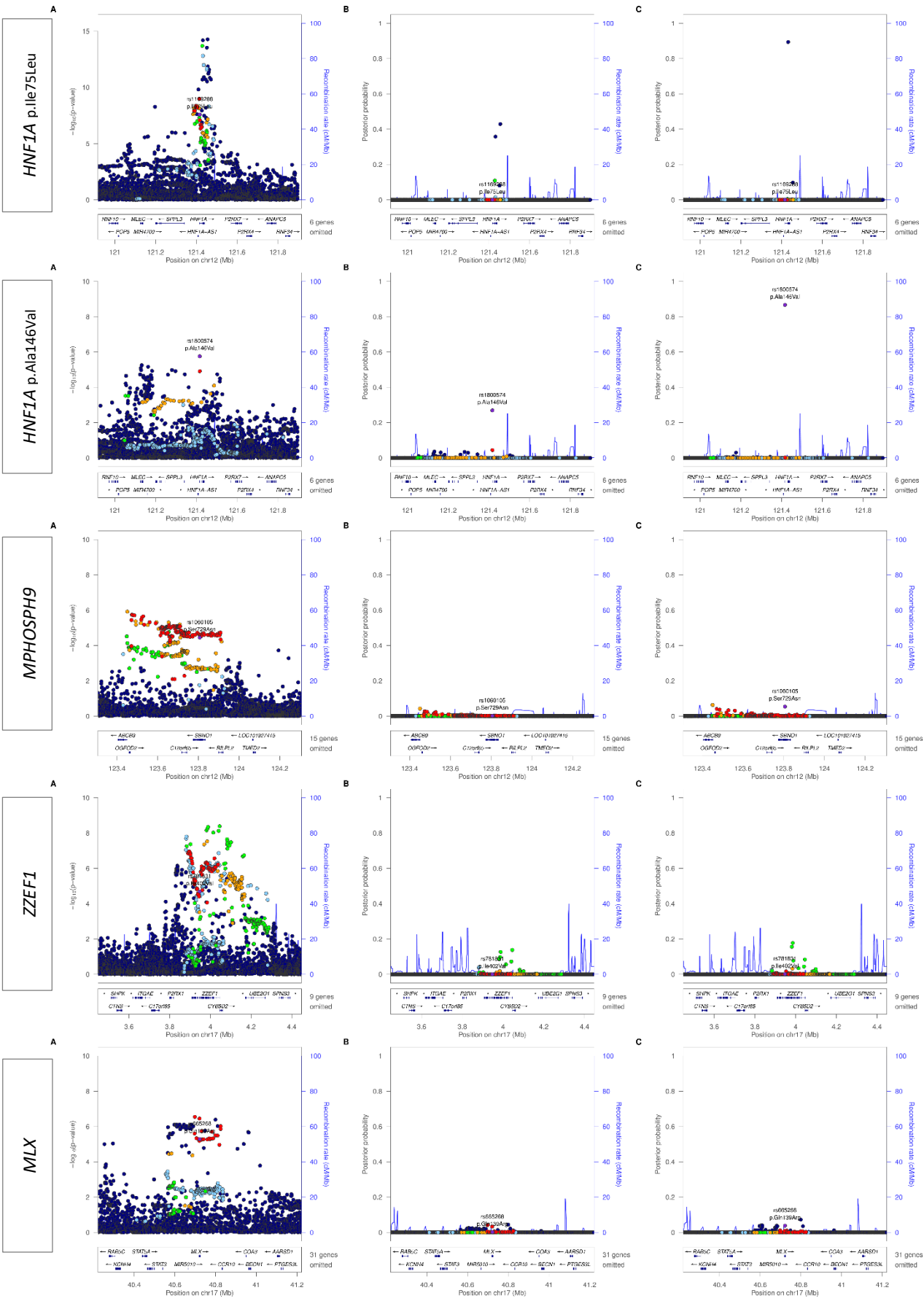


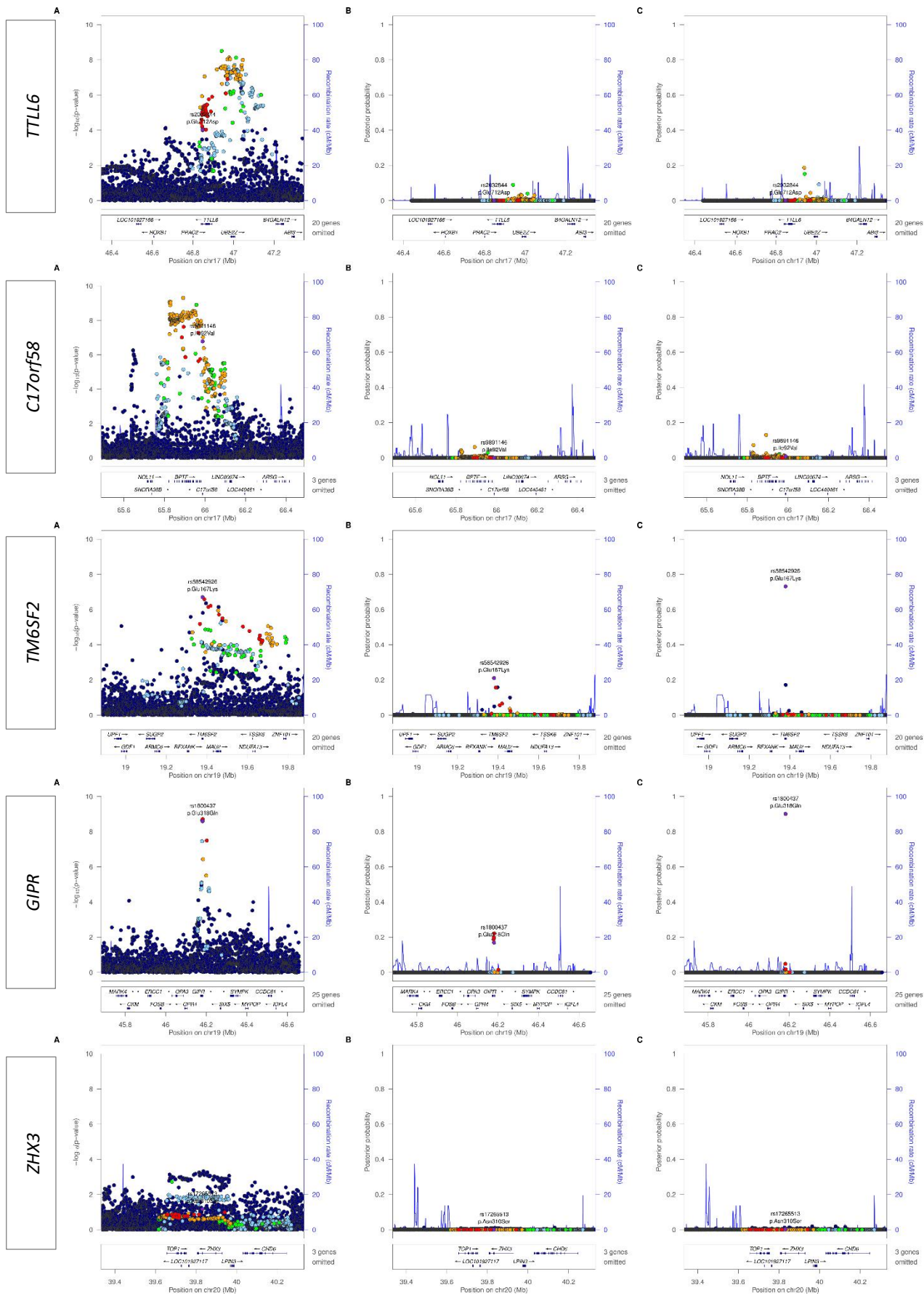


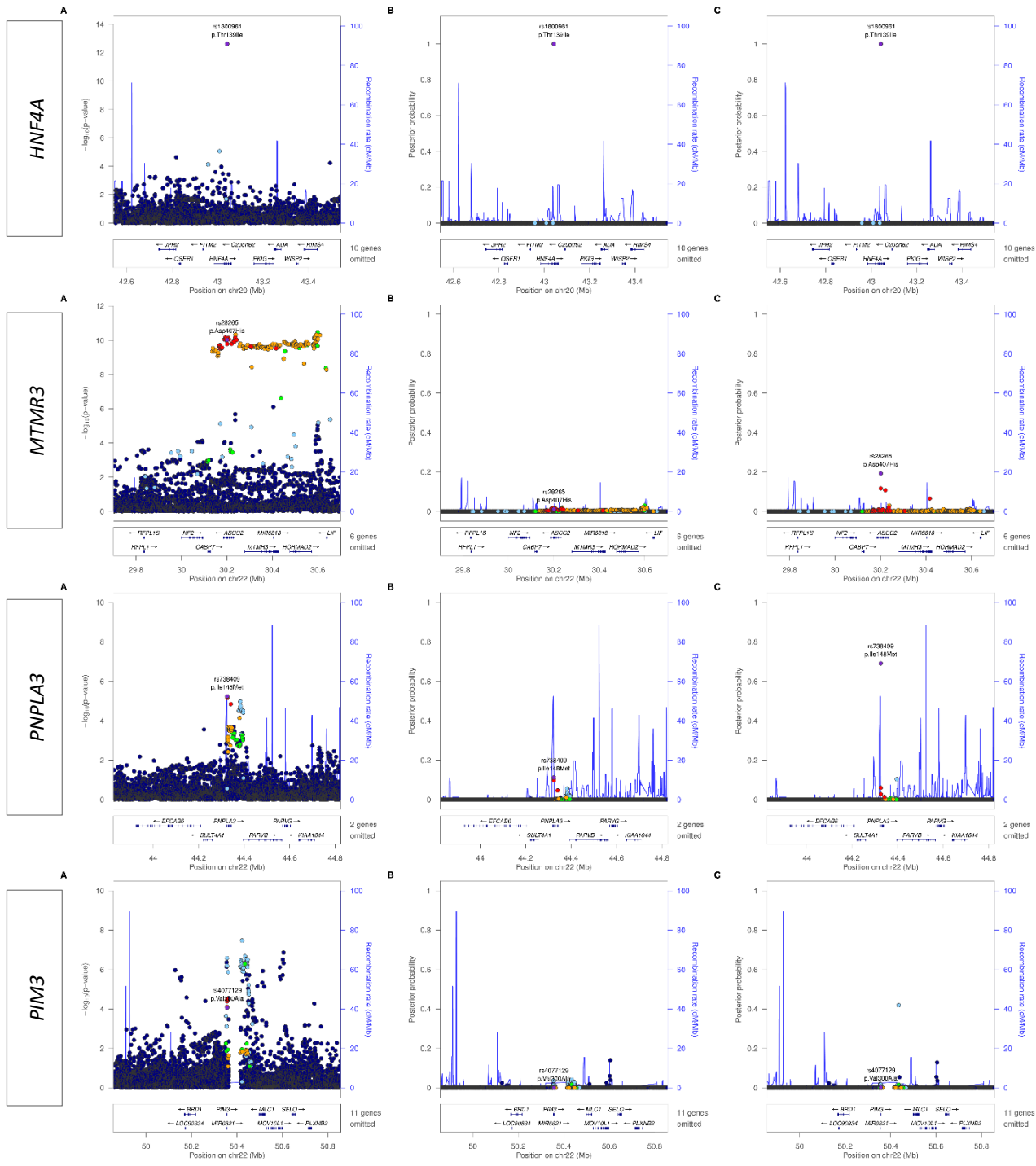










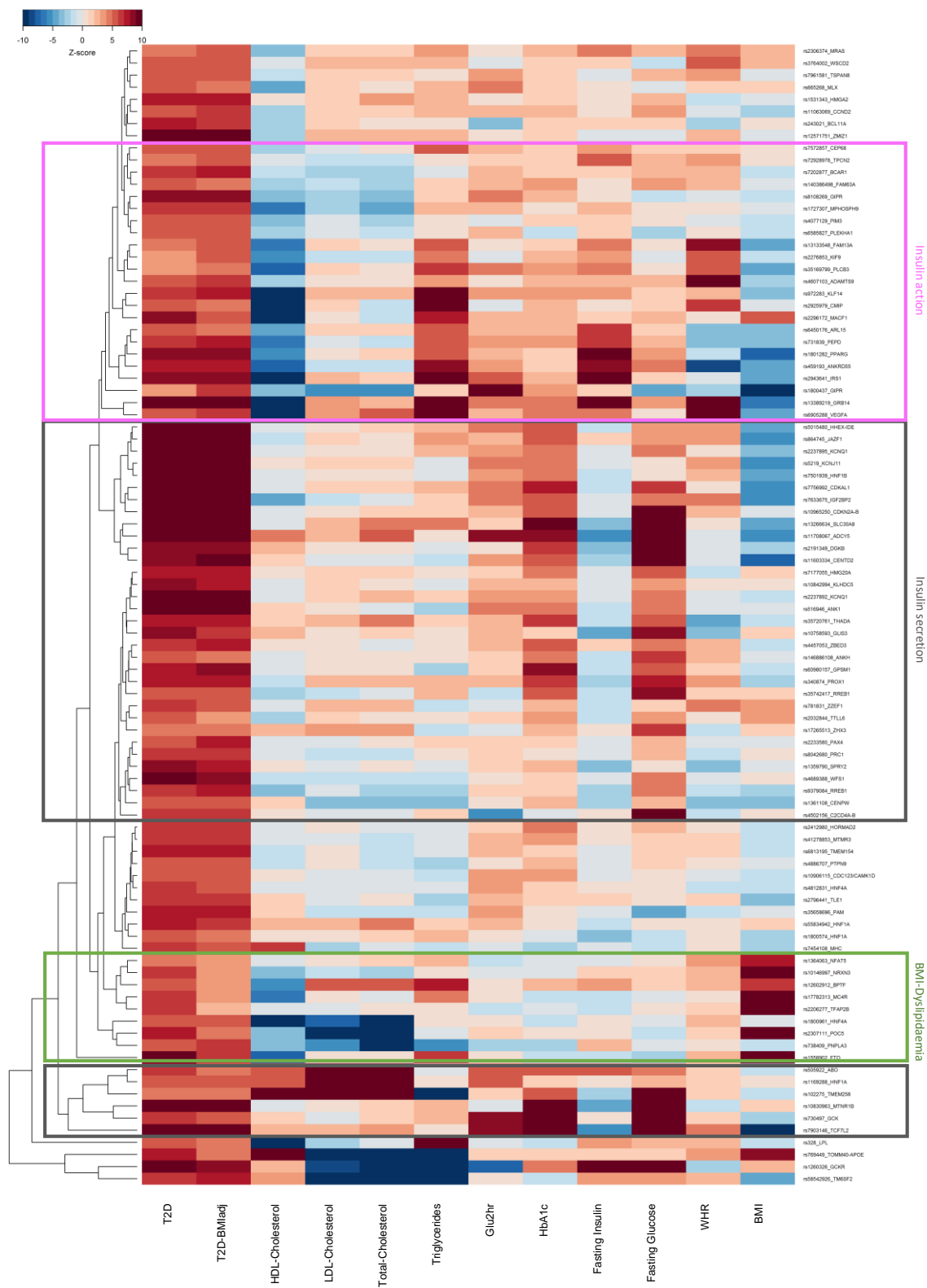


**Supplementary Figure 6 | Clustering of type 2 diabetes loci based on similarity with glycemic, anthropometric traits, and lipid levels. a)**

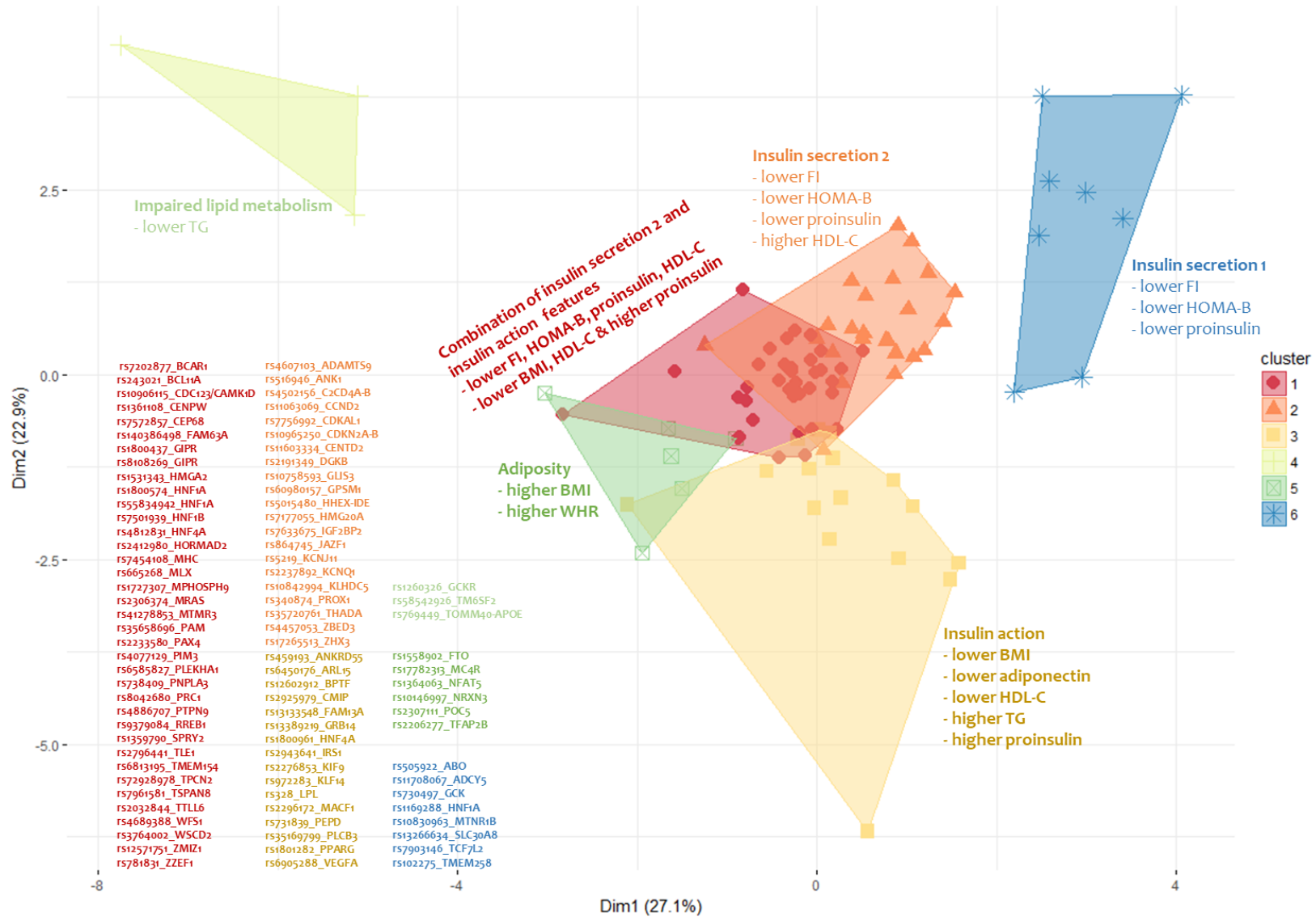
The Z-scores displayed in the heat map represent the effect of the lead T2D risk allele (*y*-axis) on the values of various metabolic and anthropometric traits (*x*-axis). Positive Z-scores in red indicate the T2D-risk allele increases the value of the trait concerned, and negative Z-scores in blue show that it is associated with a decrease in the trait value of interest. T2D loci (on *y* axis) are clustered by the complete agglomeration method and using the Euclidean distances of the Z-scores of the loci/traits, resulting in clustering of SNPs that are more significantly associated with the same set of traits. Z-scores are restricted to  $\pm 10$ . Insulin action: T2D risk allele showed higher fasting insulin levels adjusted for BMI, lower high-density lipoprotein cholesterol, and higher triglyceride levels. Insulin secretion: T2D risk allele demonstrated higher fasting glucose levels adjusted for BMI, higher 2-h glucose, higher glycated haemoglobin levels, and lower fasting insulin levels adjusted for BMI. HDL: high density lipoprotein. LDL: low density lipoprotein. Glu2hr: 2-h glucose. HbA1c: glycated haemoglobin. WHR: waist hip ratio. BMI: body mass index. **b)** Soft clustering performed using fuzzy c-means algorithm that assigns a score to a variant for each cluster. This allows each variant to be assigned to more than one cluster. Broadly variants can be assigned to six different clusters using this approach.



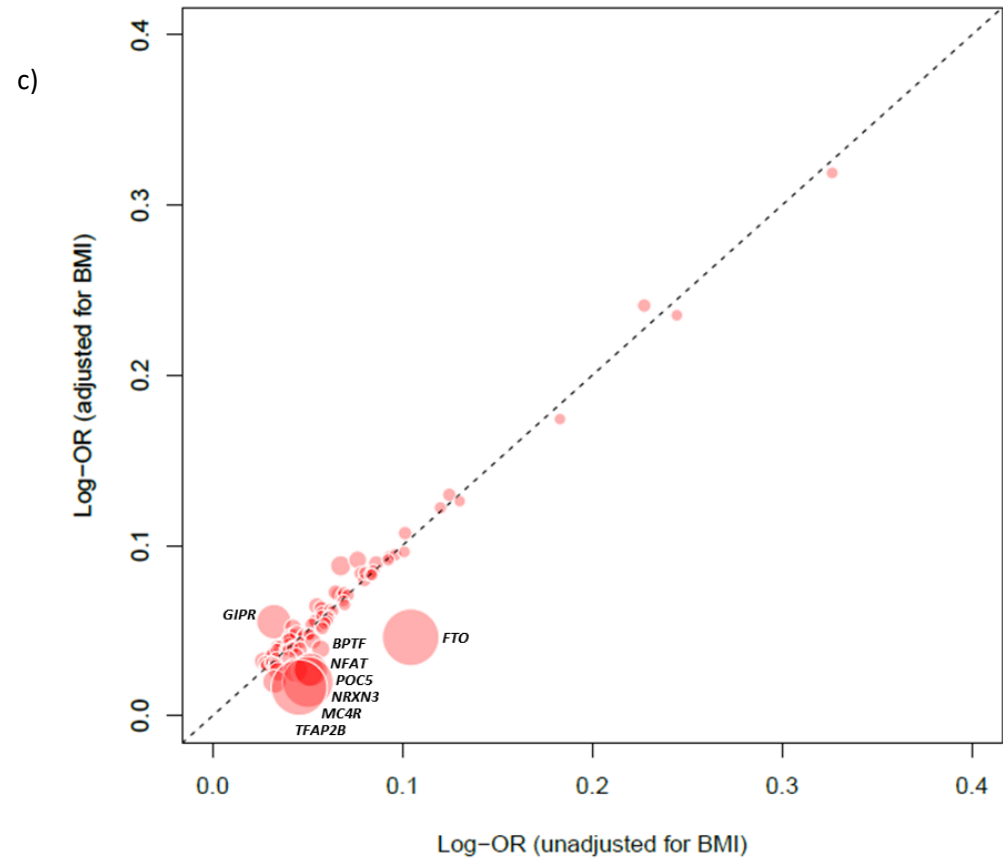
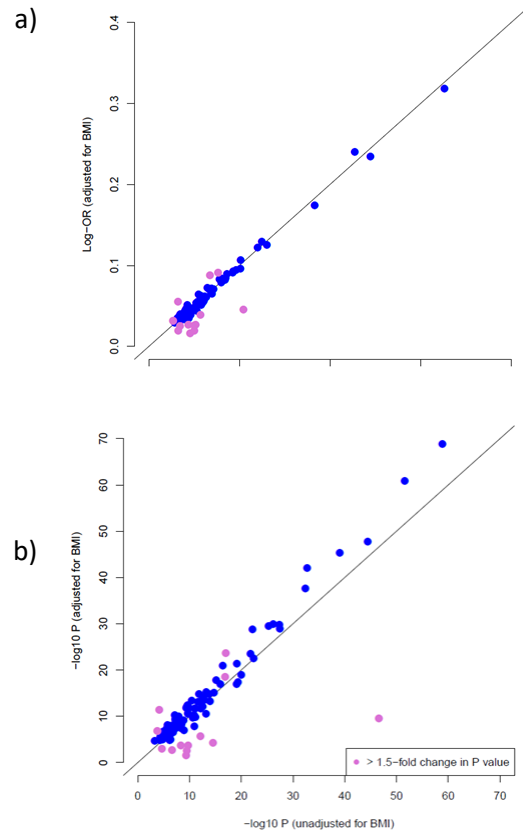
a)



b)



**Supplementary Figure 7 | Comparison of estimated effect size and  $p$ -value between BMI-adjusted and unadjusted models.** Plots comparing adjustment with BMI (x-axis) versus no adjustment for BMI (y-axis) from the trans-ethnic meta-analysis of 68,048 cases and 304,612 controls are shown for: **a)** odds ratio. Coding variants with  $>2$ -fold change ( $-\log_{10}P$  unadjusted/  $-\log_{10}P$  adjusted) are highlighted; and **b)**  $p$ -values for significant variant associations. Variants  $>1.5$ -fold change in  $p$ -value are highlighted in pink. **c)** odds ratio; where the size of the circle varies with fold change in  $p$ -values: BMI-adjusted vs BMI-unadjusted.



ii. **Supplementary Tables**

**Supplementary Tables 1 and 2 can be found in the Supplementary excel files.**

**Supplementary Table 1** | Study design, genotyping methods, quality control, and statistical analysis of studies genotyped using exome-array.

**Supplementary Table 2** | Sample size and phenotype descriptives of studies genotyped using exome-array.

**Supplementary Table 3 | Association summary statistics of coding variants attaining exome-wide significant ( $p < 2.2 \times 10^{-7}$ ) evidence of association with T2D susceptibility in the discovery analysis.**

(a) Trans-ethnic meta-analysis of 81,412 cases and 370,832.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	BMI unadjusted			BMI adjusted		
					Risk	Other		OR (95% CI)	p-value	Cochran's Q p-value	OR (95% CI)	p-value	Cochran's Q p-value
MACF1	MACF1 p.Ile39Val	rs16826069	1	39,797,055	G	A	0.212	1.06 (1.04-1.07)	$2.5 \times 10^{-14}$	0.36	1.05 (1.03-1.06)	$7.0 \times 10^{-9}$	0.82
	MACF1 p.Lys1625Asn	rs41270807	1	39,801,815	C	A	0.199	1.07 (1.05-1.09)	$2.5 \times 10^{-15}$	0.91	1.05 (1.03-1.07)	$2.5 \times 10^{-7}$	0.95
	MACF1 p.Met1424Val	rs2296172	1	39,835,817	G	A	0.193	1.06 (1.05-1.08)	$6.7 \times 10^{-16}$	0.84	1.04 (1.03-1.06)	$5.9 \times 10^{-8}$	0.89
	MACF1 p.Ala3354Thr	rs587404	1	39,908,506	A	G	0.302	1.04 (1.02-1.05)	$7.7 \times 10^{-9}$	0.30	1.03 (1.02-1.05)	$2.3 \times 10^{-6}$	0.27
FAM63A	FAM63A p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.988	1.21 (1.14-1.28)	$7.5 \times 10^{-8}$	0.29	1.19 (1.12-1.26)	$6.7 \times 10^{-7}$	0.30
GCKR	GCKR p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.630	1.06 (1.05-1.08)	$5.3 \times 10^{-25}$	0.18	1.06 (1.04-1.07)	$3.2 \times 10^{-18}$	0.44
	C2orf16 p.Ile774Val	rs1919128	2	27,801,759	A	G	0.735	1.04 (1.03-1.06)	$9.9 \times 10^{-11}$	0.62	1.04 (1.02-1.05)	$1.2 \times 10^{-8}$	0.77
	GPN1 p.Arg12Lys	rs3749147	2	27,851,918	G	A	0.763	1.04 (1.02-1.05)	$2.1 \times 10^{-8}$	0.20	1.04 (1.02-1.05)	$6.3 \times 10^{-7}$	0.36
THADA	THADA p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.895	1.08 (1.05-1.10)	$4.6 \times 10^{-15}$	0.55	1.07 (1.05-1.10)	$8.3 \times 10^{-16}$	0.59
	THADA p.Thr897Ala	rs7578597	2	43,732,823	T	C	0.898	1.06 (1.04-1.09)	$2.7 \times 10^{-9}$	0.03	1.05 (1.03-1.08)	$1.7 \times 10^{-7}$	0.024
CEP68	CEP68 p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.846	1.05 (1.04-1.07)	$8.3 \times 10^{-9}$	0.13	1.05 (1.03-1.07)	$6.6 \times 10^{-7}$	0.13
GRB14	COBLL1 p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.879	1.08 (1.06-1.11)	$8.6 \times 10^{-20}$	0.14	1.09 (1.07-1.12)	$5.0 \times 10^{-23}$	0.46
PPARG	PPARG p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.887	1.09 (1.07-1.11)	$1.4 \times 10^{-17}$	0.96	1.10 (1.07-1.12)	$2.7 \times 10^{-19}$	0.93
KIF9-PTPN23	KIF9 p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.588	1.02 (1.01-1.04)	$8.0 \times 10^{-5}$	0.84	1.03 (1.02-1.05)	$5.3 \times 10^{-8}$	0.87
	PTPN23 p.Ala818Thr	rs6780013	3	47,452,118	G	A	0.624	1.02 (1.01-1.04)	$7.0 \times 10^{-5}$	0.693	1.03 (1.02-1.04)	$3.6 \times 10^{-7}$	0.63
IGF2BP2	SEN2 p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.367	1.03 (1.01-1.04)	$1.6 \times 10^{-6}$	0.048	1.03 (1.02-1.05)	$3.0 \times 10^{-8}$	0.058
WFS1	WFS1 p.Val333Ile	rs1801212	4	6,302,519	A	G	0.748	1.07 (1.06-1.09)	$1.1 \times 10^{-24}$	0.13	1.07 (1.05-1.08)	$7.1 \times 10^{-21}$	0.15
	WFS1 p.Arg611His	rs734312	4	6,303,354	A	G	0.542	1.06 (1.04-1.07)	$2.0 \times 10^{-18}$	0.24	1.05 (1.03-1.06)	$3.7 \times 10^{-13}$	0.39
ANKH	ANKH p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.996	1.29 (1.16-1.45)	$1.4 \times 10^{-7}$	0.58	1.27 (1.13-1.41)	$3.5 \times 10^{-7}$	0.79
POC5	POC5 p.His36Arg	rs2307111	5	75,003,678	T	C	0.562	1.05 (1.04-1.07)	$1.6 \times 10^{-15}$	0.85	1.03 (1.01-1.04)	$2.1 \times 10^{-5}$	0.72
PAM-PP1P5K2	PAM p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.0450	1.13 (1.10-1.17)	$1.2 \times 10^{-16}$	0.34	1.13 (1.09-1.17)	$7.4 \times 10^{-15}$	0.66
	PP1P5K2 p.Ser1207Gly	rs36046591	5	102,537,285	G	A	0.0450	1.13 (1.09-1.17)	$1.4 \times 10^{-16}$	0.25	1.13 (1.09-1.16)	$2.8 \times 10^{-14}$	0.52
RREB1	RREB1 p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.884	1.08 (1.06-1.11)	$1.1 \times 10^{-13}$	0.75	1.10 (1.07-1.13)	$1.5 \times 10^{-17}$	0.53
	RREB1 p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.836	1.04 (1.03-1.06)	$5.5 \times 10^{-8}$	0.31	1.04 (1.02-1.06)	$2.2 \times 10^{-7}$	0.50
MHC	TCF19 p.Met131Val	rs2073721	6	31,129,616	G	A	0.749	1.04 (1.02-1.05)	$1.6 \times 10^{-10}$	0.18	1.04 (1.02-1.05)	$2.3 \times 10^{-9}$	0.36
	PRRC2A p.Leu1895Val	rs3132453	6	31,604,044	G	T	0.940	1.07 (1.05-1.10)	$9.3 \times 10^{-8}$	0.67	1.06 (1.03-1.09)	$4.9 \times 10^{-6}$	0.83
	SLC44A4 p.Met250Val	rs644827	6	31,838,441	C	T	0.559	1.03 (1.01-1.04)	$1.6 \times 10^{-5}$	0.81	1.03 (1.02-1.05)	$8.9 \times 10^{-7}$	0.80
	SLC44A4 p.Val183Ile	rs2242665	6	31,839,309	T	C	0.559	1.03 (1.01-1.04)	$1.4 \times 10^{-5}$	0.85	1.03 (1.02-1.05)	$7.1 \times 10^{-7}$	0.84
	EHMT2 p.Ser58Phe	rs115884658	6	31,864,538	A	G	0.0258	1.12 (1.08-1.17)	$4.6 \times 10^{-9}$	0.059	1.13 (1.08-1.17)	$4.2 \times 10^{-7}$	0.040
	PPT2 p.Cys5Trp	rs3134604	6	32,122,386	G	C	0.886	1.06 (1.04-1.08)	$9.4 \times 10^{-9}$	0.086	1.05 (1.03-1.07)	$4.6 \times 10^{-7}$	0.14
	BTNL2 p.Ser83Gly	rs2076530	6	32,363,816	C	T	0.421	1.03 (1.02-1.04)	$3.5 \times 10^{-5}$	0.45	1.03 (1.02-1.05)	$6.5 \times 10^{-7}$	0.52
	HLA-DQB1 p.Phe41Tyr	rs9274407	6	32,632,832	T	A	0.815	1.05 (1.03-1.07)	$6.0 \times 10^{-8}$	0.26	1.04 (1.02-1.06)	$5.4 \times 10^{-5}$	0.44
PAX4	PAX4 p.Arg190His	rs2233580	7	127,253,550	T	C	0.0294	1.36 (1.25-1.48)	$1.8 \times 10^{-12}$	0.47	1.38 (1.26-1.51)	$4.2 \times 10^{-13}$	0.50

<i>LPL</i>	<i>LPL</i> p.Ser474*	rs328	8	19,819,724	C	G	0.903	1.05 (1.03-1.08)	6.8x10 <sup>-9</sup>	0.69	1.05 (1.03-1.07)	2.3x10 <sup>-7</sup>	0.87
<i>SLC30A8</i>	<i>SLC30A8</i> p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.691	1.09 (1.08-1.11)	1.9x10 <sup>-47</sup>	0.09	1.09 (1.08-1.11)	1.3x10 <sup>-47</sup>	0.041
<i>GPSM1</i>	<i>GPSM1</i> p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.771	1.06 (1.05-1.08)	3.2x10 <sup>-16</sup>	0.20	1.06 (1.05-1.08)	6.6x10 <sup>-16</sup>	0.31
<i>KCNJ11-ABCC8</i>	<i>NUCB2</i> p.Gln338Glu	rs757081	11	17,351,683	G	C	0.320	1.04 (1.03-1.06)	8.6x10 <sup>-9</sup>	0.54	1.05 (1.04-1.07)	5.6x10 <sup>-11</sup>	0.20
	<i>KCNJ11</i> p.Val250Ile	rs5215	11	17,408,630	C	T	0.365	1.06 (1.05-1.08)	4.5x10 <sup>-21</sup>	0.66	1.07 (1.05-1.08)	3.2x10 <sup>-22</sup>	0.37
	<i>KCNJ11</i> p.Lys29Glu	rs5219	11	17,409,572	T	C	0.364	1.06 (1.05-1.07)	5.7x10 <sup>-22</sup>	0.69	1.07 (1.05-1.08)	1.5x10 <sup>-22</sup>	0.37
	<i>ABCC8</i> p.Ala1369Ser	rs757110	11	17,418,477	C	A	0.367	1.06 (1.04-1.07)	8.1x10 <sup>-19</sup>	0.66	1.06 (1.05-1.07)	5.4x10 <sup>-19</sup>	0.33
<i>PLCB3</i>	<i>PLCB3</i> p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.0585	1.04 (1.02-1.07)	0.00012	0.011	1.05 (1.03-1.08)	1.7x10 <sup>-6</sup>	0.025
<i>TPCN2</i>	<i>TPCN2</i> p.Val219Ile	rs72928978	11	68,831,364	G	A	0.890	1.05 (1.02-1.07)	5.2x10 <sup>-7</sup>	0.55	1.05 (1.03-1.07)	1.8x10 <sup>-8</sup>	0.47
	<i>TPCN2</i> p.Met484Leu	rs35264875	11	68,846,399	A	T	0.847	1.05 (1.03-1.08)	4.5x10 <sup>-5</sup>	0.24	1.07 (1.04-1.09)	9.6x10 <sup>-8</sup>	0.20
<i>CENTD2</i>	<i>ARAP1</i> p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.733	1.04 (1.02-1.05)	4.8x10 <sup>-8</sup>	0.77	1.05 (1.03-1.06)	5.2x10 <sup>-10</sup>	0.61
<i>KLHDC5</i>	<i>MRPS35</i> p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.850	1.06 (1.04-1.08)	1.4x10 <sup>-11</sup>	0.72	1.05 (1.03-1.07)	1.5x10 <sup>-8</sup>	0.85
	<i>MANSC4</i> p.Thr163Met	rs11049125	12	27,916,206	G	A	0.849	1.05 (1.04-1.07)	8.8x10 <sup>-9</sup>	0.75	1.05 (1.03-1.06)	3.0x10 <sup>-6</sup>	0.84
	<i>MANSC4</i> p.Leu157Ser	rs11049126	12	27,916,224	A	G	0.849	1.05 (1.04-1.07)	1.4x10 <sup>-8</sup>	0.73	1.05 (1.03-1.06)	3.9x10 <sup>-6</sup>	0.83
<i>WSCD2</i>	<i>WSCD2</i> p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.719	1.03 (1.02-1.05)	3.3x10 <sup>-8</sup>	0.076	1.03 (1.02-1.05)	1.2x10 <sup>-7</sup>	0.28
<i>HNF1A</i>	<i>HNF1A</i> p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.323	1.04 (1.03-1.06)	1.1x10 <sup>-11</sup>	0.00065	1.04 (1.02-1.06)	1.9x10 <sup>-10</sup>	0.0023
	<i>HNF1A</i> p.Ala146Val	rs1800574	12	121,416,864	T	C	0.029	1.11 (1.06-1.15)	6.1x10 <sup>-8</sup>	0.77	1.10 (1.06-1.15)	1.3x10 <sup>-7</sup>	0.43
<i>MPHOSPH9</i>	<i>SBNO1</i> p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.815	1.04 (1.02-1.06)	5.7x10 <sup>-7</sup>	0.87	1.04 (1.02-1.06)	1.1x10 <sup>-7</sup>	0.89
<i>ZZEF1</i>	<i>ZZEF1</i> p.Ile402Val	rs781831	17	3,947,644	C	T	0.422	1.04 (1.03-1.05)	8.3x10 <sup>-11</sup>	0.49	1.03 (1.02-1.05)	1.8x10 <sup>-7</sup>	0.87
	<i>ZZEF1</i> p.Leu360Pro	rs781852	17	3,953,102	G	A	0.400	1.04 (1.03-1.06)	8.8x10 <sup>-10</sup>	0.31	1.03 (1.02-1.05)	4.4x10 <sup>-7</sup>	0.69
<i>MLX</i>	<i>MLX</i> p.Gln139Arg	rs665268	17	40,722,029	G	A	0.294	1.04 (1.02-1.05)	2.0x10 <sup>-8</sup>	0.32	1.03 (1.02-1.04)	1.1x10 <sup>-5</sup>	0.50
<i>TTLL6-CALCOCO2</i>	<i>TTLL6</i> p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.754	1.04 (1.02-1.06)	1.2x10 <sup>-7</sup>	0.33	1.03 (1.01-1.04)	0.00098	0.30
	<i>CALCOCO2</i> p.Pro347Ala	rs10278	17	46,939,658	C	G	0.710	1.04 (1.02-1.05)	4.7x10 <sup>-7</sup>	0.72	1.03 (1.02-1.05)	3.0x10 <sup>-5</sup>	0.59
<i>C17orf58</i>	<i>C17orf58</i> p.Ile92Val	rs9891146	17	65,988,049	T	C	0.332	1.04 (1.02-1.05)	7.2x10 <sup>-7</sup>	0.20	1.02 (1.00-1.03)	0.0027	0.43
<i>CILP2</i>	<i>NCAN</i> p.Pro92Ser	rs2228603	19	19,329,924	T	C	0.0711	1.07 (1.05-1.10)	1.8x10 <sup>-10</sup>	0.025	1.08 (1.05-1.11)	3.7x10 <sup>-11</sup>	0.027
	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0755	1.07 (1.05-1.10)	4.8x10 <sup>-12</sup>	0.099	1.09 (1.06-1.11)	3.4x10 <sup>-15</sup>	0.089
	<i>ZNF101</i> Splice region	rs2304130	19	19,789,528	G	A	0.100	1.04 (1.02-1.06)	1.7x10 <sup>-5</sup>	0.29	1.05 (1.03-1.07)	3.0x10 <sup>-9</sup>	0.28
<i>GIPR</i>	<i>GIPR</i> p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.200	1.03 (1.02-1.05)	7.1x10 <sup>-5</sup>	0.96	1.06 (1.04-1.07)	6.8x10 <sup>-12</sup>	0.93
<i>ZHX3</i>	<i>ZHX3</i> p.Asn310Ser	rs17265513	20	39,832,628	C	T	0.174	1.04 (1.02-1.06)	6.8x10 <sup>-6</sup>	0.89	1.04 (1.02-1.05)	3.2x10 <sup>-5</sup>	0.88
<i>HNF4A</i>	<i>HNF4A</i> p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.0316	1.09 (1.05-1.13)	2.6x10 <sup>-8</sup>	0.0005	1.10 (1.06-1.14)	5.0x10 <sup>-8</sup>	0.0017
<i>MTMR3-ASCC2</i>	<i>ASCC2</i> p.Pro423Ser	rs36571	22	30,200,713	G	A	0.929	1.08 (1.06-1.11)	5.5x10 <sup>-10</sup>	0.20	1.09 (1.06-1.11)	5.5x10 <sup>-12</sup>	0.36
	<i>ASCC2</i> p.Asp407His	rs28265	22	30,200,761	C	G	0.925	1.09 (1.06-1.11)	2.1x10 <sup>-12</sup>	0.12	1.09 (1.07-1.12)	4.4x10 <sup>-14</sup>	0.34
	<i>ASCC2</i> p.Val123Ile	rs11549795	22	30,221,120	C	T	0.926	1.08 (1.06-1.11)	4.8x10 <sup>-12</sup>	0.077	1.09 (1.06-1.12)	1.5x10 <sup>-13</sup>	0.21
	<i>MTMR3</i> p.Asn960Ser	rs41278853	22	30,416,527	A	G	0.926	1.09 (1.06-1.11)	5.6x10 <sup>-13</sup>	0.064	1.09 (1.06-1.12)	5.0x10 <sup>-14</sup>	0.21
<i>PNPLA3</i>	<i>PNPLA3</i> p.Ile148Met	rs738409	22	44,324,727	G	C	0.239	1.04 (1.03-1.05)	2.1x10 <sup>-10</sup>	0.98	1.05 (1.03-1.06)	2.8x10 <sup>-11</sup>	0.99
<i>PIM3</i>	<i>PIM3</i> p.Val300Ala	rs4077129	22	50,356,693	T	C	0.276	1.04 (1.02-1.05)	1.9x10 <sup>-7</sup>	0.79	1.04 (1.02-1.06)	3.5x10 <sup>-8</sup>	0.51

(b) European-specific meta-analysis of 48,286 cases and 250,671 controls.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	BMI unadjusted			BMI adjusted		
					Risk	Other		OR (95% CI)	p-value	Cochran's Q p-value	OR (95% CI)	p-value	Cochran's Q p-value
MACF1	MACF1 p.Ile39Val	rs16826069	1	39,797,055	G	A	0.221	1.06 (1.04-1.08)	8.9x10 <sup>-11</sup>	0.82	1.05 (1.03-1.07)	8.8x10 <sup>-9</sup>	0.91
	MACF1 p.Lys1625Asn	rs41270807	1	39,801,815	C	A	0.217	1.06 (1.04-1.08)	4.4x10 <sup>-10</sup>	0.89	1.05 (1.03-1.07)	7.4x10 <sup>-8</sup>	0.93
	MACF1 p.Met1424Val	rs2296172	1	39,835,817	G	A	0.217	1.06 (1.04-1.08)	1.2x10 <sup>-10</sup>	0.87	1.05 (1.03-1.07)	1.2x10 <sup>-8</sup>	0.93
	MACF1 p.Ala3354Thr	rs587404	1	39,908,506	A	G	0.296	1.04 (1.02-1.06)	1.7x10 <sup>-7</sup>	0.63	1.04 (1.02-1.05)	7.3x10 <sup>-8</sup>	0.79
FAM63A	FAM63A p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.986	1.22 (1.14-1.30)	5.8x10 <sup>-8</sup>	0.43	1.20 (1.13-1.28)	5.9x10 <sup>-8</sup>	0.43
GCKR	GCKR p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.617	1.06 (1.04-1.07)	1.0x10 <sup>-15</sup>	0.088	1.05 (1.04-1.07)	9.9x10 <sup>-15</sup>	0.44
	C2orf16 p.Ile774Val	rs1919128	2	27,801,759	A	G	0.743	1.04 (1.02-1.05)	2.1x10 <sup>-6</sup>	0.43	1.03 (1.02-1.05)	4.5x10 <sup>-6</sup>	0.66
	GPN1 p.Arg12Lys	rs3749147	2	27,851,918	G	A	0.752	1.04 (1.02-1.06)	6.9x10 <sup>-6</sup>	0.15	1.03 (1.02-1.05)	2.0x10 <sup>-5</sup>	0.32
THADA	THADA p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.889	1.08 (1.05-1.10)	1.1x10 <sup>-12</sup>	0.38	1.08 (1.06-1.10)	9.9x10 <sup>-15</sup>	0.47
	THADA p.Thr897Ala	rs7578597	2	43,732,823	T	C	0.909	1.07 (1.04-1.11)	3.0x10 <sup>-9</sup>	0.42	1.08 (1.05-1.11)	1.6x10 <sup>-10</sup>	0.46
CEP68	CEP68 p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.833	1.05 (1.03-1.07)	7.9x10 <sup>-6</sup>	0.18	1.05 (1.03-1.07)	6.0x10 <sup>-6</sup>	0.18
GRB14	COBL1 p.Asu901Asp	rs7607980	2	165,551,201	T	C	0.881	1.09 (1.06-1.11)	5.0x10 <sup>-15</sup>	0.061	1.09 (1.07-1.12)	6.5x10 <sup>-19</sup>	0.31
PPARG	PPARG p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.871	1.08 (1.05-1.10)	4.8x10 <sup>-12</sup>	0.88	1.09 (1.07-1.12)	1.0x10 <sup>-16</sup>	0.83
KIF9-PTPN23	KIF9 p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.599	1.03 (1.01-1.04)	8.4x10 <sup>-5</sup>	0.40	1.03 (1.02-1.05)	6.7x10 <sup>-7</sup>	0.59
	PTPN23 p.Ala818Thr	rs6780013	3	47,452,118	G	A	0.616	1.03 (1.01-1.04)	2.5x10 <sup>-5</sup>	0.78	1.03 (1.02-1.05)	2.0x10 <sup>-7</sup>	0.79
IGF2BP2	SEN2 p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.338	1.03 (1.01-1.04)	6.7x10 <sup>-5</sup>	0.26	1.03 (1.02-1.05)	9.6x10 <sup>-6</sup>	0.25
WFS1	WFS1 p.Val333Ile	rs1801212	4	6,302,519	A	G	0.710	1.07 (1.05-1.09)	6.7x10 <sup>-20</sup>	0.16	1.06 (1.05-1.08)	2.1x10 <sup>-17</sup>	0.13
	WFS1 p.Arg611His	rs734312	4	6,303,354	A	G	0.532	1.05 (1.04-1.07)	5.6x10 <sup>-13</sup>	0.47	1.05 (1.03-1.06)	7.9x10 <sup>-12</sup>	0.65
ANKH	ANKH p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.995	1.29 (1.15-1.45)	2.0x10 <sup>-7</sup>	0.16	1.28 (1.14-1.43)	1.1x10 <sup>-7</sup>	0.32
POC5	POC5 p.His36Arg	rs2307111	5	75,003,678	T	C	0.597	1.06 (1.04-1.07)	4.8x10 <sup>-12</sup>	0.30	1.03 (1.02-1.05)	2.6x10 <sup>-6</sup>	0.55
PAM-PIIP5K2	PAM p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.051	1.13 (1.09-1.17)	5.9x10 <sup>-12</sup>	0.55	1.13 (1.09-1.17)	3.5x10 <sup>-13</sup>	0.77
	PIIP5K2 p.Ser1207Gly	rs36046591	5	102,537,285	G	A	0.051	1.12 (1.08-1.16)	1.3x10 <sup>-11</sup>	0.52	1.12 (1.09-1.16)	1.1x10 <sup>-12</sup>	0.74
RREB1	RREB1 p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.887	1.10 (1.07-1.13)	1.6x10 <sup>-12</sup>	0.98	1.09 (1.06-1.12)	1.8x10 <sup>-13</sup>	0.94
	RREB1 p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.807	1.04 (1.02-1.06)	5.8x10 <sup>-6</sup>	0.47	1.04 (1.02-1.06)	3.1x10 <sup>-6</sup>	0.64
MHC	TCF19 p.Met131Val	rs2073721	6	31,129,616	G	A	0.742	1.04 (1.02-1.06)	5.6x10 <sup>-9</sup>	0.039	1.04 (1.03-1.06)	6.1x10 <sup>-10</sup>	0.16
	PRRC2A p.Leu1895Val	rs3132453	6	31,604,044	G	T	0.926	1.07 (1.04-1.10)	3.0x10 <sup>-7</sup>	0.56	1.06 (1.03-1.09)	1.0x10 <sup>-5</sup>	0.75
	SLC44A4 p.Met250Val	rs644827	6	31,838,441	C	T	0.535	1.03 (1.02-1.05)	3.0x10 <sup>-6</sup>	0.74	1.04 (1.02-1.05)	1.8x10 <sup>-7</sup>	0.64
	SLC44A4 p.Val183Ile	rs2242665	6	31,839,309	T	C	0.535	1.03 (1.02-1.05)	1.9x10 <sup>-6</sup>	0.79	1.04 (1.02-1.05)	1.0x10 <sup>-7</sup>	0.704
	EHMT2 p.Ser58Phe	rs115884658	6	31,864,538	A	G	0.031	1.10 (1.05-1.15)	5.3x10 <sup>-6</sup>	0.13	1.13 (1.08-1.18)	4.1x10 <sup>-9</sup>	0.088
	PPT2 p.Cys5Trp	rs3134604	6	32,122,386	G	C	0.868	1.06 (1.04-1.09)	1.7x10 <sup>-8</sup>	0.15	1.06 (1.03-1.08)	1.2x10 <sup>-7</sup>	0.18
	BTNL2 p.Ser83Gly	rs2076530	6	32,363,816	C	T	0.434	1.03 (1.02-1.05)	3.8x10 <sup>-6</sup>	0.30	1.04 (1.03-1.05)	3.9x10 <sup>-9</sup>	0.48
	HLA-DQB1 p.Phe41Tyr	rs9274407	6	32,632,832	T	A	0.818	1.04 (1.02-1.07)	6.2x10 <sup>-5</sup>	0.093	1.04 (1.02-1.06)	9.2x10 <sup>-5</sup>	0.18
PAX4	PAX4 p.Arg190His	rs2233580	7	127,253,550	T	C	N/A	N/A	N/A	N/A	N/A	N/A	N/A
LPL	LPL p.Ser474*	rs328	8	19,819,724	C	G	0.902	1.05 (1.03-1.08)	3.0x10 <sup>-6</sup>	0.82	1.05 (1.03-1.07)	2.6x10 <sup>-6</sup>	0.95
SLC30A8	SLC30A8 p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.680	1.09 (1.07-1.10)	5.5x10 <sup>-30</sup>	0.12	1.09 (1.07-1.11)	7.7x10 <sup>-36</sup>	0.045
GPSM1	GPSM1 p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.747	1.07 (1.05-1.09)	4.8x10 <sup>-15</sup>	0.21	1.07 (1.05-1.08)	2.0x10 <sup>-15</sup>	0.34
	NUCB2 p.Gln338Glu	rs757081	11	17,351,683	G	C	0.340	1.05 (1.03-1.07)	1.4x10 <sup>-8</sup>	0.27	1.06 (1.04-1.08)	2.9x10 <sup>-12</sup>	0.13

KCNJ11- ABCC8	KCNJ11 p.Val250Ile	rs5215	11	17,408,630	C	T	0.389	1.06 (1.05-1.08)	3.8x10 <sup>-17</sup>	0.91	1.07 (1.05-1.08)	4.6x10 <sup>-22</sup>	0.72
	KCNJ11 p.Lys29Glu	rs5219	11	17,409,572	T	C	0.389	1.06 (1.05-1.08)	4.8x10 <sup>-17</sup>	0.91	1.07 (1.05-1.08)	6.6x10 <sup>-22</sup>	0.73
	ABCC8 p.Ala1369Ser	rs757110	11	17,418,477	C	A	0.390	1.06 (1.04-1.07)	4.9x10 <sup>-15</sup>	0.88	1.06 (1.05-1.08)	2.1x10 <sup>-19</sup>	0.72
PLCB3	PLCB3 p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.071	1.05 (1.02-1.08)	1.3x10 <sup>-5</sup>	0.067	1.06 (1.03-1.09)	1.8x10 <sup>-7</sup>	0.17
TPCN2	TPCN2 p.Val219Ile	rs72928978	11	68,831,364	G	A	0.857	1.05 (1.02-1.07)	6.7x10 <sup>-6</sup>	0.17	1.05 (1.02-1.07)	5.1x10 <sup>-6</sup>	0.13
	TPCN2 p.Met484Leu	rs35264875	11	68,846,399	A	T	0.827	1.07 (1.04-1.09)	1.6x10 <sup>-6</sup>	0.14	1.06 (1.04-1.09)	2.2x10 <sup>-6</sup>	0.18
CENTD2	ARAP1 p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.721	1.04 (1.02-1.06)	1.5x10 <sup>-5</sup>	0.63	1.05 (1.04-1.07)	2.1x10 <sup>-9</sup>	0.44
KLHDC5	MRPS35 p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.840	1.06 (1.04-1.08)	1.6x10 <sup>-9</sup>	0.49	1.05 (1.03-1.07)	2.6x10 <sup>-8</sup>	0.67
	MANSC4 p.Thr163Met	rs11049125	12	27,916,206	G	A	0.842	1.06 (1.04-1.08)	1.4x10 <sup>-7</sup>	0.68	1.05 (1.03-1.07)	7.8x10 <sup>-7</sup>	0.77
	MANSC4 p.Leu157Ser	rs11049126	12	27,916,224	A	G	0.842	1.06 (1.03-1.08)	1.8x10 <sup>-7</sup>	0.64	1.05 (1.03-1.07)	9.6x10 <sup>-7</sup>	0.75
WSCD2	WSCD2 p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.726	1.04 (1.02-1.05)	8.7x10 <sup>-8</sup>	0.023	1.04 (1.02-1.05)	6.3x10 <sup>-8</sup>	0.14
HNF1A	HNF1A p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.337	1.04 (1.02-1.06)	1.6x10 <sup>-7</sup>	0.00051	1.04 (1.02-1.05)	1.4x10 <sup>-7</sup>	0.0040
	HNF1A p.Ala146Val	rs1800574	12	121,416,864	T	C	0.033	1.11 (1.06-1.16)	3.9x10 <sup>-7</sup>	0.92	1.10 (1.06-1.15)	1.7x10 <sup>-7</sup>	0.54
MPHOSPH9	SBNO1 p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.796	1.04 (1.02-1.06)	1.1x10 <sup>-5</sup>	0.72	1.04 (1.02-1.06)	3.5x10 <sup>-6</sup>	0.76
ZZEF1	ZZEF1 p.Ile402Val	rs781831	17	3,947,644	C	T	0.403	1.05 (1.03-1.06)	3.8x10 <sup>-9</sup>	0.43	1.04 (1.02-1.05)	2.0x10 <sup>-7</sup>	0.87
	ZZEF1 p.Leu360Pro	rs781852	17	3,953,102	G	A	0.387	1.05 (1.03-1.07)	9.1x10 <sup>-11</sup>	0.57	1.04 (1.03-1.06)	7.6x10 <sup>-9</sup>	0.90
MLX	MLX p.Gln139Arg	rs665268	17	40,722,029	G	A	0.272	1.03 (1.01-1.05)	6.1x10 <sup>-5</sup>	0.73	1.03 (1.01-1.04)	0.00053	0.92
TTLL6- CALCOCO2	TTLL6 p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.754	1.04 (1.02-1.06)	4.4x10 <sup>-6</sup>	0.61	1.03 (1.01-1.05)	0.00025	0.58
	CALCOCO2 p.Pro347Ala	rs10278	17	46,939,658	C	G	0.706	1.05 (1.03-1.06)	3.1x10 <sup>-8</sup>	0.91	1.04 (1.02-1.05)	2.6x10 <sup>-6</sup>	0.74
C17orf58	C17orf58 p.Ile92Val	rs9891146	17	65,988,049	T	C	0.277	1.04 (1.02-1.06)	1.3x10 <sup>-7</sup>	0.32	1.02 (1.00-1.04)	0.00058	0.44
CILP2	NCAN p.Pro92Ser	rs2228603	19	19,329,924	T	C	0.078	1.07 (1.04-1.10)	3.5x10 <sup>-7</sup>	0.15	1.08 (1.05-1.11)	2.0x10 <sup>-9</sup>	0.23
	TM6SF2 p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.079	1.09 (1.06-1.12)	1.7x10 <sup>-10</sup>	0.71	1.09 (1.06-1.12)	1.3x10 <sup>-12</sup>	0.75
	ZNF101 Splice region	rs2304130	19	19,789,528	G	A	0.084	1.07 (1.04-1.10)	6.5x10 <sup>-8</sup>	0.36	1.08 (1.05-1.11)	3.1x10 <sup>-11</sup>	0.55
GIPR	GIPR p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.218	1.03 (1.02-1.05)	0.00021	0.84	1.06 (1.04-1.08)	3.1x10 <sup>-12</sup>	0.84
ZHX3	ZHX3 p.Asn310Ser	rs17265513	20	39,832,628	C	T	0.211	1.05 (1.03-1.07)	9.2x10 <sup>-8</sup>	0.86	1.04 (1.02-1.05)	2.9x10 <sup>-6</sup>	0.78
HNF4A	HNF4A p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.035	1.09 (1.04-1.13)	3.1x10 <sup>-6</sup>	0.00082	1.09 (1.05-1.13)	6.5x10 <sup>-7</sup>	0.0018
MTMR3- ASCC2	ASCC2 p.Pro423Ser	rs36571	22	30,200,713	G	A	0.917	1.09 (1.06-1.12)	3.0x10 <sup>-10</sup>	0.11	1.09 (1.06-1.12)	7.7x10 <sup>-12</sup>	0.42
	ASCC2 p.Asp407His	rs28265	22	30,200,761	C	G	0.916	1.09 (1.06-1.12)	5.2x10 <sup>-11</sup>	0.15	1.09 (1.06-1.12)	1.2x10 <sup>-12</sup>	0.54
	ASCC2 p.Val123Ile	rs11549795	22	30,221,120	C	T	0.916	1.09 (1.06-1.12)	2.3x10 <sup>-10</sup>	0.10	1.09 (1.06-1.12)	4.3x10 <sup>-12</sup>	0.42
	MTMR3 p.Asn960Ser	rs41278853	22	30,416,527	A	G	0.917	1.09 (1.06-1.12)	4.0x10 <sup>-11</sup>	0.075	1.09 (1.06-1.12)	1.7x10 <sup>-12</sup>	0.31
PNPLA3	PNPLA3 p.Ile148Met	rs738409	22	44,324,727	G	C	0.227	1.04 (1.02-1.06)	8.1x10 <sup>-7</sup>	0.93	1.04 (1.03-1.06)	3.0x10 <sup>-8</sup>	0.96
PIM3	PIM3 p.Val300Ala	rs4077129	22	50,356,693	T	C	0.259	1.04 (1.02-1.06)	7.0x10 <sup>-6</sup>	0.84	1.04 (1.02-1.05)	1.1x10 <sup>-5</sup>	0.49

Chr: chromosome. RAF: risk allele frequency. BMI: body mass index. OR: odds ratio. CI: confidence interval.



**Supplementary Table 4 | Summary statistics for additive, recessive and dominant models for coding variants attaining exome-wide significant evidence ( $p < 2.2 \times 10^{-7}$ ) of association with T2D susceptibility in the discovery analysis.**

(a) Trans-ethnic meta-analysis of 58,425 cases and 188,032 controls.

(i) BMI unadjusted analyses.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	Additive		Recessive		Dominant	
					Risk	Other		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
MACF1	MACF1 p.Ile39Val	rs16826069	1	39,797,055	G	A	0.210	1.05 (1.03-1.07)	8.8x10 <sup>-10</sup>	1.12 (1.07-1.17)	1.6x10 <sup>-7</sup>	1.05 (1.03-1.07)	2.2x10 <sup>-7</sup>
	MACF1 p.Lys1625Asn	rs41270807	1	39,801,815	C	A	0.195	1.06 (1.04-1.08)	1.2x10 <sup>-9</sup>	1.14 (1.08-1.20)	7.4x10 <sup>-7</sup>	1.06 (1.04-1.08)	2.2x10 <sup>-7</sup>
	MACF1 p.Met1424Val	rs2296172	1	39,835,817	G	A	0.187	1.05 (1.04-1.07)	1.4x10 <sup>-10</sup>	1.14 (1.08-1.19)	5.2x10 <sup>-8</sup>	1.05 (1.03-1.07)	7.3x10 <sup>-8</sup>
	MACF1 p.Ala3354Thr	rs587404	1	39,908,506	A	G	0.301	1.03 (1.01-1.04)	1.3x10 <sup>-5</sup>	1.04 (1.02-1.06)	5.3x10 <sup>-5</sup>	1.04 (1.01-1.07)	0.0032
FAM63A	FAM63A p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.988	1.23 (1.15-1.32)	1.2x10 <sup>-6</sup>	1.45 (0.69-3.06)	0.76	1.23 (1.15-1.32)	6.7x10 <sup>-7</sup>
GCKR	GCKR p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.642	1.06 (1.04-1.07)	8.8x10 <sup>-17</sup>	1.08 (1.05-1.10)	1.0x10 <sup>-13</sup>	1.08 (1.05-1.11)	1.5x10 <sup>-9</sup>
	C2orf16 p.Ile774Val	rs1919128	2	27,801,759	A	G	0.74	1.04 (1.02-1.06)	1.0x10 <sup>-8</sup>	1.05 (1.02-1.09)	0.00064	1.05 (1.03-1.07)	4.2x10 <sup>-8</sup>
	GPN1 p.Arg12Lys	rs3749147	2	27,851,918	G	A	0.771	1.04 (1.02-1.05)	6.7x10 <sup>-7</sup>	1.04 (1.02-1.06)	1.2x10 <sup>-5</sup>	1.06 (1.02-1.11)	0.00024
THADA	THADA p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.9	1.07 (1.04-1.09)	7.6x10 <sup>-10</sup>	1.07 (1.05-1.10)	1.9x10 <sup>-10</sup>	1.06 (0.97-1.17)	0.2
	THADA p.Thr897Ala	rs7578597	2	43,732,823	T	C	0.9	1.05 (1.02-1.07)	0.00011	1.05 (0.95-1.15)	0.18	1.05 (1.02-1.08)	0.00011
CEP68	CEP68 p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.849	1.05 (1.03-1.07)	2.4x10 <sup>-6</sup>	1.06 (1.03-1.08)	4.3x10 <sup>-6</sup>	1.09 (1.03-1.17)	0.023
GRB14	COBLL1 p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.878	1.08 (1.06-1.11)	5.7x10 <sup>-13</sup>	1.13 (1.04-1.23)	0.0036	1.09 (1.07-1.12)	7.5x10 <sup>-13</sup>
PPARG	PPARG p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.888	1.07 (1.05-1.10)	4.3x10 <sup>-10</sup>	1.17 (1.07-1.28)	0.00017	1.08 (1.05-1.10)	3.0x10 <sup>-9</sup>
KIF9-PTPN23	KIF9 p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.587	1.02 (1.01-1.04)	0.0007	1.04 (1.02-1.06)	8.9x10 <sup>-5</sup>	1.01 (0.99-1.04)	0.18
	PTPN23 p.Ala818Thr	rs6780013	3	47,452,118	G	A	0.628	1.02 (1.01-1.04)	0.0013	1.03 (1.01-1.06)	0.00082	1.02 (0.99-1.05)	0.13
IGF2BP2	SEN2 p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.374	1.03 (1.02-1.05)	2.3x10 <sup>-6</sup>	1.04 (1.02-1.06)	3.0x10 <sup>-5</sup>	1.05 (1.02-1.08)	0.001
WFS1	WFS1 p.Val333Ile	rs1801212	4	6,302,519	A	G	0.753	1.07 (1.05-1.09)	2.0x10 <sup>-18</sup>	1.08 (1.06-1.11)	3.5x10 <sup>-16</sup>	1.12 (1.07-1.16)	6.8x10 <sup>-8</sup>
	WFS1 p.Arg611His	rs734312	4	6,303,354	A	G	0.543	1.05 (1.04-1.07)	1.7x10 <sup>-11</sup>	1.06 (1.03-1.08)	1.5x10 <sup>-6</sup>	1.08 (1.06-1.11)	3.2x10 <sup>-9</sup>
ANKH	ANKH p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.996	1.20 (1.06-1.36)	0.0018	1.20 (1.06-1.35)	0.0019	3.22 (0.48-21.66)	0.24
POC5	POC5 p.His36Arg	rs2307111	5	75,003,678	T	C	0.551	1.04 (1.03-1.06)	4.7x10 <sup>-8</sup>	1.05 (1.02-1.08)	4.2x10 <sup>-5</sup>	1.06 (1.03-1.08)	9.9x10 <sup>-7</sup>
PAM-PP1P5K2	PAM p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.044	1.12 (1.07-1.16)	5.7x10 <sup>-9</sup>	1.36 (1.07-1.72)	0.0039	1.12 (1.07-1.16)	1.4x10 <sup>-8</sup>
	PP1P5K2 p.Ser1207Gly	rs36046591	5	102,537,285	G	A	0.045	1.12 (1.08-1.16)	5.0x10 <sup>-10</sup>	1.47 (1.18-1.83)	0.00035	1.12 (1.08-1.16)	2.8x10 <sup>-9</sup>
RREB1	RREB1 p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.889	1.09 (1.06-1.12)	9.1x10 <sup>-10</sup>	1.10 (1.07-1.14)	4.9x10 <sup>-10</sup>	1.12 (1.00-1.24)	0.063
	RREB1 p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.837	1.04 (1.02-1.06)	1.7x10 <sup>-6</sup>	1.05 (1.03-1.07)	5.2x10 <sup>-7</sup>	1.04 (0.98-1.09)	0.14
MHC	TCF19 p.Met131Val	rs2073721	6	31,129,616	G	A	0.747	1.03 (1.02-1.05)	1.6x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.00021	1.07 (1.03-1.11)	0.00041
	PRRC2A p.Leu1895Val	rs3132453	6	31,604,044	G	T	0.943	1.07 (1.03-1.10)	2.3x10 <sup>-5</sup>	1.07 (1.04-1.11)	1.0x10 <sup>-5</sup>	1.05 (0.90-1.23)	0.59
	SLC44A4 p.Met250Val	rs644827	6	31,838,441	C	T	0.558	1.02 (1.01-1.04)	0.00043	1.03 (1.01-1.05)	0.0062	1.04 (1.01-1.07)	0.002
	SLC44A4 p.Val183Ile	rs2242665	6	31,839,309	T	C	0.558	1.02 (1.01-1.04)	0.00036	1.03 (1.01-1.05)	0.0072	1.04 (1.01-1.07)	0.0012
	EHMT2 p.Ser58Phe	rs115884658	6	31,864,538	A	G	0.029	1.10 (1.05-1.15)	0.00081	1.10 (1.05-1.15)	0.00079	1.33 (0.98-1.81)	0.27
	PPT2 p.Cys5Trp	rs3134604	6	32,122,386	G	C	0.892	1.06 (1.03-1.08)	6.1x10 <sup>-6</sup>	1.06 (1.03-1.09)	6.3x10 <sup>-6</sup>	1.11 (1.02-1.20)	0.047
	BTNL2 p.Ser83Gly	rs2076530	6	32,363,816	C	T	0.416	1.02 (1.01-1.04)	0.00047	1.03 (1.01-1.06)	0.022	1.03 (1.01-1.05)	0.00091
	HLA-DQB1 p.Phe41Tyr	rs9274407	6	32,632,832	T	A	0.81	1.04 (1.02-1.06)	5.2x10 <sup>-5</sup>	1.05 (1.03-1.08)	2.7x10 <sup>-5</sup>	1.05 (0.99-1.11)	0.18

<i>PAX4</i>	<i>PAX4</i> p.Arg190His	rs2233580	7	127,253,550	T	C	0.084	1.39 (1.26-1.52)	1.4x10 <sup>-12</sup>	2.04 (1.35-3.09)	0.00022	1.40 (1.27-1.54)	1.1x10 <sup>-11</sup>
<i>LPL</i>	<i>LPL</i> p.Ser474*	rs328	8	19,819,724	C	G	0.905	1.05 (1.02-1.07)	3.1x10 <sup>-5</sup>	1.11 (1.01-1.22)	0.026	1.05 (1.02-1.08)	6.2x10 <sup>-5</sup>
<i>SLC30A8</i>	<i>SLC30A8</i> p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.69	1.08 (1.07-1.10)	7.4x10 <sup>-26</sup>	1.10 (1.08-1.12)	9.1x10 <sup>-23</sup>	1.13 (1.09-1.17)	2.0x10 <sup>-12</sup>
<i>GPSM1</i>	<i>GPSM1</i> p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.768	1.07 (1.05-1.09)	5.9x10 <sup>-15</sup>	1.07 (1.05-1.10)	2.2x10 <sup>-12</sup>	1.13 (1.08-1.18)	2.5x10 <sup>-8</sup>
<i>KCNJ11-ABCC8</i>	<i>NUCB2</i> p.Gln338Glu	rs757081	11	17,351,683	G	C	0.316	1.05 (1.03-1.06)	3.3x10 <sup>-7</sup>	1.07 (1.03-1.10)	0.00071	1.06 (1.03-1.08)	1.7x10 <sup>-6</sup>
	<i>KCNJ11</i> p.Val250Ile	rs5215	11	17,408,630	C	T	0.368	1.06 (1.04-1.07)	1.6x10 <sup>-13</sup>	1.09 (1.06-1.12)	3.2x10 <sup>-9</sup>	1.07 (1.05-1.09)	2.9x10 <sup>-10</sup>
	<i>KCNJ11</i> p.Lys29Glu	rs5219	11	17,409,572	T	C	0.367	1.06 (1.04-1.07)	4.2x10 <sup>-14</sup>	1.09 (1.06-1.12)	3.8x10 <sup>-10</sup>	1.07 (1.05-1.09)	1.7x10 <sup>-10</sup>
	<i>ABCC8</i> p.Ala1369Ser	rs757110	11	17,418,477	C	A	0.37	1.05 (1.04-1.07)	4.4x10 <sup>-12</sup>	1.09 (1.06-1.12)	2.3x10 <sup>-10</sup>	1.06 (1.04-1.08)	6.1x10 <sup>-8</sup>
<i>PLCB3</i>	<i>PLCB3</i> p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.061	1.03 (1.00-1.06)	0.011	1.03 (1.00-1.07)	0.007	1.01 (0.87-1.17)	0.78
<i>TPCN2</i>	<i>TPCN2</i> p.Val219Ile	rs72928978	11	68,831,364	G	A	0.888	1.05 (1.03-1.08)	2.1x10 <sup>-7</sup>	1.06 (1.03-1.09)	5.8x10 <sup>-7</sup>	1.09 (1.01-1.18)	0.017
	<i>TPCN2</i> p.Met484Leu	rs35264875	11	68,846,399	A	T	0.852	1.08 (1.05-1.11)	3.4x10 <sup>-8</sup>	1.15 (1.05-1.25)	9.6x10 <sup>-5</sup>	1.08 (1.05-1.12)	3.1x10 <sup>-7</sup>
<i>CENTD2</i>	<i>ARAP1</i> p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.73	1.03 (1.02-1.05)	7.0x10 <sup>-5</sup>	1.04 (1.02-1.06)	0.00024	1.05 (1.01-1.09)	0.0073
<i>KLHDC5</i>	<i>MRPS35</i> p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.854	1.06 (1.04-1.08)	5.8x10 <sup>-8</sup>	1.06 (1.04-1.09)	1.1x10 <sup>-7</sup>	1.09 (1.02-1.16)	0.0057
	<i>MANSC4</i> p.Thr163Met	rs11049125	12	27,916,206	G	A	0.852	1.05 (1.03-1.07)	1.1x10 <sup>-6</sup>	1.06 (1.04-1.08)	2.2x10 <sup>-6</sup>	1.09 (1.02-1.16)	0.014
	<i>MANSC4</i> p.Leu157Ser	rs11049126	12	27,916,224	A	G	0.852	1.05 (1.03-1.07)	1.5x10 <sup>-6</sup>	1.09 (1.02-1.16)	0.016	1.06 (1.03-1.08)	2.8x10 <sup>-6</sup>
<i>WSCD2</i>	<i>WSCD2</i> p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.714	1.03 (1.01-1.04)	5.4x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.00062	1.04 (1.01-1.08)	0.0007
<i>HNF1A</i>	<i>HNF1A</i> p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.323	1.04 (1.02-1.05)	1.1x10 <sup>-6</sup>	1.08 (1.04-1.12)	2.9x10 <sup>-6</sup>	1.03 (1.01-1.06)	0.00063
	<i>HNF1A</i> p.Ala146Val	rs1800574	12	121,416,864	T	C	0.03	1.10 (1.05-1.15)	2.5x10 <sup>-5</sup>	1.10 (1.05-1.16)	2.5x10 <sup>-5</sup>	1.08 (0.77-1.50)	0.26
<i>MPHOSPH9</i>	<i>SBNO1</i> p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.818	1.04 (1.02-1.06)	3.5x10 <sup>-6</sup>	1.06 (1.03-1.08)	2.3x10 <sup>-7</sup>	1.01 (0.96-1.06)	0.47
<i>ZZEF1</i>	<i>ZZEF1</i> p.Ile402Val	rs781831	17	3,947,644	C	T	0.425	1.04 (1.03-1.06)	3.3x10 <sup>-9</sup>	1.07 (1.05-1.10)	3.6x10 <sup>-8</sup>	1.04 (1.02-1.07)	1.8x10 <sup>-5</sup>
	<i>ZZEF1</i> p.Leu360Pro	rs781852	17	3,953,102	G	A	0.402	1.04 (1.03-1.06)	1.1x10 <sup>-8</sup>	1.08 (1.05-1.10)	1.2x10 <sup>-7</sup>	1.04 (1.02-1.06)	2.9x10 <sup>-5</sup>
<i>MLX</i>	<i>MLX</i> p.Gln139Arg	rs665268	17	40,722,029	G	A	0.301	1.03 (1.02-1.05)	3.4x10 <sup>-6</sup>	1.04 (1.01-1.08)	0.0097	1.04 (1.02-1.06)	6.7x10 <sup>-6</sup>
<i>TTL6-CALCOCO2</i>	<i>TTL6</i> p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.76	1.03 (1.02-1.05)	0.00035	1.04 (1.02-1.06)	0.0014	1.05 (1.01-1.10)	0.0084
	<i>CALCOCO2</i> p.Pro347Ala	rs10278	17	46,939,658	C	G	0.712	1.04 (1.02-1.05)	2.7x10 <sup>-6</sup>	1.05 (1.01-1.09)	0.0032	1.05 (1.03-1.07)	8.6x10 <sup>-6</sup>
<i>C17orf58</i>	<i>C17orf58</i> p.Ile92Val	rs9891146	17	65,988,049	T	C	0.346	1.03 (1.02-1.05)	1.1x10 <sup>-5</sup>	1.06 (1.02-1.09)	0.00029	1.03 (1.01-1.06)	0.00026
<i>CILP2</i>	<i>NCAN</i> p.Pro92Ser	rs2228603	19	19,329,924	T	C	0.071	1.08 (1.05-1.11)	7.1x10 <sup>-8</sup>	1.08 (1.04-1.11)	1.2x10 <sup>-6</sup>	1.33 (1.16-1.53)	2.6x10 <sup>-5</sup>
	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.077	1.08 (1.06-1.11)	5.5x10 <sup>-10</sup>	1.08 (1.05-1.11)	2.0x10 <sup>-8</sup>	1.29 (1.15-1.46)	5.2x10 <sup>-6</sup>
	<i>ZNF101</i> Splice region	rs2304130	19	19,789,528	G	A	0.102	1.04 (1.02-1.06)	0.00043	1.13 (1.04-1.24)	0.00077	1.04 (1.01-1.06)	0.0035
<i>GIPR</i>	<i>GIPR</i> p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.2	1.03 (1.01-1.05)	0.0024	1.03 (1.01-1.05)	0.012	1.06 (1.02-1.12)	0.01
<i>ZHX3</i>	<i>ZHX3</i> p.Asn310Ser	rs17265513	20	39,832,628	C	T	0.172	1.04 (1.02-1.06)	1.1x10 <sup>-5</sup>	1.08 (1.03-1.14)	0.00065	1.04 (1.02-1.07)	4.8x10 <sup>-5</sup>
<i>HNF4A</i>	<i>HNF4A</i> p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.032	1.08 (1.04-1.13)	1.4x10 <sup>-5</sup>	1.09 (1.04-1.13)	7.2x10 <sup>-6</sup>	1.06 (0.78-1.42)	0.98
<i>MTMR3-ASCC2</i>	<i>ASCC2</i> p.Pro423Ser	rs36571	22	30,200,713	G	A	0.933	1.08 (1.05-1.11)	7.2x10 <sup>-7</sup>	1.08 (1.05-1.11)	1.3x10 <sup>-6</sup>	1.16 (1.01-1.33)	0.011
	<i>ASCC2</i> p.Asp407His	rs28265	22	30,200,761	C	G	0.928	1.09 (1.06-1.12)	3.0x10 <sup>-8</sup>	1.17 (1.03-1.33)	0.0054	1.09 (1.06-1.12)	6.0x10 <sup>-8</sup>
	<i>ASCC2</i> p.Val123Ile	rs11549795	22	30,221,120	C	T	0.929	1.08 (1.05-1.11)	9.8x10 <sup>-8</sup>	1.08 (1.05-1.12)	1.6x10 <sup>-7</sup>	1.14 (1.01-1.30)	0.012
	<i>MTMR3</i> p.Asn960Ser	rs41278853	22	30,416,527	A	G	0.929	1.08 (1.05-1.11)	2.6x10 <sup>-8</sup>	1.18 (1.04-1.34)	0.0036	1.09 (1.06-1.12)	6.8x10 <sup>-8</sup>
<i>PNPLA3</i>	<i>PNPLA3</i> p.Ile148Met	rs738409	22	44,324,727	G	C	0.241	1.04 (1.03-1.06)	7.1x10 <sup>-8</sup>	1.09 (1.05-1.14)	1.4x10 <sup>-5</sup>	1.04 (1.02-1.06)	9.0x10 <sup>-6</sup>
<i>PIM3</i>	<i>PIM3</i> p.Val300Ala	rs4077129	22	50,356,693	T	C	0.283	1.04 (1.02-1.06)	1.3x10 <sup>-7</sup>	1.08 (1.04-1.12)	1.0x10 <sup>-5</sup>	1.04 (1.02-1.06)	2.5x10 <sup>-5</sup>

## (ii) BMI adjusted analyses.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	Additive		Recessive		Dominant	
					Risk	Other		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
MACF1	MACF1 p.Ile39Val	rs16826069	1	39,797,055	G	A	0.210	1.05 (1.03-1.07)	1.3x10 <sup>-9</sup>	1.11 (1.07-1.16)	3.4x10 <sup>-8</sup>	1.05 (1.03-1.07)	4.7x10 <sup>-7</sup>
	MACF1 p.Lys1625Asn	rs41270807	1	39,801,815	C	A	0.195	1.05 (1.03-1.07)	1.8x10 <sup>-7</sup>	1.12 (1.07-1.18)	3.3x10 <sup>-6</sup>	1.05 (1.03-1.07)	1.5x10 <sup>-5</sup>
	MACF1 p.Met1424Val	rs2296172	1	39,835,817	G	A	0.187	1.05 (1.03-1.06)	2.7x10 <sup>-8</sup>	1.12 (1.07-1.17)	2.6x10 <sup>-7</sup>	1.04 (1.02-1.06)	5.8x10 <sup>-6</sup>
	MACF1 p.Ala3354Thr	rs587404	1	39,908,506	A	G	0.301	1.03 (1.02-1.04)	7.3x10 <sup>-6</sup>	1.04 (1.02-1.05)	7.1x10 <sup>-5</sup>	1.05 (1.02-1.08)	0.00065
FAM63A	FAM63A p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.988	1.21 (1.14-1.29)	1.2x10 <sup>-6</sup>	1.66 (0.83-3.32)	0.46	1.21 (1.14-1.29)	7.6x10 <sup>-7</sup>
GCKR	GCKR p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.642	1.05 (1.04-1.07)	1.0x10 <sup>-15</sup>	1.07 (1.05-1.09)	3.0x10 <sup>-12</sup>	1.08 (1.05-1.11)	7.3x10 <sup>-10</sup>
	C2orf16 p.Ile774Val	rs1919128	2	27,801,759	A	G	0.740	1.04 (1.02-1.05)	1.7x10 <sup>-8</sup>	1.05 (1.02-1.09)	0.00052	1.05 (1.03-1.07)	9.2x10 <sup>-8</sup>
	GPN1 p.Arg12Lys	rs3749147	2	27,851,918	G	A	0.771	1.04 (1.02-1.05)	8.7x10 <sup>-7</sup>	1.04 (1.02-1.06)	1.4x10 <sup>-5</sup>	1.06 (1.02-1.10)	0.0003
THADA	THADA p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.900	1.07 (1.05-1.09)	4.7x10 <sup>-11</sup>	1.08 (1.05-1.10)	6.6x10 <sup>-12</sup>	1.06 (0.97-1.15)	0.23
	THADA p.Thr897Ala	rs7578597	2	43,732,823	T	C	0.900	1.05 (1.02-1.07)	6.3x10 <sup>-5</sup>	1.03 (0.94-1.13)	0.30	1.05 (1.02-1.08)	4.4x10 <sup>-5</sup>
CEP68	CEP68 p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.849	1.05 (1.03-1.07)	2.4x10 <sup>-6</sup>	1.05 (1.03-1.07)	4.7x10 <sup>-6</sup>	1.09 (1.02-1.15)	0.020
GRB14	COBLL1 p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.878	1.09 (1.07-1.11)	1.1x10 <sup>-16</sup>	1.13 (1.05-1.22)	0.00059	1.10 (1.08-1.13)	1.6x10 <sup>-16</sup>
PPARG	PPARG p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.888	1.09 (1.06-1.11)	1.3x10 <sup>-14</sup>	1.19 (1.10-1.30)	3.5x10 <sup>-6</sup>	1.09 (1.06-1.12)	2.4x10 <sup>-13</sup>
KIF9-PTPN23	KIF9 p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.587	1.03 (1.02-1.04)	5.2x10 <sup>-6</sup>	1.05 (1.03-1.07)	1.6x10 <sup>-6</sup>	1.03 (1.00-1.05)	0.016
	PTPN23 p.Ala818Thr	rs6780013	3	47,452,118	G	A	0.628	1.03 (1.01-1.04)	2.2x10 <sup>-5</sup>	1.04 (1.02-1.06)	2.9x10 <sup>-5</sup>	1.03 (1.00-1.06)	0.016
IGF2BP2	SEN2 p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.374	1.04 (1.02-1.05)	2.3x10 <sup>-7</sup>	1.04 (1.02-1.06)	3.0x10 <sup>-6</sup>	1.05 (1.03-1.08)	0.00041
WFS1	WFS1 p.Val333Ile	rs1801212	4	6,302,519	A	G	0.753	1.06 (1.05-1.08)	1.2x10 <sup>-17</sup>	1.07 (1.05-1.09)	3.8x10 <sup>-15</sup>	1.11 (1.07-1.15)	1.2x10 <sup>-8</sup>
	WFS1 p.Arg611His	rs734312	4	6,303,354	A	G	0.543	1.05 (1.03-1.06)	7.8x10 <sup>-11</sup>	1.06 (1.03-1.08)	9.3x10 <sup>-7</sup>	1.07 (1.05-1.10)	5.2x10 <sup>-8</sup>
ANKH	ANKH p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.996	1.20 (1.07-1.34)	0.0016	1.19 (1.07-1.34)	0.0016	2.59 (0.41-16.13)	0.38
POC5	POC5 p.His36Arg	rs2307111	5	75,003,678	T	C	0.551	1.02 (1.01-1.04)	0.0064	1.02 (1.00-1.05)	0.034	1.03 (1.01-1.05)	0.012
PAM-PP1P5K2	PAM p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.0440	1.12 (1.08-1.16)	1.7x10 <sup>-9</sup>	1.41 (1.13-1.76)	0.00071	1.12 (1.08-1.16)	6.9x10 <sup>-9</sup>
	PP1P5K2 p.Ser1207Gly	rs36046591	5	102,537,285	G	A	0.0450	1.12 (1.08-1.16)	1.3x10 <sup>-10</sup>	1.50 (1.22-1.85)	7.3x10 <sup>-5</sup>	1.12 (1.08-1.16)	1.1x10 <sup>-9</sup>
RREB1	RREB1 p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.889	1.09 (1.06-1.12)	4.9x10 <sup>-11</sup>	1.11 (1.07-1.14)	7.0x10 <sup>-12</sup>	1.08 (0.98-1.19)	0.17
	RREB1 p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.837	1.04 (1.02-1.06)	1.6x10 <sup>-6</sup>	1.05 (1.03-1.07)	8.8x10 <sup>-7</sup>	1.04 (0.99-1.10)	0.082
MHC	TCF19 p.Met131Val	rs2073721	6	31,129,616	G	A	0.747	1.04 (1.02-1.05)	1.4x10 <sup>-6</sup>	1.04 (1.02-1.06)	5.0x10 <sup>-5</sup>	1.08 (1.04-1.12)	2.9x10 <sup>-5</sup>
	PRRC2A p.Leu1895Val	rs3132453	6	31,604,044	G	T	0.943	1.05 (1.02-1.08)	0.00015	1.06 (1.03-1.09)	4.3x10 <sup>-5</sup>	1.00 (0.87-1.16)	0.94
	SLC44A4 p.Met250Val	rs644827	6	31,838,441	C	T	0.558	1.03 (1.01-1.04)	4.6x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.00094	1.04 (1.02-1.07)	0.00044
	SLC44A4 p.Val183Ile	rs2242665	6	31,839,309	T	C	0.558	1.03 (1.01-1.04)	3.6x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.0011	1.04 (1.02-1.07)	0.00024
	EHMT2 p.Ser58Phe	rs115884658	6	31,864,538	A	G	0.0290	1.12 (1.08-1.17)	5.3x10 <sup>-6</sup>	1.12 (1.07-1.17)	6.7x10 <sup>-6</sup>	1.48 (1.12-1.96)	0.059
	PPT2 p.Cys5Trp	rs3134604	6	32,122,386	G	C	0.892	1.05 (1.03-1.07)	1.0x10 <sup>-5</sup>	1.06 (1.03-1.08)	3.9x10 <sup>-6</sup>	1.07 (0.98-1.15)	0.19
	BTNL2 p.Ser83Gly	rs2076530	6	32,363,816	C	T	0.416	1.03 (1.02-1.04)	6.1x10 <sup>-6</sup>	1.05 (1.02-1.07)	0.00062	1.04 (1.02-1.06)	7.0x10 <sup>-5</sup>
HLA-DQB1 p.Phe41Tyr	rs9274407	6	32,632,832	T	A	0.810	1.04 (1.02-1.06)	5.7x10 <sup>-5</sup>	1.05 (1.03-1.08)	7.7x10 <sup>-6</sup>	1.03 (0.97-1.09)	0.51	
PAX4	PAX4 p.Arg190His	rs2233580	7	127,253,550	T	C	0.0840	1.38 (1.26-1.51)	2.6x10 <sup>-12</sup>	2.04 (1.35-3.07)	0.00025	1.38 (1.26-1.53)	2.3x10 <sup>-11</sup>
LPL	LPL p.Ser474*	rs328	8	19,819,724	C	G	0.905	1.05 (1.02-1.07)	3.6x10 <sup>-5</sup>	1.11 (1.02-1.21)	0.014	1.05 (1.02-1.07)	8.8x10 <sup>-5</sup>
SLC30A8	SLC30A8 p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.690	1.09 (1.07-1.10)	3.20E-34	1.10 (1.08-1.12)	8.4x10 <sup>-30</sup>	1.14 (1.11-1.17)	9.2x10 <sup>-17</sup>
GPSM1	GPSM1 p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.768	1.06 (1.05-1.08)	1.7x10 <sup>-15</sup>	1.07 (1.05-1.09)	3.0x10 <sup>-13</sup>	1.11 (1.07-1.16)	4.3x10 <sup>-8</sup>
KCNJ11-ABCC8	NUCB2 p.Gln338Glu	rs757081	11	17,351,683	G	C	0.316	1.05 (1.04-1.07)	3.1x10 <sup>-10</sup>	1.08 (1.04-1.11)	1.5x10 <sup>-5</sup>	1.06 (1.04-1.09)	6.4x10 <sup>-9</sup>
	KCNJ11 p.Val250Ile	rs5215	11	17,408,630	C	T	0.368	1.06 (1.05-1.08)	3.3x10 <sup>-18</sup>	1.10 (1.07-1.13)	3.7x10 <sup>-13</sup>	1.07 (1.05-1.09)	4.8x10 <sup>-13</sup>

	<i>KCNJ11</i> p.Lys29Glu	rs5219	11	17,409,572	T	C	0.367	1.06 (1.05-1.08)	4.7x10 <sup>-18</sup>	1.10 (1.07-1.13)	2.8x10 <sup>-13</sup>	1.07 (1.05-1.09)	6.6x10 <sup>-13</sup>
	<i>ABCC8</i> p.Ala1369Ser	rs757110	11	17,418,477	C	A	0.370	1.06 (1.04-1.07)	1.3x10 <sup>-15</sup>	1.10 (1.07-1.13)	2.3x10 <sup>-13</sup>	1.06 (1.04-1.08)	4.7x10 <sup>-10</sup>
<i>PLCB3</i>	<i>PLCB3</i> p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.0610	1.05 (1.02-1.07)	0.00047	1.05 (1.02-1.08)	0.00019	1.00 (0.87-1.15)	0.76
<i>TPCN2</i>	<i>TPCN2</i> p.Val219Ile	rs72928978	11	68,831,364	G	A	0.888	1.05 (1.03-1.07)	2.4x10 <sup>-7</sup>	1.06 (1.03-1.08)	4.6x10 <sup>-7</sup>	1.07 (1.00-1.15)	0.024
	<i>TPCN2</i> p.Met484Leu	rs35264875	11	68,846,399	A	T	0.852	1.07 (1.04-1.10)	1.5x10 <sup>-7</sup>	1.11 (1.02-1.21)	0.0006	1.08 (1.04-1.11)	6.3x10 <sup>-7</sup>
<i>CENTD2</i>	<i>ARAP1</i> p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.730	1.04 (1.03-1.06)	9.2x10 <sup>-8</sup>	1.05 (1.03-1.07)	8.3x10 <sup>-7</sup>	1.07 (1.03-1.11)	0.00032
<i>KLHDC5</i>	<i>MRPS35</i> p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.854	1.05 (1.03-1.07)	5.8x10 <sup>-7</sup>	1.06 (1.04-1.08)	4.9x10 <sup>-7</sup>	1.06 (1.00-1.13)	0.029
	<i>MANSC4</i> p.Thr163Met	rs11049125	12	27,916,206	G	A	0.852	1.05 (1.03-1.07)	3.9x10 <sup>-6</sup>	1.05 (1.03-1.08)	4.3x10 <sup>-6</sup>	1.07 (1.01-1.14)	0.041
	<i>MANSC4</i> p.Leu157Ser	rs11049126	12	27,916,224	A	G	0.852	1.05 (1.03-1.07)	4.8x10 <sup>-6</sup>	1.07 (1.01-1.14)	0.047	1.05 (1.03-1.08)	5.1x10 <sup>-6</sup>
<i>WSCD2</i>	<i>WSCD2</i> p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.714	1.03 (1.01-1.04)	3.7x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.00028	1.04 (1.00-1.07)	0.0013
<i>HNF1A</i>	<i>HNF1A</i> p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.323	1.04 (1.02-1.05)	3.4x10 <sup>-7</sup>	1.08 (1.04-1.12)	8.6x10 <sup>-7</sup>	1.03 (1.01-1.06)	0.00028
	<i>HNF1A</i> p.Ala146Val	rs1800574	12	121,416,864	T	C	0.0300	1.09 (1.05-1.14)	2.4x10 <sup>-5</sup>	1.10 (1.05-1.14)	2.4x10 <sup>-5</sup>	1.11 (0.81-1.51)	0.25
<i>MPHOSPH9</i>	<i>SBNO1</i> p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.818	1.04 (1.02-1.06)	9.2x10 <sup>-7</sup>	1.05 (1.03-1.07)	9.6x10 <sup>-8</sup>	1.02 (0.97-1.07)	0.28
<i>ZZEF1</i>	<i>ZZEF1</i> p.Ile402Val	rs781831	17	3,947,644	C	T	0.425	1.03 (1.02-1.05)	2.2x10 <sup>-7</sup>	1.06 (1.04-1.09)	3.1x10 <sup>-7</sup>	1.03 (1.02-1.05)	0.0004
	<i>ZZEF1</i> p.Leu360Pro	rs781852	17	3,953,102	G	A	0.402	1.04 (1.02-1.05)	5.2x10 <sup>-7</sup>	1.06 (1.04-1.09)	1.5x10 <sup>-6</sup>	1.04 (1.02-1.06)	0.00037
<i>MLX</i>	<i>MLX</i> p.Gln139Arg	rs665268	17	40,722,029	G	A	0.301	1.03 (1.01-1.04)	3.1x10 <sup>-5</sup>	1.04 (1.00-1.07)	0.029	1.04 (1.02-1.06)	4.8x10 <sup>-5</sup>
<i>TTL6-CALCOCO2</i>	<i>TTL6</i> p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.760	1.03 (1.01-1.04)	0.0050	1.03 (1.01-1.05)	0.007	1.03 (0.99-1.07)	0.094
	<i>CALCOCO2</i> p.Pro347Ala	rs10278	17	46,939,658	C	G	0.712	1.03 (1.02-1.05)	6.0x10 <sup>-5</sup>	1.04 (1.00-1.07)	0.016	1.04 (1.02-1.06)	9.8x10 <sup>-5</sup>
<i>C17orf58</i>	<i>C17orf58</i> p.Ile92Val	rs9891146	17	65,988,049	T	C	0.346	1.02 (1.00-1.03)	0.013	1.03 (1.00-1.06)	0.039	1.02 (1.00-1.04)	0.036
<i>CILP2</i>	<i>NCAN</i> p.Pro92Ser	rs2228603	19	19,329,924	T	C	0.0710	1.08 (1.05-1.11)	1.5x10 <sup>-8</sup>	1.07 (1.04-1.10)	8.5x10 <sup>-7</sup>	1.38 (1.22-1.57)	1.7x10 <sup>-7</sup>
	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0770	1.09 (1.06-1.11)	5.6x10 <sup>-12</sup>	1.08 (1.06-1.11)	8.4x10 <sup>-10</sup>	1.35 (1.21-1.51)	4.3x10 <sup>-8</sup>
	<i>ZNF101</i> Splice region	rs2304130	19	19,789,528	G	A	0.102	1.05 (1.03-1.07)	5.5x10 <sup>-6</sup>	1.17 (1.07-1.27)	2.8x10 <sup>-5</sup>	1.05 (1.02-1.07)	0.00013
<i>GIPR</i>	<i>GIPR</i> p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.200	1.05 (1.03-1.07)	6.1x10 <sup>-9</sup>	1.05 (1.03-1.07)	1.2x10 <sup>-7</sup>	1.09 (1.05-1.14)	0.00011
<i>ZHX3</i>	<i>ZHX3</i> p.Asu310Ser	rs17265513	20	39,832,628	C	T	0.172	1.03 (1.02-1.05)	0.00012	1.08 (1.03-1.13)	0.00027	1.03 (1.01-1.05)	0.00086
<i>HNF4A</i>	<i>HNF4A</i> p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.032	1.08 (1.04-1.12)	6.8x10 <sup>-6</sup>	1.08 (1.04-1.13)	5.0x10 <sup>-6</sup>	1.15 (0.87-1.52)	0.62
<i>MTMR3-ASCC2</i>	<i>ASCC2</i> p.Pro423Ser	rs36571	22	30,200,713	G	A	0.933	1.08 (1.05-1.11)	2.9x10 <sup>-8</sup>	1.08 (1.05-1.11)	8.4x10 <sup>-8</sup>	1.18 (1.04-1.34)	0.0027
	<i>ASCC2</i> p.Asp407His	rs28265	22	30,200,761	C	G	0.928	1.09 (1.06-1.12)	1.0x10 <sup>-9</sup>	1.20 (1.06-1.35)	0.00081	1.09 (1.06-1.12)	3.9x10 <sup>-9</sup>
	<i>ASCC2</i> p.Val123Ile	rs11549795	22	30,221,120	C	T	0.929	1.08 (1.06-1.11)	3.9x10 <sup>-9</sup>	1.09 (1.06-1.12)	1.1x10 <sup>-8</sup>	1.17 (1.04-1.32)	0.0023
	<i>MTMR3</i> p.Asu960Ser	rs41278853	22	30,416,527	A	G	0.929	1.08 (1.06-1.11)	1.6x10 <sup>-9</sup>	1.19 (1.06-1.35)	0.00078	1.09 (1.06-1.12)	7.1x10 <sup>-9</sup>
<i>PNPLA3</i>	<i>PNPLA3</i> p.Ile148Met	rs738409	22	44,324,727	G	C	0.241	1.05 (1.03-1.06)	2.3x10 <sup>-9</sup>	1.10 (1.06-1.14)	7.5x10 <sup>-7</sup>	1.05 (1.03-1.07)	1.0x10 <sup>-6</sup>
<i>PIM3</i>	<i>PIM3</i> p.Val300Ala	rs4077129	22	50,356,693	T	C	0.283	1.04 (1.02-1.05)	8.1x10 <sup>-7</sup>	1.08 (1.04-1.13)	1.9x10 <sup>-5</sup>	1.04 (1.02-1.06)	7.3x10 <sup>-5</sup>

(b) European meta-analysis of 41,066 cases and 136,024 controls.

(i) BMI unadjusted analyses.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	Additive		Recessive		Dominant	
					Risk	Other		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
MACF1	MACF1 p.Ile39Val	rs16826069	1	39,797,055	G	A	0.223	1.06 (1.04-1.08)	2.6x10 <sup>-10</sup>	1.13 (1.07-1.19)	3.2x10 <sup>-7</sup>	1.06 (1.03-1.08)	7.9x10 <sup>-8</sup>
	MACF1 p.Lys1625Asn	rs41270807	1	39,801,815	C	A	0.217	1.06 (1.04-1.08)	2.4x10 <sup>-9</sup>	1.15 (1.09-1.21)	4.7x10 <sup>-7</sup>	1.06 (1.04-1.09)	6.5x10 <sup>-7</sup>
	MACF1 p.Met1424Val	rs2296172	1	39,835,817	G	A	0.218	1.06 (1.04-1.08)	2.9x10 <sup>-10</sup>	1.14 (1.08-1.20)	6.4x10 <sup>-8</sup>	1.06 (1.03-1.08)	1.8x10 <sup>-7</sup>
	MACF1 p.Ala3354Thr	rs587404	1	39,908,506	A	G	0.295	1.03 (1.02-1.05)	7.8x10 <sup>-6</sup>	1.05 (1.01-1.10)	0.0012	1.04 (1.02-1.06)	8.9x10 <sup>-5</sup>
FAM63A	FAM63A p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.986	1.25 (1.16-1.34)	6.5x10 <sup>-9</sup>	1.25 (1.16-1.34)	7.8x10 <sup>-9</sup>	2.03 (0.92-4.48)	0.14
GCKR	GCKR p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.618	1.06 (1.04-1.07)	1.3x10 <sup>-12</sup>	1.07 (1.05-1.10)	1.9x10 <sup>-10</sup>	1.07 (1.04-1.11)	5.3x10 <sup>-7</sup>
	C2orf16 p.Ile774Val	rs1919128	2	27,801,759	A	G	0.743	1.03 (1.02-1.05)	6.2x10 <sup>-6</sup>	1.04 (1.02-1.07)	2.4x10 <sup>-5</sup>	1.05 (1.00-1.09)	0.0057
	GPN1 p.Arg12Lys	rs3749147	2	27,851,918	G	A	0.752	1.03 (1.01-1.06)	2.1x10 <sup>-5</sup>	1.04 (1.02-1.07)	0.00013	1.05 (1.00-1.10)	0.0035
THADA	THADA p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.892	1.07 (1.04-1.10)	2.4x10 <sup>-9</sup>	1.08 (1.05-1.11)	4.7x10 <sup>-10</sup>	1.06 (0.96-1.17)	0.27
	THADA p.Thr897Ala	rs7578597	2	43,732,823	T	C	0.914	1.07 (1.04-1.11)	2.2x10 <sup>-6</sup>	1.08 (1.04-1.12)	1.7x10 <sup>-6</sup>	1.09 (0.94-1.26)	0.21
CEP68	CEP68 p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.831	1.05 (1.02-1.07)	6.1x10 <sup>-5</sup>	1.05 (1.02-1.08)	0.00012	1.09 (1.02-1.17)	0.032
GRB14	COBLL1 p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.881	1.08 (1.06-1.11)	1.4x10 <sup>-11</sup>	1.09 (1.06-1.12)	3.9x10 <sup>-11</sup>	1.15 (1.05-1.26)	0.0026
PPARG	PPARG p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.869	1.07 (1.04-1.10)	3.4x10 <sup>-8</sup>	1.07 (1.04-1.10)	9.0x10 <sup>-8</sup>	1.15 (1.04-1.26)	0.0044
KIF9-PTPN23	KIF9 p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.598	1.02 (1.00-1.04)	0.0047	1.03 (1.01-1.06)	0.0022	1.01 (0.98-1.05)	0.19
	PTPN23 p.Ala818Thr	rs6780013	3	47,452,118	G	A	0.616	1.02 (1.01-1.04)	0.0016	1.03 (1.01-1.06)	0.0024	1.02 (0.99-1.06)	0.055
IGF2BP2	SEN2 p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.337	1.03 (1.02-1.05)	5.4x10 <sup>-5</sup>	1.05 (1.02-1.09)	0.007	1.04 (1.02-1.06)	0.00021
WFS1	WFS1 p.Val333Ile	rs1801212	4	6,302,519	A	G	0.708	1.07 (1.05-1.09)	2.5x10 <sup>-17</sup>	1.08 (1.06-1.11)	1.7x10 <sup>-14</sup>	1.12 (1.08-1.16)	1.3x10 <sup>-8</sup>
	WFS1 p.Arg611His	rs734312	4	6,303,354	A	G	0.530	1.05 (1.03-1.07)	1.2x10 <sup>-10</sup>	1.06 (1.03-1.08)	1.2x10 <sup>-6</sup>	1.08 (1.05-1.11)	1.6x10 <sup>-8</sup>
ANKH	ANKH p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.996	1.21 (1.07-1.37)	0.00080	1.21 (1.07-1.37)	0.00085	3.22 (0.46-22.36)	0.25
POC5	POC5 p.His36Arg	rs2307111	5	75,003,678	T	C	0.595	1.04 (1.03-1.06)	2.0x10 <sup>-7</sup>	1.06 (1.03-1.09)	5.6x10 <sup>-6</sup>	1.06 (1.03-1.10)	7.8x10 <sup>-5</sup>
PAM-PP1P5K2	PAM p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.051	1.12 (1.07-1.16)	1.5x10 <sup>-8</sup>	1.31 (1.03-1.67)	0.021	1.12 (1.07-1.16)	2.6x10 <sup>-8</sup>
	PP1P5K2 p.Ser1207Gly	rs36046591	5	102,537,285	G	A	0.051	1.12 (1.08-1.16)	2.9x10 <sup>-9</sup>	1.43 (1.14-1.80)	0.0018	1.12 (1.07-1.16)	1.2x10 <sup>-8</sup>
RREB1	RREB1 p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.888	1.09 (1.05-1.12)	6.7x10 <sup>-8</sup>	1.10 (1.06-1.14)	5.1x10 <sup>-8</sup>	1.11 (0.99-1.25)	0.057
	RREB1 p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.806	1.04 (1.02-1.06)	2.0x10 <sup>-5</sup>	1.05 (1.03-1.07)	8.6x10 <sup>-6</sup>	1.04 (0.98-1.11)	0.18
MHC	TCF19 p.Met131Val	rs2073721	6	31,129,616	G	A	0.742	1.04 (1.02-1.05)	1.0x10 <sup>-5</sup>	1.04 (1.01-1.06)	0.00017	1.08 (1.03-1.13)	0.00045
	PRRC2A p.Leu1895Val	rs3132453	6	31,604,044	G	T	0.928	1.06 (1.03-1.10)	2.9x10 <sup>-5</sup>	1.07 (1.04-1.11)	1.6x10 <sup>-5</sup>	1.06 (0.91-1.24)	0.42
	SLC44A4 p.Met250Val	rs644827	6	31,838,441	C	T	0.537	1.03 (1.01-1.04)	0.00015	1.03 (1.01-1.06)	0.0046	1.04 (1.02-1.07)	0.00071
	SLC44A4 p.Val183Ile	rs2242665	6	31,839,309	T	C	0.536	1.03 (1.01-1.05)	0.00011	1.03 (1.01-1.06)	0.0054	1.05 (1.02-1.08)	0.00034
	EHMT2 p.Ser58Phe	rs115884658	6	31,864,538	A	G	0.0320	1.10 (1.05-1.15)	0.00018	1.33 (0.98-1.81)	0.28	1.10 (1.05-1.15)	0.00018
	PPT2 p.Cys5Trp	rs3134604	6	32,122,386	G	C	0.870	1.06 (1.04-1.09)	6.9x10 <sup>-7</sup>	1.07 (1.04-1.10)	6.1x10 <sup>-7</sup>	1.10 (1.01-1.21)	0.064
	BTNL2 p.Ser83Gly	rs2076530	6	32,363,816	C	T	0.430	1.03 (1.01-1.05)	9.5x10 <sup>-5</sup>	1.04 (1.01-1.07)	0.0024	1.04 (1.02-1.06)	0.00087
HLA-DQB1	HLA-DQB1 p.Phe41Tyr	rs9274407	6	32,632,832	T	A	0.816	1.05 (1.02-1.07)	8.8x10 <sup>-5</sup>	1.06 (1.03-1.08)	4.3x10 <sup>-5</sup>	1.05 (0.98-1.12)	0.26
PAX4	PAX4 p.Arg190His	rs2233580	7	127,253,550	T	C	N/A	N/A	N/A	N/A	N/A	N/A	N/A
LPL	LPL p.Ser474*	rs328	8	19,819,724	C	G	0.903	1.05 (1.02-1.08)	0.00024	1.05 (1.02-1.08)	0.00022	1.08 (0.97-1.20)	0.19
SLC30A8	SLC30A8 p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.678	1.08 (1.06-1.10)	1.7x10 <sup>-20</sup>	1.09 (1.07-1.12)	4.3x10 <sup>-18</sup>	1.12 (1.08-1.16)	8.4x10 <sup>-10</sup>
GPSM1	GPSM1 p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.744	1.07 (1.05-1.09)	5.4x10 <sup>-15</sup>	1.08 (1.05-1.10)	2.3x10 <sup>-12</sup>	1.13 (1.08-1.19)	3.8x10 <sup>-8</sup>

KCNJ11- ABCC8	NUCB2 p.Gln338Glu	rs757081	11	17,351,683	G	C	0.341	1.05 (1.03-1.07)	6.2x10 <sup>-8</sup>	1.08 (1.04-1.12)	8.7x10 <sup>-5</sup>	1.06 (1.04-1.09)	1.5x10 <sup>-6</sup>
	KCNJ11 p.Val250Ile	rs5215	11	17,408,630	C	T	0.394	1.06 (1.04-1.08)	1.4x10 <sup>-13</sup>	1.09 (1.06-1.12)	6.9x10 <sup>-9</sup>	1.07 (1.05-1.10)	3.4x10 <sup>-10</sup>
	KCNJ11 p.Lys29Glu	rs5219	11	17,409,572	T	C	0.394	1.06 (1.04-1.08)	2.1x10 <sup>-13</sup>	1.09 (1.06-1.12)	6.4x10 <sup>-9</sup>	1.07 (1.05-1.10)	5.8x10 <sup>-10</sup>
	ABCC8 p.Ala1369Ser	rs757110	11	17,418,477	C	A	0.394	1.06 (1.04-1.07)	5.6x10 <sup>-12</sup>	1.09 (1.06-1.12)	2.2x10 <sup>-9</sup>	1.06 (1.04-1.09)	6.1x10 <sup>-8</sup>
PLCB3	PLCB3 p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.0730	1.04 (1.01-1.07)	0.0022	1.01 (0.86-1.18)	0.66	1.04 (1.01-1.07)	0.0012
TPCN2	TPCN2 p.Val219Ile	rs72928978	11	68,831,364	G	A	0.850	1.05 (1.03-1.08)	1.6x10 <sup>-5</sup>	1.05 (1.03-1.08)	4.0x10 <sup>-5</sup>	1.09 (1.01-1.18)	0.026
	TPCN2 p.Met484Leu	rs35264875	11	68,846,399	A	T	0.821	1.07 (1.04-1.10)	1.5x10 <sup>-6</sup>	1.08 (1.04-1.11)	1.0x10 <sup>-5</sup>	1.14 (1.04-1.25)	0.0012
CENTD2	ARAP1 p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.719	1.03 (1.01-1.06)	0.00050	1.04 (1.02-1.07)	0.00086	1.05 (1.00-1.10)	0.028
KLHDC5	MRPS35 p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.842	1.06 (1.04-1.08)	4.7x10 <sup>-8</sup>	1.07 (1.04-1.09)	7.7x10 <sup>-8</sup>	1.09 (1.02-1.17)	0.012
	MANSC4 p.Thr163Met	rs11049125	12	27,916,206	G	A	0.843	1.06 (1.04-1.08)	8.6x10 <sup>-8</sup>	1.07 (1.04-1.09)	2.3x10 <sup>-7</sup>	1.10 (1.02-1.18)	0.0072
	MANSC4 p.Leu157Ser	rs11049126	12	27,916,224	A	G	0.843	1.06 (1.04-1.08)	1.1x10 <sup>-7</sup>	1.07 (1.04-1.09)	2.7x10 <sup>-7</sup>	1.10 (1.02-1.18)	0.0084
WSCD2	WSCD2 p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.723	1.03 (1.01-1.05)	3.0x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.0019	1.07 (1.03-1.12)	3.7x10 <sup>-5</sup>
HNF1A	HNF1A p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.343	1.03 (1.01-1.05)	2.6x10 <sup>-5</sup>	1.08 (1.04-1.13)	2.7x10 <sup>-6</sup>	1.02 (1.00-1.05)	0.011
	HNF1A p.Ala146Val	rs1800574	12	121,416,864	T	C	0.0330	1.11 (1.06-1.16)	1.0x10 <sup>-5</sup>	1.13 (0.80-1.60)	0.25	1.11 (1.06-1.16)	1.2x10 <sup>-5</sup>
MPHOSPH9	SBNO1 p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.796	1.04 (1.02-1.06)	3.8x10 <sup>-5</sup>	1.05 (1.03-1.08)	1.9x10 <sup>-6</sup>	1.00 (0.95-1.06)	0.78
ZZEF1	ZZEF1 p.Ile402Val	rs781831	17	3,947,644	C	T	0.404	1.05 (1.03-1.07)	3.3x10 <sup>-9</sup>	1.08 (1.05-1.11)	4.4x10 <sup>-7</sup>	1.05 (1.03-1.08)	2.9x10 <sup>-6</sup>
	ZZEF1 p.Leu360Pro	rs781852	17	3,953,102	G	A	0.387	1.05 (1.04-1.07)	1.6x10 <sup>-10</sup>	1.09 (1.06-1.12)	9.0x10 <sup>-8</sup>	1.06 (1.04-1.08)	2.3x10 <sup>-7</sup>
MLX	MLX p.Gln139Arg	rs665268	17	40,722,029	G	A	0.270	1.03 (1.01-1.05)	0.00012	1.04 (0.99-1.08)	0.047	1.04 (1.02-1.06)	0.00015
TTLL6- CALCOCO2	TTLL6 p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.756	1.04 (1.02-1.06)	9.7x10 <sup>-5</sup>	1.05 (1.02-1.07)	0.00038	1.06 (1.01-1.11)	0.0087
	CALCOCO2 p.Pro347Ala	rs10278	17	46,939,658	C	G	0.707	1.05 (1.03-1.06)	1.5x10 <sup>-7</sup>	1.06 (1.04-1.08)	1.6x10 <sup>-7</sup>	1.05 (1.01-1.09)	0.0060
C17orf58	C17orf58 p.Ile92Val	rs9891146	17	65,988,049	T	C	0.280	1.04 (1.02-1.06)	9.8x10 <sup>-6</sup>	1.08 (1.04-1.13)	0.00021	1.04 (1.01-1.06)	0.00044
CILP2	NCAN p.Pro92Ser	rs2228603	19	19,329,924	T	C	0.0780	1.07 (1.03-1.10)	3.8x10 <sup>-5</sup>	1.31 (1.13-1.52)	0.00013	1.06 (1.03-1.10)	0.00036
	TM6SF2 p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0800	1.09 (1.06-1.12)	6.8x10 <sup>-9</sup>	1.33 (1.16-1.53)	1.2x10 <sup>-5</sup>	1.08 (1.05-1.12)	2.2x10 <sup>-7</sup>
	ZNF101 Splice region	rs2304130	19	19,789,528	G	A	0.0830	1.06 (1.03-1.10)	1.4x10 <sup>-5</sup>	1.18 (1.04-1.35)	0.0039	1.06 (1.03-1.10)	6.6x10 <sup>-5</sup>
GIPR	GIPR p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.222	1.03 (1.01-1.05)	0.0061	1.06 (1.00-1.12)	0.034	1.03 (1.01-1.05)	0.019
ZHX3	ZHX3 p.Asn310Ser	rs17265513	20	39,832,628	C	T	0.214	1.04 (1.02-1.06)	4.6x10 <sup>-6</sup>	1.07 (1.02-1.13)	0.013	1.05 (1.02-1.07)	8.2x10 <sup>-6</sup>
HNF4A	HNF4A p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.0360	1.07 (1.02-1.11)	0.00046	1.06 (0.77-1.46)	0.88	1.07 (1.02-1.12)	0.00031
MTMR3- ASCC2	ASCC2 p.Pro423Ser	rs36571	22	30,200,713	G	A	0.918	1.08 (1.05-1.11)	1.7x10 <sup>-6</sup>	1.08 (1.05-1.12)	2.2x10 <sup>-6</sup>	1.15 (1.00-1.33)	0.048
	ASCC2 p.Asp407His	rs28265	22	30,200,761	C	G	0.918	1.08 (1.05-1.12)	4.0x10 <sup>-7</sup>	1.09 (1.05-1.12)	5.6x10 <sup>-7</sup>	1.16 (1.01-1.33)	0.032
	ASCC2 p.Val123Ile	rs11549795	22	30,221,120	C	T	0.918	1.08 (1.05-1.11)	1.3x10 <sup>-6</sup>	1.08 (1.05-1.12)	1.5x10 <sup>-6</sup>	1.14 (0.99-1.31)	0.057
	MTMR3 p.Asn960Ser	rs41278853	22	30,416,527	A	G	0.918	1.08 (1.05-1.11)	2.4x10 <sup>-7</sup>	1.09 (1.05-1.12)	3.8x10 <sup>-7</sup>	1.17 (1.02-1.34)	0.026
PNPLA3	PNPLA3 p.Ile148Met	rs738409	22	44,324,727	G	C	0.229	1.04 (1.02-1.06)	5.6x10 <sup>-6</sup>	1.11 (1.05-1.16)	1.8x10 <sup>-5</sup>	1.04 (1.02-1.06)	0.00041
PIM3	PIM3 p.Val300Ala	rs4077129	22	50,356,693	T	C	0.260	1.03 (1.01-1.06)	9.6x10 <sup>-5</sup>	1.07 (1.02-1.12)	0.0016	1.03 (1.01-1.06)	0.0018

(ii) BMI adjusted analyses.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	Additive		Recessive		Dominant	
					Risk	Other		OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
MACF1	MACF1 p.Ile39Val	rs16826069	1	39,797,055	G	A	0.223	1.05 (1.03-1.07)	5.1x10 <sup>-9</sup>	1.11 (1.06-1.17)	9.0x10 <sup>-7</sup>	1.05 (1.03-1.07)	1.0x10 <sup>-6</sup>
	MACF1 p.Lys1625Asn	rs41270807	1	39,801,815	C	A	0.217	1.05 (1.03-1.07)	8.7x10 <sup>-8</sup>	1.13 (1.07-1.19)	1.5x10 <sup>-6</sup>	1.05 (1.03-1.08)	1.3x10 <sup>-5</sup>
	MACF1 p.Met1424Val	rs2296172	1	39,835,817	G	A	0.218	1.05 (1.03-1.07)	6.4x10 <sup>-9</sup>	1.13 (1.07-1.18)	1.6x10 <sup>-7</sup>	1.05 (1.03-1.07)	2.5x10 <sup>-6</sup>

	<i>MACF1</i> p.Ala3354Thr	rs587404	1	39,908,506	A	G	0.295	1.04 (1.02-1.05)	1.4x10 <sup>-6</sup>	1.06 (1.02-1.10)	0.00012	1.04 (1.02-1.06)	5.1x10 <sup>-5</sup>
<i>FAM63A</i>	<i>FAM63A</i> p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.986	1.23 (1.15-1.31)	7.7x10 <sup>-9</sup>	1.22 (1.15-1.31)	1.1x10 <sup>-8</sup>	2.23 (1.06-4.67)	0.054
<i>GCKR</i>	<i>GCKR</i> p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.618	1.05 (1.04-1.07)	1.6x10 <sup>-12</sup>	1.07 (1.04-1.09)	1.0x10 <sup>-9</sup>	1.07 (1.04-1.10)	1.4x10 <sup>-7</sup>
	<i>C2orf16</i> p.Ile774Val	rs1919128	2	27,801,759	A	G	0.743	1.03 (1.02-1.05)	5.0x10 <sup>-6</sup>	1.04 (1.02-1.06)	2.5x10 <sup>-5</sup>	1.05 (1.00-1.09)	0.0038
	<i>GNP1</i> p.Arg12Lys	rs3749147	2	27,851,918	G	A	0.752	1.03 (1.01-1.05)	2.3x10 <sup>-5</sup>	1.04 (1.02-1.06)	0.00012	1.05 (1.00-1.09)	0.0041
<i>THADA</i>	<i>THADA</i> p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.892	1.07 (1.05-1.10)	6.0x10 <sup>-11</sup>	1.08 (1.06-1.11)	5.8x10 <sup>-12</sup>	1.05 (0.95-1.15)	0.32
	<i>THADA</i> p.Thr897Ala	rs7578597	2	43,732,823	T	C	0.914	1.07 (1.04-1.10)	7.3x10 <sup>-7</sup>	1.08 (1.04-1.11)	2.8x10 <sup>-7</sup>	1.05 (0.91-1.21)	0.40
<i>CEP68</i>	<i>CEP68</i> p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.831	1.04 (1.02-1.06)	3.8x10 <sup>-5</sup>	1.04 (1.02-1.07)	9.5x10 <sup>-5</sup>	1.09 (1.02-1.16)	0.020
<i>GRB14</i>	<i>COBLL1</i> p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.881	1.09 (1.07-1.12)	5.7x10 <sup>-15</sup>	1.10 (1.07-1.13)	1.4x10 <sup>-14</sup>	1.14 (1.05-1.25)	0.00076
<i>PPARG</i>	<i>PPARG</i> p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.869	1.08 (1.06-1.11)	3.5x10 <sup>-12</sup>	1.09 (1.06-1.12)	1.8x10 <sup>-11</sup>	1.17 (1.08-1.28)	0.00029
<i>KIF9-PTPN23</i>	<i>KIF9</i> p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.598	1.03 (1.01-1.04)	6.2x10 <sup>-5</sup>	1.04 (1.02-1.06)	0.00011	1.03 (1.00-1.06)	0.018
	<i>PTPN23</i> p.Ala818Thr	rs6780013	3	47,452,118	G	A	0.616	1.03 (1.01-1.05)	1.9x10 <sup>-5</sup>	1.04 (1.02-1.06)	8.0x10 <sup>-5</sup>	1.03 (1.00-1.06)	0.0053
<i>IGF2BP2</i>	<i>SENP2</i> p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.337	1.03 (1.02-1.05)	1.1x10 <sup>-5</sup>	1.06 (1.02-1.09)	0.0037	1.04 (1.02-1.06)	4.3x10 <sup>-5</sup>
<i>WFS1</i>	<i>WFS1</i> p.Val333Ile	rs1801212	4	6,302,519	A	G	0.708	1.06 (1.05-1.08)	7.6x10 <sup>-15</sup>	1.07 (1.05-1.10)	1.9x10 <sup>-12</sup>	1.10 (1.06-1.14)	2.2x10 <sup>-7</sup>
	<i>WFS1</i> p.Arg611His	rs734312	4	6,303,354	A	G	0.530	1.05 (1.03-1.06)	1.0x10 <sup>-9</sup>	1.05 (1.03-1.08)	1.6x10 <sup>-6</sup>	1.07 (1.04-1.10)	3.1x10 <sup>-7</sup>
<i>ANKH</i>	<i>ANKH</i> p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.996	1.21 (1.08-1.36)	0.00062	1.21 (1.07-1.35)	0.00062	2.59 (0.40-16.85)	0.39
<i>POC5</i>	<i>POC5</i> p.His36Arg	rs2307111	5	75,003,678	T	C	0.595	1.03 (1.01-1.04)	0.0012	1.03 (1.01-1.05)	0.011	1.04 (1.01-1.07)	0.0045
<i>PAM-PP1P5K2</i>	<i>PAM</i> p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.0510	1.12 (1.08-1.16)	2.2x10 <sup>-9</sup>	1.37 (1.09-1.72)	0.0056	1.12 (1.07-1.16)	6.1x10 <sup>-9</sup>
	<i>PP1P5K2</i> p.Ser1207Gly	rs36046591	5	102,537,285	G	A	0.0510	1.12 (1.08-1.16)	4.2x10 <sup>-10</sup>	1.47 (1.18-1.82)	0.00054	1.12 (1.08-1.16)	2.6x10 <sup>-9</sup>
<i>RREB1</i>	<i>RREB1</i> p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.888	1.09 (1.05-1.12)	5.3x10 <sup>-9</sup>	1.10 (1.06-1.13)	1.2x10 <sup>-9</sup>	1.07 (0.95-1.19)	0.16
	<i>RREB1</i> p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.806	1.04 (1.02-1.06)	2.0x10 <sup>-5</sup>	1.04 (1.02-1.07)	1.4x10 <sup>-5</sup>	1.05 (0.99-1.11)	0.11
<i>MHC</i>	<i>TCF19</i> p.Met131Val	rs2073721	6	31,129,616	G	A	0.742	1.04 (1.02-1.06)	7.9x10 <sup>-7</sup>	1.04 (1.02-1.06)	4.8x10 <sup>-5</sup>	1.08 (1.04-1.13)	3.0x10 <sup>-5</sup>
	<i>PRRC2A</i> p.Leu1895Val	rs3132453	6	31,604,044	G	T	0.928	1.05 (1.02-1.08)	0.00038	1.06 (1.03-1.09)	0.00016	1.01 (0.87-1.16)	0.83
	<i>SLC44A4</i> p.Met250Val	rs644827	6	31,838,441	C	T	0.537	1.03 (1.02-1.05)	2.5x10 <sup>-5</sup>	1.04 (1.01-1.06)	0.0011	1.05 (1.02-1.07)	0.00022
	<i>SLC44A4</i> p.Val183Ile	rs2242665	6	31,839,309	T	C	0.536	1.03 (1.02-1.05)	1.7x10 <sup>-5</sup>	1.04 (1.01-1.06)	0.0013	1.05 (1.02-1.08)	9.3x10 <sup>-5</sup>
	<i>EHMT2</i> p.Ser58Phe	rs115884658	6	31,864,538	A	G	0.0320	1.13 (1.08-1.17)	5.9x10 <sup>-7</sup>	1.48 (1.11-1.97)	0.065	1.12 (1.08-1.17)	7.7x10 <sup>-7</sup>
	<i>PPT2</i> p.Cys5Trp	rs3134604	6	32,122,386	G	C	0.870	1.06 (1.03-1.08)	2.4x10 <sup>-6</sup>	1.06 (1.04-1.09)	8.4x10 <sup>-7</sup>	1.06 (0.97-1.15)	0.29
	<i>BTNL2</i> p.Ser83Gly	rs2076530	6	32,363,816	C	T	0.430	1.04 (1.02-1.05)	3.2x10 <sup>-7</sup>	1.06 (1.03-1.09)	1.9x10 <sup>-5</sup>	1.05 (1.02-1.07)	3.6x10 <sup>-5</sup>
	<i>HLA-DQB1</i> p.Phe41Tyr	rs9274407	6	32,632,832	T	A	0.816	1.04 (1.02-1.06)	8.1x10 <sup>-5</sup>	1.06 (1.03-1.08)	1.3x10 <sup>-5</sup>	1.03 (0.97-1.09)	0.64
<i>PAX4</i>	<i>PAX4</i> p.Arg190His	rs2233580	7	127,253,550	T	C	N/A	N/A	N/A	N/A	N/A	N/A	N/A
<i>LPL</i>	<i>LPL</i> p.Ser474*	rs328	8	19,819,724	C	G	0.903	1.05 (1.02-1.07)	0.00014	1.05 (1.02-1.08)	0.00016	1.08 (0.98-1.20)	0.12
<i>SLC30A8</i>	<i>SLC30A8</i> p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.678	1.08 (1.06-1.10)	6.3x10 <sup>25</sup>	1.09 (1.07-1.12)	1.8x10 <sup>21</sup>	1.13 (1.09-1.17)	2.2x10 <sup>-12</sup>
<i>GPSM1</i>	<i>GPSM1</i> p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.744	1.07 (1.05-1.09)	2.1x10 <sup>-15</sup>	1.08 (1.05-1.10)	3.0x10 <sup>-13</sup>	1.12 (1.07-1.17)	1.6x10 <sup>-7</sup>
<i>KCNJ11-ABCC8</i>	<i>NUCB2</i> p.Gln338Glu	rs757081	11	17,351,683	G	C	0.341	1.06 (1.04-1.08)	2.0x10 <sup>-11</sup>	1.09 (1.05-1.14)	6.6x10 <sup>-7</sup>	1.07 (1.05-1.10)	4.6x10 <sup>-9</sup>
	<i>KCNJ11</i> p.Val250Ile	rs5215	11	17,408,630	C	T	0.394	1.07 (1.05-1.08)	8.5x10 <sup>-18</sup>	1.10 (1.07-1.13)	1.8x10 <sup>-12</sup>	1.08 (1.06-1.10)	2.3x10 <sup>-12</sup>
	<i>KCNJ11</i> p.Lys29Glu	rs5219	11	17,409,572	T	C	0.394	1.07 (1.05-1.08)	1.5x10 <sup>-17</sup>	1.10 (1.07-1.13)	1.6x10 <sup>-12</sup>	1.08 (1.05-1.10)	4.4x10 <sup>-12</sup>
	<i>ABCC8</i> p.Ala1369Ser	rs757110	11	17,418,477	C	A	0.394	1.06 (1.05-1.08)	8.9x10 <sup>-16</sup>	1.10 (1.07-1.13)	7.5x10 <sup>-13</sup>	1.07 (1.05-1.09)	6.9x10 <sup>-10</sup>
<i>PLCB3</i>	<i>PLCB3</i> p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.0730	1.05 (1.02-1.08)	3.9x10 <sup>-5</sup>	1.00 (0.87-1.16)	0.68	1.06 (1.03-1.09)	1.2x10 <sup>-5</sup>
<i>TPCN2</i>	<i>TPCN2</i> p.Val219Ile	rs72928978	11	68,831,364	G	A	0.850	1.05 (1.02-1.07)	1.2x10 <sup>-5</sup>	1.05 (1.03-1.08)	1.9x10 <sup>-5</sup>	1.07 (0.99-1.15)	0.056
	<i>TPCN2</i> p.Met484Leu	rs35264875	11	68,846,399	A	T	0.821	1.07 (1.04-1.10)	2.9x10 <sup>-6</sup>	1.07 (1.04-1.11)	8.7x10 <sup>-6</sup>	1.11 (1.02-1.21)	0.007
<i>CENTD2</i>	<i>ARAP1</i> p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.719	1.05 (1.03-1.07)	4.3x10 <sup>-7</sup>	1.06 (1.03-1.08)	2.1x10 <sup>-6</sup>	1.07 (1.03-1.12)	0.0011
<i>KLHDC5</i>	<i>MRPS35</i> p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.842	1.05 (1.03-1.07)	8.6x10 <sup>-7</sup>	1.06 (1.04-1.08)	6.3x10 <sup>-7</sup>	1.06 (1.00-1.14)	0.060

	<i>MANSC4</i> p.Thr163Met	rs11049125	12	27,916,206	G	A	0.843	1.05 (1.03-1.07)	6.3x10 <sup>-7</sup>	1.06 (1.03-1.08)	8.3x10 <sup>-7</sup>	1.08 (1.01-1.15)	0.031
	<i>MANSC4</i> p.Leu157Ser	rs11049126	12	27,916,224	A	G	0.843	1.05 (1.03-1.07)	7.5x10 <sup>-7</sup>	1.06 (1.03-1.08)	9.5x10 <sup>-7</sup>	1.07 (1.01-1.15)	0.034
<i>WSCD2</i>	<i>WSCD2</i> p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.723	1.03 (1.01-1.05)	3.6x10 <sup>-5</sup>	1.03 (1.01-1.05)	0.00096	1.06 (1.01-1.10)	0.00024
<i>HNF1A</i>	<i>HNF1A</i> p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.343	1.03 (1.01-1.05)	1.7x10 <sup>-5</sup>	1.08 (1.04-1.12)	1.7x10 <sup>-6</sup>	1.02 (1.00-1.05)	0.0078
	<i>HNF1A</i> p.Ala146Val	rs1800574	12	121,416,864	T	C	0.0330	1.10 (1.05-1.14)	9.0x10 <sup>-6</sup>	1.16 (0.84-1.60)	0.23	1.10 (1.05-1.15)	1.1x10 <sup>-5</sup>
<i>MPHOSPH9</i>	<i>SBNO1</i> p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.796	1.04 (1.02-1.06)	1.3x10 <sup>-5</sup>	1.05 (1.03-1.07)	1.3x10 <sup>-6</sup>	1.01 (0.96-1.07)	0.44
<i>ZZEF1</i>	<i>ZZEF1</i> p.Ile402Val	rs781831	17	3,947,644	C	T	0.404	1.04 (1.02-1.05)	2.2x10 <sup>-7</sup>	1.06 (1.04-1.10)	4.1x10 <sup>-6</sup>	1.04 (1.02-1.06)	8.3x10 <sup>-5</sup>
	<i>ZZEF1</i> p.Leu360Pro	rs781852	17	3,953,102	G	A	0.387	1.04 (1.03-1.06)	1.7x10 <sup>-8</sup>	1.07 (1.04-1.10)	2.6x10 <sup>-6</sup>	1.05 (1.03-1.07)	5.6x10 <sup>-6</sup>
<i>MLX</i>	<i>MLX</i> p.Gln139Arg	rs665268	17	40,722,029	G	A	0.270	1.03 (1.01-1.04)	0.00088	1.03 (0.99-1.07)	0.13	1.03 (1.01-1.05)	0.00072
<i>TLL6-CALCOCO2</i>	<i>TLL6</i> p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.756	1.03 (1.01-1.05)	0.0014	1.04 (1.02-1.06)	0.002	1.04 (0.99-1.08)	0.073
	<i>CALCOCO2</i> p.Pro347Ala	rs10278	17	46,939,658	C	G	0.707	1.04 (1.02-1.06)	3.6x10 <sup>-6</sup>	1.05 (1.03-1.07)	2.0x10 <sup>-6</sup>	1.04 (1.00-1.08)	0.028
<i>C17orf58</i>	<i>C17orf58</i> p.Ile92Val	rs9891146	17	65,988,049	T	C	0.280	1.02 (1.00-1.04)	0.0091	1.04 (1.00-1.09)	0.025	1.02 (0.99-1.04)	0.042
<i>CILP2</i>	<i>NCAN</i> p.Pro92Ser	rs2228603	19	19,329,924	T	C	0.0780	1.08 (1.05-1.11)	4.5x10 <sup>-7</sup>	1.34 (1.17-1.54)	1.5x10 <sup>-5</sup>	1.07 (1.04-1.10)	8.9x10 <sup>-6</sup>
	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0800	1.09 (1.06-1.12)	5.7x10 <sup>-11</sup>	1.38 (1.21-1.57)	3.5x10 <sup>-7</sup>	1.09 (1.06-1.12)	6.0x10 <sup>-9</sup>
	<i>ZNF101</i> Splice region	rs2304130	19	19,789,528	G	A	0.0830	1.08 (1.05-1.11)	2.4x10 <sup>-8</sup>	1.25 (1.11-1.41)	9.1x10 <sup>-5</sup>	1.07 (1.04-1.11)	4.5x10 <sup>-7</sup>
<i>GIPR</i>	<i>GIPR</i> p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.222	1.05 (1.04-1.07)	7.8x10 <sup>-9</sup>	1.09 (1.04-1.15)	0.00059	1.06 (1.04-1.08)	6.8x10 <sup>-8</sup>
<i>ZHX3</i>	<i>ZHX3</i> p.Asn310Ser	rs17265513	20	39,832,628	C	T	0.214	1.03 (1.01-1.05)	8.1x10 <sup>-5</sup>	1.07 (1.02-1.13)	0.0084	1.03 (1.01-1.06)	0.00032
<i>HNF4A</i>	<i>HNF4A</i> p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.0360	1.07 (1.02-1.11)	0.00026	1.15 (0.86-1.56)	0.72	1.07 (1.02-1.11)	0.00023
<i>MTMR3-ASCC2</i>	<i>ASCC2</i> p.Pro423Ser	rs36571	22	30,200,713	G	A	0.918	1.08 (1.05-1.11)	4.2x10 <sup>-8</sup>	1.09 (1.05-1.12)	9.1x10 <sup>-8</sup>	1.17 (1.03-1.34)	0.012
	<i>ASCC2</i> p.Asp407His	rs28265	22	30,200,761	C	G	0.918	1.09 (1.06-1.12)	8.9x10 <sup>-9</sup>	1.09 (1.06-1.12)	2.3x10 <sup>-8</sup>	1.19 (1.04-1.35)	0.0064
	<i>ASCC2</i> p.Val123Ile	rs11549795	22	30,221,120	C	T	0.918	1.08 (1.05-1.11)	2.7x10 <sup>-8</sup>	1.09 (1.06-1.12)	5.6x10 <sup>-8</sup>	1.17 (1.03-1.33)	0.013
	<i>MTMR3</i> p.Asn960Ser	rs41278853	22	30,416,527	A	G	0.918	1.08 (1.06-1.11)	1.0x10 <sup>-8</sup>	1.09 (1.06-1.12)	3.0x10 <sup>-8</sup>	1.19 (1.05-1.36)	0.0058
<i>PNPLA3</i>	<i>PNPLA3</i> p.Ile148Met	rs738409	22	44,324,727	G	C	0.229	1.04 (1.03-1.06)	4.8x10 <sup>-7</sup>	1.11 (1.06-1.16)	1.2x10 <sup>-6</sup>	1.04 (1.02-1.06)	0.00011
<i>PIM3</i>	<i>PIM3</i> p.Val300Ala	rs4077129	22	50,356,693	T	C	0.260	1.03 (1.01-1.05)	0.00014	1.07 (1.02-1.11)	0.0011	1.03 (1.01-1.05)	0.0027

Chr: chromosome. RAF: risk allele frequency. OR: odds ratio. CI: confidence interval.



**Supplementary Table 5 | Index coding variants for distinct T2D association signals attaining exome-wide significance ( $p < 2.2 \times 10^{-7}$ ) in trans-ethnic meta-analysis of 73,033 cases and 362,354 controls in the discovery analysis.**

(a) Summary of conditional analysis of index coding variants.

Locus	Variant annotation	rs ID	Chr	Position	Alleles		RAF	Conditioning variant	BMI unadjusted		BMI adjusted	
					Risk	Other			OR (95% CI)	p-value	OR (95% CI)	p-value
<i>MACF1</i>	<i>MACF1</i> p.Met1424Val	rs2296172	1	39,835,817	G	A	0.193	Unconditional	1.06 (1.05-1.08)	$6.7 \times 10^{-16}$	1.04 (1.03-1.06)	$5.9 \times 10^{-8}$
<i>FAM63A</i>	<i>FAM63A</i> p.Tyr95Asn	rs140386498	1	150,972,959	A	T	0.988	Unconditional	1.21 (1.14-1.28)	$7.5 \times 10^{-8}$	1.19 (1.12-1.26)	$6.7 \times 10^{-7}$
<i>GCKR</i>	<i>GCKR</i> p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.630	Unconditional	1.06 (1.05-1.08)	$5.3 \times 10^{-25}$	1.06 (1.04-1.07)	$3.2 \times 10^{-18}$
<i>THADA</i>	<i>THADA</i> p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.895	Unconditional	1.08 (1.05-1.10)	$4.6 \times 10^{-15}$	1.07 (1.05-1.10)	$8.3 \times 10^{-16}$
<i>CEP68</i>	<i>CEP68</i> p.Gly74Ser	rs7572857	2	65,296,798	G	A	0.846	Unconditional	1.05 (1.04-1.07)	$8.3 \times 10^{-9}$	1.05 (1.03-1.07)	$6.6 \times 10^{-7}$
<i>GRB14</i>	<i>COBLL1</i> p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.879	Unconditional	1.08 (1.06-1.11)	$8.6 \times 10^{-20}$	1.09 (1.07-1.12)	$5.0 \times 10^{-23}$
<i>PPARG</i>	<i>PPARG</i> p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.887	Unconditional	1.09 (1.07-1.11)	$1.4 \times 10^{-17}$	1.10 (1.07-1.12)	$2.7 \times 10^{-19}$
<i>KIF9</i>	<i>KIF9</i> p.Arg638Trp	rs2276853	3	47,282,303	A	G	0.588	Unconditional	1.02 (1.01-1.04)	$8.0 \times 10^{-5}$	1.03 (1.02-1.05)	$5.3 \times 10^{-8}$
<i>IGF2BP2</i>	<i>SENP2</i> p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.367	Unconditional	1.03 (1.01-1.04)	$1.6 \times 10^{-6}$	1.03 (1.02-1.05)	$3.0 \times 10^{-8}$
<i>WFS1</i>	<i>WFS1</i> p.Val333Ile	rs1801212	4	6,302,519	A	G	0.748	Unconditional	1.07 (1.06-1.09)	$1.1 \times 10^{-24}$	1.07 (1.05-1.08)	$7.1 \times 10^{-21}$
<i>ANKH</i>	<i>ANKH</i> p.Arg187Gln	rs146886108	5	14,751,305	C	T	0.996	Unconditional	1.29 (1.16-1.45)	$1.4 \times 10^{-7}$	1.27 (1.13-1.41)	$3.5 \times 10^{-7}$
<i>POC5</i>	<i>POC5</i> p.His36Arg	rs2307111	5	75,003,678	T	C	0.562	Unconditional	1.05 (1.04-1.07)	$1.6 \times 10^{-15}$	1.03 (1.01-1.04)	$2.1 \times 10^{-5}$
<i>PAM-PIIP5K2</i>	<i>PAM</i> p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.0450	Unconditional	1.13 (1.10-1.17)	$1.2 \times 10^{-16}$	1.13 (1.09-1.17)	$7.4 \times 10^{-15}$
<i>RREB1</i>	<i>RREB1</i> p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.884	<i>RREB1</i> p.Ser1499Tyr	1.08 (1.06-1.11)	$3.1 \times 10^{-13}$	1.10 (1.07-1.13)	$8.5 \times 10^{-17}$
	<i>RREB1</i> p.Ser1499Tyr	rs35742417	6	7,247,344	C	A	0.836	<i>RREB1</i> p.Asp1171Asn	1.04 (1.03-1.06)	$2.3 \times 10^{-9}$	1.05 (1.02-1.07)	$7.5 \times 10^{-10}$
<i>MHC</i>	<i>TCF19</i> p.Met131Val	rs2073721	6	31,129,616	G	A	0.749	Unconditional	1.04 (1.02-1.05)	$1.6 \times 10^{-10}$	1.04 (1.02-1.05)	$2.3 \times 10^{-9}$
<i>PAX4</i>	<i>PAX4</i> p.Arg190His	rs2233580	7	127,253,550	T	C	0.0294	Unconditional	1.36 (1.25-1.48)	$1.8 \times 10^{-12}$	1.38 (1.26-1.51)	$4.2 \times 10^{-13}$
<i>LPL</i>	<i>LPL</i> p.Ser474*	rs328	8	19,819,724	C	G	0.903	Unconditional	1.05 (1.03-1.08)	$6.8 \times 10^{-9}$	1.05 (1.03-1.07)	$2.3 \times 10^{-7}$
<i>SLC30A8</i>	<i>SLC30A8</i> p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.691	Unconditional	1.09 (1.08-1.11)	$1.9 \times 10^{-47}$	1.09 (1.08-1.11)	$1.3 \times 10^{-47}$
<i>GPSM1</i>	<i>GPSM1</i> p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.771	Unconditional	1.06 (1.05-1.08)	$3.2 \times 10^{-16}$	1.06 (1.05-1.08)	$6.6 \times 10^{-16}$
<i>KCNJ11-ABCC8</i>	<i>KCNJ11</i> p.Lys29Glu	rs5219	11	17,409,572	T	C	0.364	Unconditional	1.06 (1.05-1.07)	$5.7 \times 10^{-22}$	1.07 (1.05-1.08)	$1.5 \times 10^{-22}$
<i>PLCB3</i>	<i>PLCB3</i> p.Ser778Leu	rs35169799	11	64,031,241	T	C	0.0585	Unconditional	1.04 (1.02-1.07)	0.00012	1.05 (1.03-1.08)	$1.7 \times 10^{-6}$
<i>TPCN2</i>	<i>TPCN2</i> p.Val219Ile	rs72928978	11	68,831,364	G	A	0.890	Unconditional	1.05 (1.02-1.07)	$5.2 \times 10^{-7}$	1.05 (1.03-1.07)	$1.8 \times 10^{-8}$
<i>CENTD2</i>	<i>ARAP1</i> p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.733	Unconditional	1.04 (1.02-1.05)	$4.8 \times 10^{-8}$	1.05 (1.03-1.06)	$5.2 \times 10^{-10}$
<i>KLHDC5</i>	<i>MRPS35</i> p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.850	Unconditional	1.06 (1.04-1.08)	$1.4 \times 10^{-11}$	1.05 (1.03-1.07)	$1.5 \times 10^{-8}$
<i>WSCD2</i>	<i>WSCD2</i> p.Thr113Ile	rs3764002	12	108,618,630	C	T	0.719	Unconditional	1.03 (1.02-1.05)	$3.3 \times 10^{-8}$	1.03 (1.02-1.05)	$1.2 \times 10^{-7}$
<i>HNF1A</i>	<i>HNF1A</i> p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.323	<i>HNF1A</i> p.Ala146Val	1.05 (1.03-1.08)	$1.3 \times 10^{-8}$	1.05 (1.02-1.06)	$1.5 \times 10^{-7}$
	<i>HNF1A</i> p.Ala146Val	rs1800574	12	121,416,864	T	C	0.029	<i>HNF1A</i> p.Ile75Leu	1.10 (1.05-1.14)	$1.3 \times 10^{-6}$	1.10 (1.06-1.15)	$6.9 \times 10^{-7}$
<i>MPHOSPH9</i>	<i>SBNO1</i> p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.815	Unconditional	1.04 (1.02-1.06)	$5.7 \times 10^{-7}$	1.04 (1.02-1.06)	$1.1 \times 10^{-7}$
<i>ZZEF1</i>	<i>ZZEF1</i> p.Ile402Val	rs781831	17	3,947,644	C	T	0.422	Unconditional	1.04 (1.03-1.05)	$8.3 \times 10^{-11}$	1.03 (1.02-1.05)	$1.8 \times 10^{-7}$
<i>MLX</i>	<i>MLX</i> p.Gln139Arg	rs665268	17	40,722,029	G	A	0.294	Unconditional	1.04 (1.02-1.05)	$2.0 \times 10^{-8}$	1.03 (1.02-1.04)	$1.1 \times 10^{-5}$
<i>TTL6</i>	<i>TTL6</i> p.Glu712Asp	rs2032844	17	46,847,364	C	A	0.754	Unconditional	1.04 (1.02-1.06)	$1.2 \times 10^{-7}$	1.03 (1.01-1.04)	0.00098
<i>C17orf58</i>	<i>C17orf58</i> p.Ile92Val	rs9891146	17	65,988,049	T	C	0.332	Unconditional	1.04 (1.02-1.05)	$7.2 \times 10^{-7}$	1.02 (1.00-1.03)	0.0027
<i>CILP2</i>	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0755	Unconditional	1.07 (1.05-1.10)	$4.8 \times 10^{-12}$	1.09 (1.06-1.11)	$3.4 \times 10^{-15}$

<i>GIPR</i>	<i>GIPR</i> p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.200	Unconditional	1.03 (1.02-1.05)	7.1x10 <sup>-5</sup>	1.06 (1.04-1.07)	6.8x10 <sup>-12</sup>
<i>ZHX3</i>	<i>ZHX3</i> p.Asn310Ser	rs17265513	20	39,832,628	C	T	0.174	Unconditional	1.04 (1.02-1.06)	6.8x10 <sup>-6</sup>	1.04 (1.02-1.05)	3.2x10 <sup>-5</sup>
<i>HNF4A</i>	<i>HNF4A</i> p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.0316	Unconditional	1.09 (1.05-1.13)	2.6x10 <sup>-8</sup>	1.10 (1.06-1.14)	5.0x10 <sup>-8</sup>
<i>MTMR3-ASCC2</i>	<i>ASCC2</i> p.Asp407His	rs28265	22	30,200,761	C	G	0.925	Unconditional	1.09 (1.06-1.11)	2.1x10 <sup>-12</sup>	1.09 (1.07-1.12)	4.4x10 <sup>-14</sup>
<i>PNPLA3</i>	<i>PNPLA3</i> p.Ile148Met	rs738409	22	44,324,727	G	C	0.239	Unconditional	1.04 (1.03-1.05)	2.1x10 <sup>-10</sup>	1.05 (1.03-1.06)	2.8x10 <sup>-11</sup>
<i>PIM3</i>	<i>PIM3</i> p.Val300Ala	rs4077129	22	50,356,693	T	C	0.276	Unconditional	1.04 (1.02-1.05)	1.9x10 <sup>-7</sup>	1.04 (1.02-1.06)	3.5x10 <sup>-8</sup>

(b) Summary of conditional analysis of index coding variants and non-coding GWAS lead variants.

Locus	Index coding variant	rs ID	Chr	Position	Alleles		RAF	BMI unadjusted		BMI adjusted		Conditioning variant	BMI unadjusted	BMI adjusted	
					Risk	Other		OR (95% CI)	p-value	OR (95% CI)	p-value		p-value	p-value	
<i>GCKR</i>	<i>GCKR</i> p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.630	1.06 (1.05-1.08)	5.3x10 <sup>-25</sup>	1.06 (1.04-1.07)	3.2x10 <sup>-18</sup>	rs780094	1.0x10 <sup>-5</sup>	1.5x10 <sup>-6</sup>	
		rs780094	2	27,741,237	C	T	0.634	1.06 (1.05-1.07)	6.8x10 <sup>-22</sup>	1.06 (1.04-1.07)	1.8x10 <sup>-17</sup>		<i>GCKR</i> p.Pro446Leu	0.094	0.22
<i>THADA</i>	<i>THADA</i> p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.895	1.08 (1.05-1.10)	4.6x10 <sup>-15</sup>	1.07 (1.05-1.10)	8.3x10 <sup>-16</sup>	rs10495903	4.9x10 <sup>-6</sup>	6.8x10 <sup>-7</sup>	
		rs10495903	2	43,806,918	C	T	0.878	1.06 (1.04-1.08)	2.6x10 <sup>-10</sup>	1.05 (1.03-1.07)	7.9x10 <sup>-8</sup>		<i>THADA</i> p.Cys845Tyr	0.25	0.61
<i>GRB14</i>	<i>COBLL1</i> p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.879	1.08 (1.06-1.11)	8.6x10 <sup>-20</sup>	1.09 (1.07-1.12)	5.0x10 <sup>-23</sup>	rs13389219	1.2x10 <sup>-5</sup>	1.2x10 <sup>-6</sup>	
		rs13389219	2	165,528,876	C	T	0.622	1.07 (1.05-1.08)	2.8x10 <sup>-24</sup>	1.07 (1.06-1.09)	1.3x10 <sup>-29</sup>		<i>COBLL1</i> p.Asn901Asp	3.1x10 <sup>-13</sup>	4.0x10 <sup>-17</sup>
<i>IGF2BP2</i>	<i>SEN2</i> p.Thr291Lys	rs6762208	3	185,331,165	A	C	0.367	1.03 (1.01-1.04)	1.6x10 <sup>-6</sup>	1.03 (1.02-1.05)	3.0x10 <sup>-8</sup>	rs4402960	0.54	0.87	
		rs4402960	3	185,511,687	T	G	0.333	1.10 (1.09-1.11)	7.4x10 <sup>-54</sup>	1.10 (1.08-1.11)	8.3x10 <sup>-49</sup>		<i>SEN2</i> p.Thr291Lys	4.2x10 <sup>-47</sup>	3.1x10 <sup>-39</sup>
<i>WFS1</i>	<i>WFS1</i> p.Val333Ile	rs1801212	4	6,302,519	A	G	0.748	1.07 (1.06-1.09)	1.1x10 <sup>-24</sup>	1.07 (1.05-1.08)	7.1x10 <sup>-21</sup>	rs1801214	3.9x10 <sup>-5</sup>	2.3x10 <sup>-6</sup>	
		rs1801214	4	6,303,022	T	C	0.637	1.06 (1.05-1.07)	9.9x10 <sup>-21</sup>	1.05 (1.04-1.07)	3.2x10 <sup>-15</sup>		<i>WFS1</i> p.Val333Ile	0.0019	0.014
<i>RREB1</i>	<i>RREB1</i> p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.884	1.08 (1.06-1.11)	3.1x10 <sup>-13</sup>	1.10 (1.07-1.13)	8.5x10 <sup>-17</sup>	rs9505118	1.4x10 <sup>-7</sup>	3.4x10 <sup>-10</sup>	
		rs9505118	6	7,290,437	A	G	0.599	1.04 (1.02-1.05)	2.0x10 <sup>-8</sup>	1.04 (1.02-1.05)	7.6x10 <sup>-9</sup>		<i>RREB1</i> p.Asp1171Asn	1.0x10 <sup>-6</sup>	2.2x10 <sup>-6</sup>
		rs35742417	6	7,247,344	C	A	0.836	1.04 (1.03-1.06)	2.3x10 <sup>-9</sup>	1.05 (1.02-1.07)	7.5x10 <sup>-10</sup>		rs9505118	0.0014	0.0051
		rs9505118	6	7,290,437	A	G	0.599	1.04 (1.02-1.05)	2.0x10 <sup>-8</sup>	1.04 (1.02-1.05)	7.6x10 <sup>-9</sup>		<i>RREB1</i> p.Ser1499Tyr	0.00011	3.3x10 <sup>-5</sup>
<i>SLC30A8</i>	<i>SLC30A8</i> p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.691	1.09 (1.08-1.11)	1.9x10 <sup>-47</sup>	1.09 (1.08-1.11)	1.3x10 <sup>-47</sup>	rs3802177	2.3x10 <sup>-5</sup>	6.1x10 <sup>-4</sup>	
		rs3802177	8	118,185,025	G	A	0.690	1.09 (1.08-1.11)	3.1x10 <sup>-41</sup>	1.09 (1.08-1.11)	2.4x10 <sup>-40</sup>		<i>SLC30A8</i> p.Arg276Trp	0.61	0.98
<i>CENTD2</i>	<i>ARAP1</i> p.Gln802Glu	rs56200889	11	72,408,055	G	C	0.733	1.04 (1.02-1.05)	4.8x10 <sup>-8</sup>	1.05 (1.03-1.06)	5.2x10 <sup>-10</sup>	rs11603334	0.94	0.80	
		rs11603334	11	72,432,985	G	A	0.851	1.07 (1.06-1.09)	9.5x10 <sup>-18</sup>	1.09 (1.07-1.11)	1.7x10 <sup>-24</sup>		<i>ARAP1</i> p.Gln802Glu	7.8x10 <sup>-10</sup>	6.2x10 <sup>-16</sup>
<i>KLHDC5</i>	<i>MRPS35</i> p.Gly43Arg	rs1127787	12	27,867,727	G	A	0.850	1.06 (1.04-1.08)	1.4x10 <sup>-11</sup>	1.05 (1.03-1.07)	1.5x10 <sup>-8</sup>	rs10842994	0.0029	0.039	
		rs10842994	12	27,965,150	C	T	0.824	1.06 (1.05-1.08)	9.4x10 <sup>-16</sup>	1.06 (1.04-1.08)	7.6x10 <sup>-13</sup>		<i>MRPS35</i> p.Gly43Arg	7.0x10 <sup>-8</sup>	4.1x10 <sup>-8</sup>
<i>HNF1A</i>	<i>HNF1A</i> p.Ile75Leu	rs1169288	12	121,416,650	C	A	0.323	1.05 (1.03-1.08)	1.3x10 <sup>-8</sup>	1.05 (1.02-1.06)	1.5x10 <sup>-7</sup>	rs7957197	8.6x10 <sup>-6</sup>	1.2x10 <sup>-5</sup>	
		rs7957197	12	121,460,686	T	A	0.818	1.04 (1.02-1.06)	2.5x10 <sup>-9</sup>	1.05 (1.02-1.06)	3.3x10 <sup>-7</sup>		<i>HNF1A</i> p.Ile75Leu	1.7x10 <sup>-5</sup>	9.9x10 <sup>-5</sup>
		rs1800574	12	121,416,864	T	C	0.029	1.10 (1.05-1.14)	1.3x10 <sup>-6</sup>	1.10 (1.06-1.15)	6.9x10 <sup>-7</sup>		rs7957197	4.1x10 <sup>-6</sup>	7.9x10 <sup>-6</sup>
		rs7957197	12	121,460,686	T	A	0.818	1.04 (1.02-1.06)	2.5x10 <sup>-9</sup>	1.05 (1.02-1.06)	3.3x10 <sup>-7</sup>		<i>HNF1A</i> p.Ala146Val	2.2x10 <sup>-8</sup>	2.1x10 <sup>-6</sup>
<i>MPHOSPH9</i>	<i>SBNO1</i> p.Ser729Asn	rs1060105	12	123,806,219	C	T	0.815	1.04 (1.02-1.06)	5.7x10 <sup>-7</sup>	1.04 (1.02-1.06)	1.1x10 <sup>-7</sup>	rs1727307	0.46	0.27	
		rs1727307	12	123,575,742	G	A	0.694	1.04 (1.03-1.05)	3.2x10 <sup>-10</sup>	1.04 (1.03-1.05)	6.2x10 <sup>-10</sup>		<i>SBNO1</i> p.Ser729Asn	0.00013	0.00012
<i>CILP2</i>	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0755	1.07 (1.05-1.10)	4.8x10 <sup>-12</sup>	1.09 (1.06-1.11)	3.4x10 <sup>-15</sup>	rs10401969	0.16	0.19	
		rs10401969	19	19,407,718	C	T	0.086	1.07 (1.04-1.09)	5.6x10 <sup>-9</sup>	1.08 (1.06-1.10)	9.2x10 <sup>-12</sup>		<i>TM6SF2</i> p.Glu167Lys	0.90	0.48
<i>GIPR</i>	<i>GIPR</i> p.Glu318Gln	rs1800437	19	46,181,392	C	G	0.200	1.03 (1.02-1.05)	7.1x10 <sup>-5</sup>	1.06 (1.04-1.07)	6.8x10 <sup>-12</sup>	rs8108269	0.0071	9.7x10 <sup>-9</sup>	
		rs8108269	19	46,158,513	G	T	0.328	1.06 (1.04-1.07)	8.3x10 <sup>-17</sup>	1.06 (1.04-1.07)	5.2x10 <sup>-16</sup>		<i>GIPR</i> p.Glu318Gln	8.3x10 <sup>-12</sup>	1.0x10 <sup>-11</sup>
<i>HNF4A</i>	<i>HNF4A</i> p.Thr139Ile	rs1800961	20	43,042,364	T	C	0.0316	1.09 (1.05-1.13)	2.6x10 <sup>-8</sup>	1.10 (1.06-1.14)	5.0x10 <sup>-8</sup>	rs4812831	4.8x10 <sup>-8</sup>	8.6x10 <sup>-9</sup>	
		rs4812831	20	43,018,260	A	G	0.130	1.06 (1.04-1.08)	8.5x10 <sup>-10</sup>	1.06 (1.04-1.08)	1.3x10 <sup>-8</sup>		<i>HNF4A</i> p.Thr139Ile	8.5x10 <sup>-9</sup>	4.9x10 <sup>-9</sup>

Chr: chromosome. RAF: risk allele frequency. BMI: body mass index. OR: odds ratio. CI: confidence interval.

**Supplementary Table 6 | Comparison of summary statistics for T2D coding variant association signals obtained from trans-ethnic meta-analysis of: (i) 73,033 cases and 362,354 controls in the present study; and (ii) 34,809 cases and 57,985 controls from the T2D-GENES/GoT2D study.**

Locus	Variant	rs ID	Chr	Position	Alleles		RAF	Trans-ethnic meta-analysis				Trans-ethnic meta-analysis from T2D-GENES/GoT2D	
					Risk	Other		BMI unadjusted		BMI adjusted		OR (95% CI)	p-value
								OR (95% CI)	p-value	OR (95% CI)	p-value		
<i>GCKR</i>	<i>GCKR</i> p.Pro446Leu	rs1260326	2	27,730,940	C	T	0.630	1.06 (1.05-1.08)	5.3x10 <sup>-25</sup>	1.06 (1.04-1.07)	3.2x10 <sup>-18</sup>	1.07 (1.04-1.10)	1.2x10 <sup>-9</sup>
<i>THADA</i>	<i>THADA</i> p.Cys845Tyr	rs35720761	2	43,519,977	C	T	0.895	1.08 (1.05-1.10)	4.6x10 <sup>-15</sup>	1.07 (1.05-1.10)	8.3x10 <sup>-16</sup>	1.12 (1.07-1.16)	3.3x10 <sup>-10</sup>
<i>GRB14</i>	<i>COBLL1</i> p.Asn901Asp	rs7607980	2	165,551,201	T	C	0.879	1.08 (1.06-1.11)	8.6x10 <sup>-20</sup>	1.09 (1.07-1.12)	5.0x10 <sup>-23</sup>	1.15 (1.11-1.19)	8.3x10 <sup>-15</sup>
<i>PPARG</i>	<i>PPARG</i> p.Pro12Ala	rs1801282	3	12,393,125	C	G	0.887	1.09 (1.07-1.11)	1.4x10 <sup>-17</sup>	1.10 (1.07-1.12)	2.7x10 <sup>-19</sup>	1.11 (1.07-1.15)	4.2x10 <sup>-8</sup>
<i>WFS1</i>	<i>WFS1</i> p.Val333Ile	rs1801212	4	6,302,519	A	G	0.748	1.07 (1.06-1.09)	1.1x10 <sup>-24</sup>	1.07 (1.05-1.08)	7.1x10 <sup>-21</sup>	1.09 (1.06-1.12)	9.0x10 <sup>-14</sup>
<i>PAM-PP1P5K2</i>	<i>PAM</i> p.Asp336Gly	rs35658696	5	102,338,811	G	A	0.0450	1.13 (1.10-1.17)	1.2x10 <sup>-16</sup>	1.13 (1.09-1.17)	7.4x10 <sup>-15</sup>	1.17 (1.11-1.24)	5.7x10 <sup>-10</sup>
<i>RREB1</i>	<i>RREB1</i> p.Asp1171Asn	rs9379084	6	7,231,843	G	A	0.884	1.08 (1.06-1.11)	3.1x10 <sup>-13</sup>	1.10 (1.07-1.13)	8.5x10 <sup>-17</sup>	1.13 (1.09-1.18)	4.0x10 <sup>-9</sup>
<i>PAX4</i>	<i>PAX4</i> p.Arg190His	rs2233580	7	127,253,550	T	C	0.0294	1.36 (1.25-1.48)	1.8x10 <sup>-12</sup>	1.38 (1.26-1.51)	4.2x10 <sup>-13</sup>	1.79 (1.47-2.19)	9.3x10 <sup>-9</sup>
<i>SLC30A8</i>	<i>SLC30A8</i> p.Arg276Trp	rs13266634	8	118,184,783	C	T	0.691	1.09 (1.08-1.11)	1.9x10 <sup>-47</sup>	1.09 (1.08-1.11)	1.3x10 <sup>-47</sup>	1.14 (1.11-1.17)	4.8x10 <sup>-23</sup>
<i>GPSM1</i>	<i>GPSM1</i> p.Ser391Leu	rs60980157	9	139,235,415	C	T	0.771	1.06 (1.05-1.08)	3.2x10 <sup>-16</sup>	1.06 (1.05-1.08)	6.6x10 <sup>-16</sup>	1.09 (1.06-1.12)	1.7x10 <sup>-9</sup>
<i>KCNJ11-ABCC8</i>	<i>KCNJ11</i> p.Lys29Glu	rs5219	11	17,409,572	T	C	0.364	1.06 (1.05-1.07)	5.7x10 <sup>-22</sup>	1.07 (1.05-1.08)	1.5x10 <sup>-22</sup>	1.07 (1.05-1.10)	9.0x10 <sup>-10</sup>
<i>CILP2</i>	<i>TM6SF2</i> p.Glu167Lys	rs58542926	19	19,379,549	T	C	0.0755	1.07 (1.05-1.10)	4.8x10 <sup>-12</sup>	1.09 (1.06-1.11)	3.4x10 <sup>-15</sup>	1.14 (1.10-1.19)	3.2x10 <sup>-10</sup>
<i>MTMR3-ASCC2</i>	<i>ASCC2</i> p.Asp407His	rs28265	22	30,200,761	C	G	0.925	1.09 (1.06-1.11)	2.1x10 <sup>-12</sup>	1.09 (1.07-1.12)	4.4x10 <sup>-14</sup>	1.12 (1.08-1.17)	1.1x10 <sup>-7</sup>

Chr: chromosome. RAF: risk allele frequency. BMI: body mass index. OR: odds ratio. CI: confidence interval.

**Supplementary Table 7 | Lead SNPs for non-coding T2D association signals attaining genome-wide significance ( $p < 5 \times 10^{-8}$ ) that map outside previously established susceptibility loci.**

(a) Trans-ethnic meta- analyses of 73,033 cases and 362,354 controls.

Locus	Lead SNP	Chr	Position	Alleles		RAF	BMI unadjusted		BMI adjusted	
				Risk	Other		OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
<b><i>Loci overlapping with novel coding association signals</i></b>										
<i>POC5-ANKDD1B</i>	rs40060	5	74,967,386	T	C	0.597	1.04 (1.03-1.06)	$1.3 \times 10^{-12}$	1.02 (1.01-1.04)	0.00038
<i>LPL</i>	rs17482753	8	19,832,646	G	T	0.904	1.06 (1.04-1.08)	$4.1 \times 10^{-8}$	1.05 (1.03-1.07)	$5.6 \times 10^{-7}$
<i>C17orf58-BPTF</i>	rs12602912	17	65,870,073	T	C	0.238	1.04 (1.03-1.06)	$4.7 \times 10^{-9}$	1.03 (1.01-1.04)	0.00016
<b><i>Loci not overlapping with novel coding association signals</i></b>										
<i>MRAS</i>	rs2306374	3	138,119,952	C	T	0.136	1.04 (1.02-1.06)	$6.5 \times 10^{-6}$	1.05 (1.03-1.07)	$1.9 \times 10^{-7}$
<i>FAM13A</i>	rs13133548	4	89,740,128	A	G	0.490	1.03 (1.02-1.04)	$8.3 \times 10^{-7}$	1.03 (1.02-1.05)	$5.0 \times 10^{-8}$
<i>VEGFA</i>	rs6905288	6	43,758,873	A	G	0.603	1.03 (1.02-1.05)	$5.5 \times 10^{-7}$	1.04 (1.03-1.05)	$5.8 \times 10^{-11}$
<i>TFAP2B</i>	rs2206277	6	50,798,526	T	C	0.195	1.05 (1.03-1.07)	$4.3 \times 10^{-10}$	1.02 (1.00-1.03)	0.022
<i>ABO</i>	rs505922	9	136,149,229	C	T	0.371	1.04 (1.03-1.05)	$9.1 \times 10^{-10}$	1.03 (1.02-1.04)	$9.4 \times 10^{-7}$
<i>PLEKHA1</i>	rs6585827	10	124,165,615	G	A	0.498	1.03 (1.02-1.05)	$8.1 \times 10^{-8}$	1.04 (1.02-1.05)	$9.5 \times 10^{-9}$
<i>TMEM258</i>	rs102275	11	61,557,803	T	C	0.638	1.03 (1.02-1.04)	$1.2 \times 10^{-5}$	1.03 (1.02-1.04)	$1.2 \times 10^{-5}$
<i>NRXN3</i>	rs10146997	14	79,945,162	G	A	0.225	1.05 (1.03-1.06)	$1.8 \times 10^{-10}$	1.03 (1.01-1.04)	0.00020
<i>PTPN9</i>	rs4886707	15	75,755,467	C	T	0.718	1.04 (1.02-1.05)	$3.8 \times 10^{-8}$	1.04 (1.03-1.05)	$4.3 \times 10^{-9}$
<i>NFAT5</i>	rs1364063	16	69,588,572	T	C	0.621	1.03 (1.01-1.04)	$2.3 \times 10^{-5}$	1.02 (1.01-1.03)	0.00094
<i>CMIP1</i>	rs2925979	16	81,534,790	T	C	0.305	1.04 (1.02-1.05)	$2.5 \times 10^{-8}$	1.03 (1.02-1.05)	$1.0 \times 10^{-5}$
<i>HORMAD2</i>	rs2412980	22	30,592,069	C	T	0.926	1.08 (1.06-1.11)	$2.6 \times 10^{-11}$	1.09 (1.06-1.11)	$2.8 \times 10^{-11}$

(b) European-specific meta-analysis of 45,927 cases and 248,489 controls.

Locus	Lead SNP	Chr	Position	Alleles		RAF	BMI unadjusted		BMI adjusted	
				Risk	Other		OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
<b><i>Loci overlapping with novel coding association signals</i></b>										
<i>POC5-ANKDD1B</i>	rs40060	5	74,967,386	T	C	0.642	1.05 (1.03-1.07)	$2.8 \times 10^{-11}$	1.03 (1.01-1.04)	$7.8 \times 10^{-5}$
<i>LPL</i>	rs17482753	8	19,832,646	G	T	0.902	1.05 (1.03-1.07)	$1.1 \times 10^{-5}$	1.09 (1.07-1.11)	$8.0 \times 10^{-6}$
<i>C17orf58-BPTF</i>	rs12602912	17	65,870,073	T	C	0.207	1.05 (1.03-1.07)	$1.1 \times 10^{-8}$	1.03 (1.01-1.05)	0.00011
<b><i>Loci not overlapping with novel coding association signals</i></b>										
<i>MRAS</i>	rs2306374	3	138,119,952	C	T	0.164	1.09 (1.08-1.11)	$4.3 \times 10^{-7}$	1.09 (1.08-1.11)	$2.8 \times 10^{-9}$
<i>FAM13A</i>	rs13133548	4	89,740,128	A	G	0.471	1.06 (1.05-1.08)	$3.6 \times 10^{-6}$	1.05 (1.04-1.07)	$4.8 \times 10^{-8}$
<i>VEGFA</i>	rs6905288	6	43,758,873	A	G	0.563	1.03 (1.01-1.04)	$3.2 \times 10^{-5}$	1.04 (1.02-1.06)	$3.0 \times 10^{-8}$
<i>TFAP2B</i>	rs2206277	6	50,798,526	T	C	0.188	1.03 (1.02-1.05)	$7.1 \times 10^{-6}$	1.04 (1.02-1.05)	0.228
<i>ABO</i>	rs505922	9	136,149,229	C	T	0.362	1.04 (1.02-1.05)	$2.7 \times 10^{-6}$	1.04 (1.03-1.06)	$8.4 \times 10^{-6}$

<i>PLEKHA1</i>	rs6585827	10	124,165,615	G	A	0.501	1.05 (1.04-1.07)	1.8x10 <sup>-6</sup>	1.06 (1.05-1.07)	2.0x10 <sup>-8</sup>
<i>TMEM258</i>	rs102275	11	61,557,803	T	C	0.645	1.04 (1.02-1.05)	1.1x10 <sup>-6</sup>	1.04 (1.02-1.06)	5.0x10 <sup>-8</sup>
<i>NRXN3</i>	rs10146997	14	79,945,162	G	A	0.222	1.05 (1.03-1.07)	5.3x10 <sup>-10</sup>	1.03 (1.01-1.04)	0.00067
<i>PTPN9</i>	rs4886707	15	75,755,467	C	T	0.761	1.04 (1.02-1.06)	1.5x10 <sup>-6</sup>	1.04 (1.02-1.05)	1.2x10 <sup>-6</sup>
<i>NFAT5</i>	rs1364063	16	69,588,572	T	C	0.579	1.04 (1.03-1.06)	2.5x10 <sup>-8</sup>	1.02 (1.01-1.04)	0.00018
<i>CMIP1</i>	rs2925979	16	81,534,790	T	C	0.304	1.04 (1.02-1.05)	2.1x10 <sup>-5</sup>	1.04 (1.02-1.05)	7.7x10 <sup>-6</sup>
<i>HORMAD2</i>	rs2412980	22	30,592,069	C	T	0.917	1.09 (1.06-1.12)	4.2x10 <sup>-9</sup>	1.09 (1.06-1.11)	4.2x10 <sup>-10</sup>

Chr: chromosome. RAF: risk allele frequency. BMI: body mass index. OR: odds ratio. CI: confidence interval.

Supplementary Table 8 | Summary of gene-based signals at *FAM63A* and *PAM*, including single-variant *p*-values.

Gene-based analysis (58,425 cases and 188,032 controls)								Variants included in the masks							
Gene	Mask	Trans-ethnic (58,425 cases and 188,032 controls)			European (41,066 cases and 136,024 controls)			rs ID	Chr	Position	Variant annotation	Trans-ethnic		European	
		Number of variants in the mask	<i>P</i> <sub>burden</sub>	<i>P</i> <sub>SKAT</sub>	Number of variants in the mask	<i>P</i> <sub>burden</sub>	<i>P</i> <sub>SKAT</sub>					MAF (%)	<i>P</i>	MAF (%)	<i>P</i>
<i>FAM63</i>	Strict	8	6.2x10 <sup>-7</sup>	9.7x10 <sup>-9</sup>	8	4.1x10 <sup>-7</sup>	4.0x10 <sup>-9</sup>	rs146551660	1	150970119	p.Thr295Met	0.062	0.079	0.039	0.00042
	Broad	10	2.1x10 <sup>-7</sup>	8.5x10 <sup>-9</sup>	10	4.6x10 <sup>-8</sup>	<b>3.1x10<sup>-9</sup></b>	1:150970216	1	150970216	p.Arg263*	0.0085	0.80	0.0050	0.25
								rs143579361	1	150970680	p.His209Tyr	0.13	0.18	0.15	0.17
								rs139059568	1	150971879	p.Arg174Gln	0.028	0.12	0.032	0.13
								rs150431391	1	150971880	p.Arg174*	0.014	0.29	0.018	0.24
								rs138246511	1	150971949	p.Gln151*	0.0082	0.47	0.023	0.34
								rs140386498	1	150972959	p.Tyr95Asn	1.1	2x10 <sup>-8</sup>	1.4	1x10 <sup>-8</sup>
								rs145467872	1	150973013	p.Asp77Asn	0.15	0.65	0.16	0.63
								rs142215084	1	150974740	p.Trp166*	0.074	0.98	0.077	0.88
								rs138505497	1	150974828	p.Glu137Gly	0.062	0.85	0.020	0.18
<i>PAM</i>	Strict	7	2.6x10 <sup>-8</sup>	1.1x10 <sup>-8</sup>	7	4.3x10 <sup>-8</sup>	2.7x10 <sup>-8</sup>	rs199856250	5	102201978	p.Val27Ile	0.0077	0.54	0.011	0.17
	Broad	17	1.4x10 <sup>-7</sup>	<b>8.2x10<sup>-9</sup></b>	15	3.0x10 <sup>-7</sup>	1.5x10 <sup>-8</sup>	rs200066052	5	102203047	p.Ser54Pro	0.029	0.91	0.030	0.90
								rs201199380	5	102203059	p.Ala58Thr	0.034	0.81	0.035	0.72
								rs181340861	5	102260735	p.Arg144Gln	0.056	0.73	0.019	0.90
								rs145099851	5	102282583	p.Arg190His	0.10	0.28	0.12	0.17
								rs201009674	5	102285612	p.Val244Ala	0.062	0.88	0.071	0.82
								rs147370276	5	102295628	p.Glu319Gln	0.0090	0.97	0.009	0.97
								rs61729214	5	102295724	p.Val351Met	0.041	0.52	0.012	0.65
								rs139660283	5	102309859	p.Arg401Lys	0.015	0.92	0.011	0.75
								rs145710876	5	102310011	p.Ile452Val	0.059	0.35	0.00	-
								rs144310649	5	102310060	p.Leu468Ser	0.027	0.13	0.028	0.60
								rs114049029	5	102310135	p.Thr493Ile	0.16	0.59	0.00	-
								rs150469595	5	102338783	p.Ile554Val	0.046	0.73	0.047	0.74
								rs35658696	5	102338811	p.Asp563Gly	4.0	7x10 <sup>-9</sup>	5.0	3.1x10 <sup>-8</sup>
								rs186632214	5	102343266	p.Arg707Gln	0.016	0.50	0.0073	0.43
								rs200646882	5	102345565	p.Arg776Cys	0.014	0.69	0.014	0.38
								rs137865834	5	102364597	p.Gly918Glu	0.028	0.98	0.027	0.91

Chr: chromosome. MAF: minor allele frequency. Variants included only in the strict mask are highlighted in grey.

**Supplementary Tables 9, 10, and 11 can be found in the Supplementary excel files.**

**Supplementary Table 9** | Study characteristics and analysis details of studies included in the DIAGRAM consortium GWAS.

**Supplementary Table 10** | Summary of fine-mapping analyses with functionally unweighted and annotation informed prior.

**Supplementary Table 11** | Association of T2D signals with various metabolic and anthropometric traits.

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#### iv. Consortium membership

##### Exome BP Consortium

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