Large-scale association analysis provides insights into the genetic architecture and pathophysiology of type 2 diabetes

Supplementary Note

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Contents

Resources interrogated for expression analyses

We identified proxies (CEU r^2>0.8) for each lead T2D SNP in novel susceptibility loci (also including *GRB14* and *HMG20A*). We interrogated public databases and unpublished resources for *cis*-eQTL expression with these SNPs in multiple tissues: fresh lymphocytes[1]; fresh leukocytes[2]; leukocytes from individuals with Celiac disease[3]; lymphoblastoid cell lines (LCL) derived from asthmatic children[4]; LCL from HapMap[5,6]; peripheral blood monocytes[7,8]; omental and subcutaneous fat[9,10]; endometrial carcinomas[11]; brain cortex[7,12]; three studies of brain regions including prefrontal cortex, visual cortex and cerebellum (Emilsson, personal communication); liver[13-15]; osteoblasts[16]; skin[17]; and additional fibroblast, T cell and LCL samples[18].

Biological hypotheses related to disease pathogenesis tested with GSEA

Adipocytokine signalling. Adipocytokines have been implicated in the development of insulin resistance. Leptin and adiponectin are potential insulin sensitizers and TNF-alpha is a potential insulin antagonist[19].

Amyloid metabolism. The islet amyloid polypeptide inhibits insulin and glucagon secretion from pancreatic beta-islet cells. Islet amyloid deposits have been associated with T2D and pancreatic beta-cell loss[20,21].

Branched-chain amino acid metabolism. Elevated branched-chain amino acid plasma levels are associated with high insulin resistance and/or low circulating levels of insulin in T2D cases. The branched-chain amino acids, isoleucine, leucine and valine, are strong predictors of future diabetes. Leucine acutely stimulates insulin secretion in pancreatic beta cells[22-24].

Cell cycle. Several cell cycle regulators lie in previously established T2D loci, including *CDKN2B/A*, *CDKN1C*, and *CCNE2*. The majority of these genes regulate CDK4 or CDK6, shown to play a role in beta-islet pancreatic cell proliferation, which in turn may affect insulin secretion. These regulators may also have an effect on peripheral tissues relevant to T2D[25-27].

Circadian rhythm. Several studies showed that people with an altered circadian rhythm have an increased risk of developing T2D. *MTNR1B* regulates circardian rhythm and contains common variants associated with T2D, fasting glucose, and pancreatic beta-cell function, suggesting a causal role for circadian rhythm in T2D. The melatonin system was shown to regulate glucose homeostasis[28-32].

Endoplasmic reticulum (ER) stress response (unfolded protein response). *WFS1*, a component of the unfolded protein response, lies near common variants associated with T2D and harbours rare mutations associated with Wolfram syndrome, a rare syndrome that causes diabetes mellitus, amongst other disorders. *WFS1* is up-regulated during insulin secretion. Inactivation of *WFS1* in beta-cells causes ER stress and dysfunction. Furthermore, *EIF2AK3*, a key component of the ER stress response pathway, contains rare mutations that cause neonatal diabetes[33-35].

Fatty acid metabolism. Elevated plasma free fatty acid (FFA) concentrations are linked with the onset of skeletal muscle and hepatic insulin resistance and are associated with T2D. Elevated blood fatty-acid concentrations reduce muscle glucose uptake, and increase liver glucose production, contributing to elevated blood glucose levels. FFA also affects insulin secretion from the pancreas. However, in pre-diabetic patients, FFA stimulation of insulin secretion is not sufficient to fully compensate for the FFA-induced insulin resistance, leading to hyperglycaemia[36,37].

Glycolysis and gluconeogenesis. Glucokinase, *GCK*, the first glycolytic enzyme, and *GCKR*, a regulator of *GCK*, contain or lie near common SNPs associated with T2D. Studies have shown that hepatic gluconeogenesis is increased in people with T2D compared with controls following overnight fasting[38,39].

Inflammation. Elevated levels of the inflammatory cytokines, TNF-alpha and IL-6, and the C-reactive protein that rises in response to inflammation, predict the development of T2D. However, whether inflammation is a primary cause of T2D or secondary to hyperglycaemia (or other T2D features) is not yet clear. A potential mechanism of causality is through macrophages that release cytokines, causing neighbouring liver, muscle or fat cells to become insulin resistant. Inflammation in pancreatic islets could also lead to a decrease in beta-cell mass affecting insulin secretion levels[40-43].

Insulin signalling. Alterations in insulin signalling may lead to insulin resistance in peripheral tissues such as fat, liver and muscle, a major risk factor for T2D[27,44].

Insulin synthesis and secretion. Insufficient insulin secretion is one of the major causes of T2D. Many of the established T2D common SNP associations lie near genes implicated in beta-cell function, such as *KCNJ11* and *ABCC8*. These ATP sensitive potassium channel subunits, proximal to each other on the chromosome, are targets of anti-diabetes drugs (sulfonylurea and/or meglitinides) that lead to an increase in insulin secretion. Mutations in these genes are also associated with different forms of neonatal diabetes[27,44].

Mitochondrial dysfunction. Mitochondrial dysfunction has been implicated in both rare and common forms of diabetes. T2D cases have less mitochondria in their skeletal muscle, and oxidative phosphorylation genes are collectively down-regulated in muscle, compared with healthy individuals. However, pronounced genetic evidence for a causal effect of decreased mitochondrial activity on T2D has not yet been shown[45-47].

NOTCH signalling. *NOTCH2* contains a common variant associated with T2D. NOTCH signalling plays a role in pancreas development[35,48].

PPARG signalling. *PPARG* contains a common variant associated with T2D, and is the target of thiazolidinedione (TZD) drugs, used clinically to reduce insulin resistance in T2D patients. *PPARG* plays a role in fat, liver and muscle[49,50].

Vitamin D metabolism. Vitamin D deficiency has been suggested to be associated with T2D and insulin resistance. Vitamin D may also play a role in insulin secretion by promoting calcium absorption in the pancreas[51-53].

WNT signalling. A strong common variant association signal lies in an intron of *TCF7L2*, a transcription factor that regulates WNT targets. The WNT signalling pathway may play a role in both the insulin secretion and insulin sensitivity features of T2D. For example, WNT signalling activation in the pancreas leads to pancreatic beta cell proliferation, and improved insulin sensitivity in skeletal muscle[54-57].

References

1. Goring HH, *et al*. (2007). Discovery of expression QTLs using large-scale transcriptional profiling in human lymphocytes. *Nat Genet* 39: 1208-16.
2. Idaghdour Y, *et al*. (2010). Geographical genomics of human leukocyte gene expression variation in southern Morocco. *Nat Genet* 42: 62-7.
3. Heap GA, *et al*. (2009). Complex nature of SNP genotype effects on gene expression in primary human leucocytes. *BMC Med Genomics* 2: 1.
4. Dixon AL, *et al*. (2007). A genome-wide association study of global gene expression. *Nat Genet* 39: 1202-7.
5. Stranger BE, *et al*. (2007). Population genomics of human gene expression. *Nat Genet* 39: 1217-24.
6. Kwan T, *et al*. (2008). Genome-wide analysis of transcript isoform variation in humans. *Nat Genet* 40: 225-31.
7. Heinzen EL, *et al*. (2008). Tissue-specific genetic control of splicing: implications for the study of complex traits. *PLoS Biol* 6: e1.
8. Zeller T, *et al*. (2010). Genetics and beyond - the transcriptome of human monocytes and disease susceptibility. *PLoS One* 5: e10693.
9. Emilsson V, *et al*. (2008). Genetics of gene expression and its effect on disease. *Nature* 452: 423-8.
10. Fehrmann RS, *et al*. (2011). Trans-eQTLs reveal that independent genetic variants associated with a complex phenotype converge on intermediate genes with a major role for the HLA. *PLoS Genet* 7: e1002197.
11. Kompass KS, Witte JS (2011). Co-regulatory expression quantitative trait loci mapping: method and application to endometrial cancer. *BMC Med Genomics* 4: 6.
12. Webster JA, *et al*. (2009). Genetic control of human brain transcript expression in Alzheimer disease. *Am J Hum Genet* 84: 445-58.
13. Schadt EE, *et al*. (2008). Mapping the genetic architecture of gene expression in human liver. *PLoS Biol* 6: e107.
14. Greenawalt DM, *et al*. (2011). A survey of the genetics of stomach, liver and adipose gene expression from a morbidly obese cohort. *Genome Res* 21: 1008-16.
15. Innocenti F, *et al*. (2011). Identification, replication, and functional fine-mapping of expression quantitative trait loci in primary human liver tissue. *PLoS Genet* 7: e1002078.
16. Grundberg E, *et al*. (2009). Population genomics in a disease targeted primary cell model. *Genome Res* 19: 1942-52.

17. Ding J, *et al*. (2010). Gene expression in skin and lymphoblastoid cells: refined statistical method reveals extensive overlap in *cis*-eQTL signals. *Am J Hum Genet* 87: 779-89.
18. Dimas AS, *et al*. (2009). Common regulatory variation impacts gene expression in a cell type-dependent manner. *Science* 325: 1246-50.
19. Pittas AG, *et al*. (2004). Adipocytokines and insulin resistance. *J Clin Endocrinol Metab* 89: 447-52.
20. Westermark P (2011). Amyloid in the islets of Langerhans: thoughts and some historical aspects. *Uppsala J Med Sciences* 116: 81-9.
21. Westermark P, *et al*. (2011). Islet amyloid polypeptide, islet amyloid, and diabetes mellitus. *Physiological Rev* 91: 795-826.
22. Shaham O, *et al*. (2008). Metabolic profiling of the human response to a glucose challenge reveals distinct axes of insulin sensitivity. *Molecular Systems Biology* 4: 214.
23. Wang TJ, *et al*. (2011). Metabolite profiles and the risk of developing diabetes. *Nat Medicine* 17: 448-53.
24. Yang J, *et al*. (2010). Leucine metabolism in regulation of insulin secretion from pancreatic beta cells. *Nutrition Reviews* 68: 270-9.
25. Rane SG, *et al*. (1999). Loss of Cdk4 expression causes insulin-deficient diabetes and Cdk4 activation results in beta-islet cell hyperplasia. *Nat Genet* 22: 44-52.
26. Fiaschi-Taesch NM, *et al*. (2010). Induction of human beta-cell proliferation and engraftment using a single G1/S regulatory molecule, cdk6. *Diabetes* 59: 1926-36.
27. Voight BF, *et al*. (2010). Twelve type 2 diabetes susceptibility loci identified through large-scale association analysis. *Nat Genet* 42: 579-89.
28. Prokopenko I, *et al*. (2009). Variants in *MTNR1B* influence fasting glucose levels. *Nat Genet* 41: 77-81.
29. Bouatia-Naji N, *et al*. (2009). A variant near *MTNR1B* is associated with increased fasting plasma glucose levels and type 2 diabetes risk. *Nat Genet* 41: 89-94.
30. Lyssenko V, *et al*. (2009). Common variant in *MTNR1B* associated with increased risk of type 2 diabetes and impaired early insulin secretion. *Nat Genet* 41: 82-8.
31. Gangwisch JE (2009). Epidemiological evidence for the links between sleep, circadian rhythms and metabolism. *Obesity Reviews* 10: 37-45.
32. Müssig K, *et al*. (2010). Genetic variants in *MTNR1B* affecting insulin secretion. *Ann Medicine* 42: 387-93.
33. Fonseca SG, *et al*. (2005). *WFS1* is a novel component of the unfolded protein response and maintains homeostasis of the endoplasmic reticulum in pancreatic beta-cells. *J Biological Chem* 280: 39609-15.
34. Yamada T, *et al*. (2006). *WFS1*-deficiency increases endoplasmic reticulum stress impairs cell cycle progression and triggers the apoptotic pathway specifically in pancreatic beta-cells. *Hum Mol Genet* 15: 1600-9.
35. Zeggini E, et al. (2008). Meta-analysis of genome-wide association data and large-scale replication identifies additional susceptibility loci for type 2 diabetes. *Nat Genet* 40: 638-45.
36. Boden G, Shulman GI (2002). Free fatty acids in obesity and type 2 diabetes: defining their role in the development of insulin resistance and beta-cell dysfunction. *Eur J Clinical Investigation* 32: 14-23.

37. Boden G (2005). Free fatty acids and insulin secretion in humans. *Curr Diabetes Reports* 5:167-170.
38. Magnusson I, *et al*. (1992). Increased rate of gluconeogenesis in type II diabetes mellitus: A 13C nuclear magnetic resonance study. *J Clinical Investigation* 90: 1323-7.
39. Dupuis J, *et al*. (2010). New genetic loci implicated in fasting glucose homeostasis and their impact on type 2 diabetes risk. *Nat Genet* 42: 105-16.
40. Pickup JC (2004). Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. *Diabetes Care* 27:813-23.
41. Pradhan AD, *et al*. (2001). C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA* 286: 327-34.
42. Dandona P, *et al*. (2004). Inflammation: the link between insulin resistance, obesity and diabetes. *Trends Immunol* 25: 4-7.
43. Donath MY, *et al*. (2009). Islet inflammation impairs the pancreatic beta-cell in type 2 diabetes. *Physiology* 24: 325-31.
44. Muoio DM, Newgard CB (2008). Mechanisms of disease: molecular and metabolic mechanisms of insulin resistance and beta-cell failure in type 2 diabetes. *Nat Rev Mol Cell Biol* 9: 193-205.
45. Mootha VK, *et al*. (2003). PGC-1alpha-responsive genes involved in oxidative phosphorylation are coordinately downregulated in human diabetes. Nat Genet, 34: 267-73.
46. Dumas J-F, *et al*. (2009). Is skeletal muscle mitochondrial dysfunction a cause or an indirect consequence of insulin resistance in humans? *Diabetes and Metabolism* 35: 159-167.
47. Segrè AV, *et al*. (2010). Common inherited variation in mitochondrial genes is not enriched for associations with type 2 diabetes or related glycemic traits. *PLoS Genet* 12: e1001058.
48. Kim W, *et al*. (2010). Notch signaling in pancreatic endocrine cell and diabetes. *Biochemical and Biophysical Research Communications* 392: 247-51.
49. Florez JC, et al. (2007). Effects of the type 2 diabetes-associated PPARG P12A polymorphism on progression to diabetes and response to troglitazone. *J Clin Endocrinol Metabolism* 92: 1502-9.
50. Rosen ED, Spiegelman BM (2001). PPARgamma: a nuclear regulator of metabolism, differentiation, and cell growth. *J Biolog Chem* 276: 37731-4.
51. Boucher BJ (2011). Vitamin D insufficiency and diabetes risks. *Current Drug Targets* 12: 61-87.
52. Wolden-Kirk H, *et al*. (2011). Vitamin D and diabetes: its importance for beta cell and immune function. *Mol Cellular Endocrinol* 347: 106-20.
53. Mitri J, *et al*. (2011). Vitamin D and type 2 diabetes: a systematic review. *Eur J Clin Nutrition* 65: 1005-15.
54. Abiola M, *et al*. (2009). Activation of Wnt/beta-catenin signaling increases insulin sensitivity through a reciprocal regulation of Wnt10b and SREBP-1c in skeletal muscle cells. *PloS One* 4: e8509.
55. Jin T, Liu L (2008). The Wnt signaling pathway effector *TCF7L2* and type 2 diabetes mellitus. *Mol Endocrinol* 22: 2383-92.
56. Perry JRB, *et al*. (2009). Interrogating type 2 diabetes genome-wide association data using a biological pathway-based approach. *Diabetes* 58: 1463-7.

57. Saxena R, *et al*. (2006). Common single nucleotide polymorphisms in *TCF7L2* are reproducibly associated with type 2 diabetes and reduce the insulin response to glucose in nondiabetic individuals. *Diabetes* 55: 2890-5.

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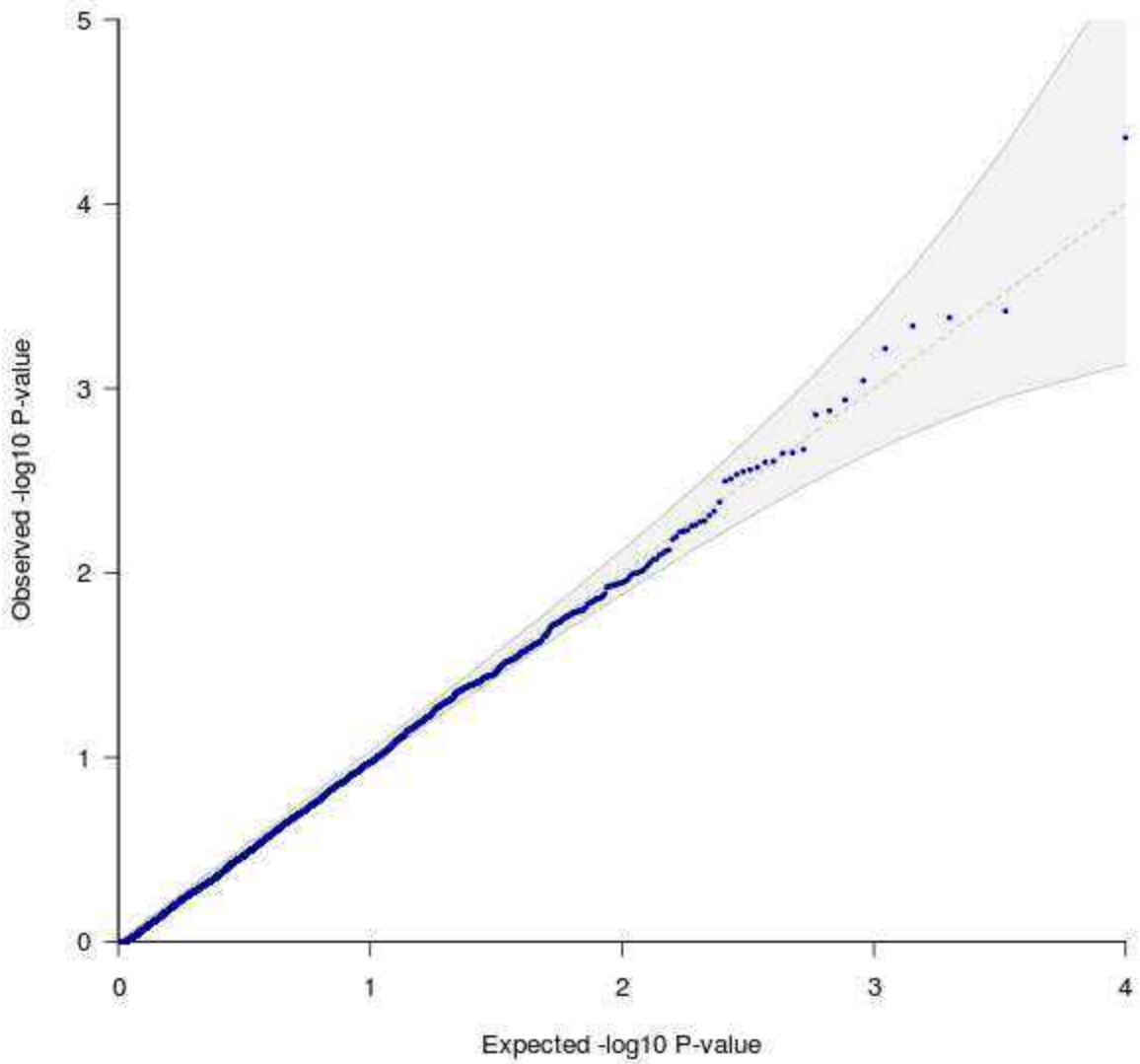
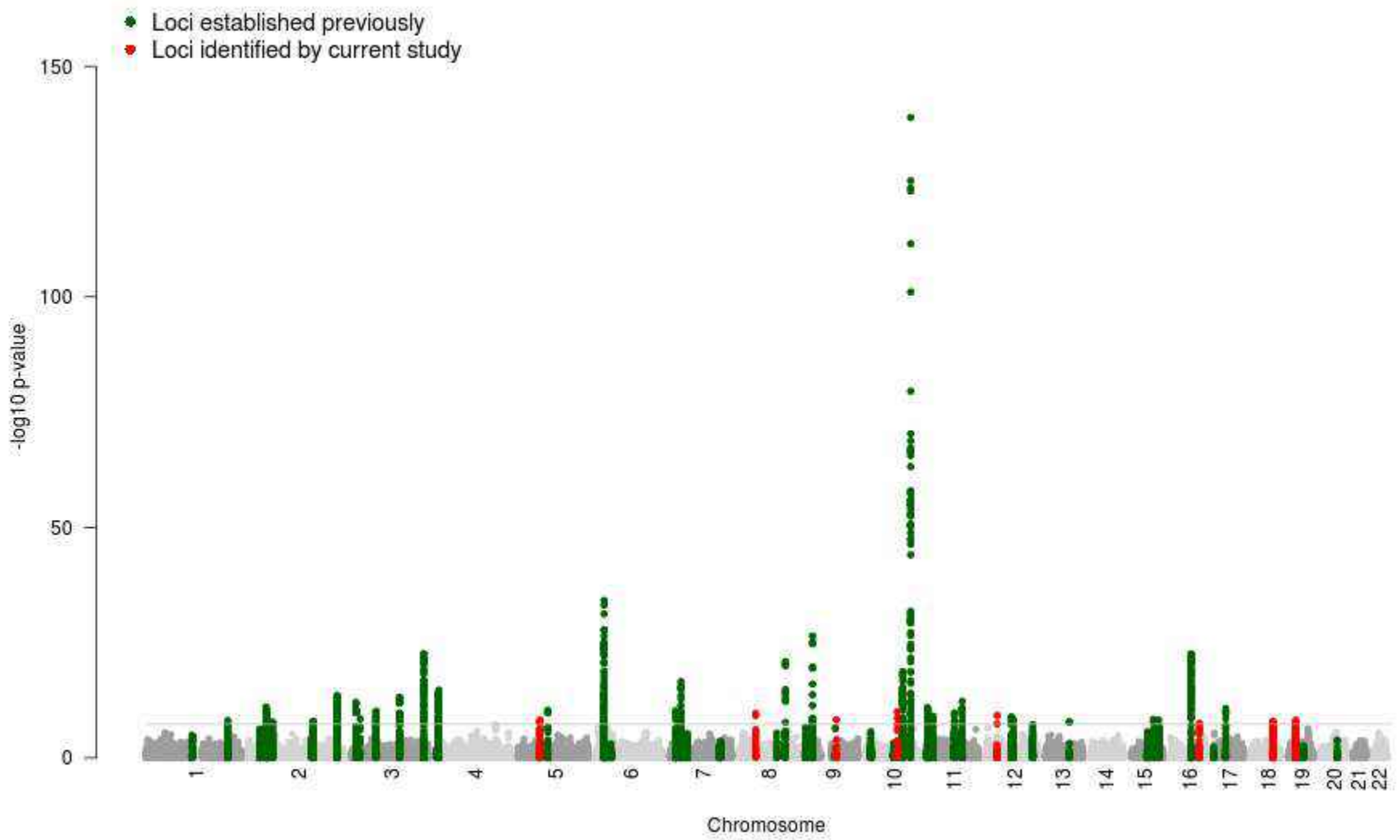
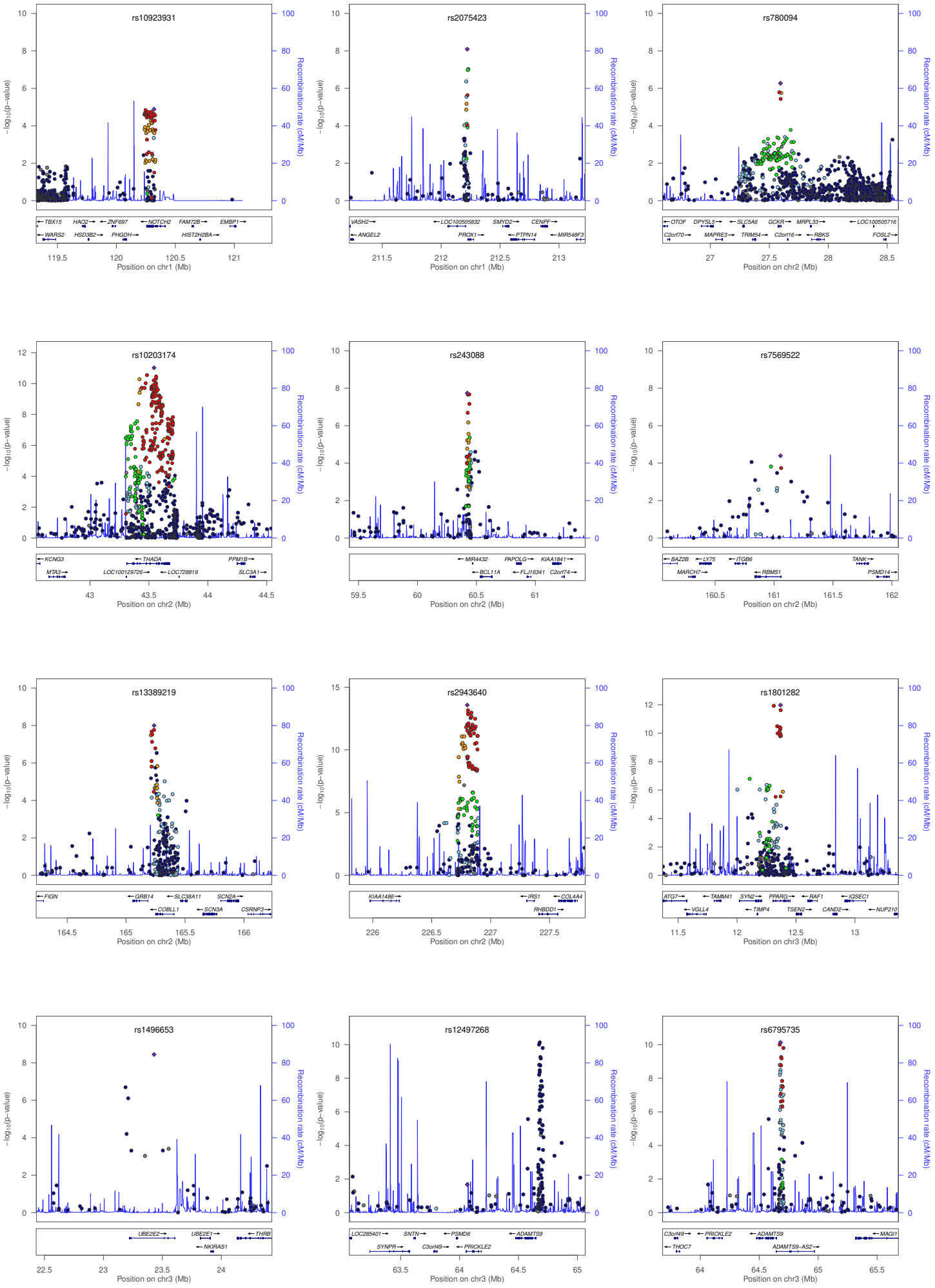
Supplementary Figure 1. QQ-plot for heterogeneity in allelic odds ratios between Stage 2 European descent meta-analysis and PROMIS. Each point represents a Metabochip SNP passing quality control in the Stage 2 meta-analysis. The y-axis corresponds to the observed $\log_{10}$ p-value from Cochran's Q-statistic of heterogeneity. The x-axis corresponds to the corresponding expected $\log_{10}$ p-value under the null hypothesis of no heterogeneity in allelic odds ratios between the Stage 2 European meta-analysis and PROMIS. The grey funnel represents 95% confidence limits for the expected p-values.



Supplementary Figure 2. Manhattan plot for the combined meta-analysis. Previously established loci are highlighted in green. Novel loci achieving genome-wide significance in the present study are highlighted in red.



Supplementary Figure 3. Regional plots of novel and established T2D susceptibility loci. Each point represents a Metabochip SNP passing quality control in our combined meta-analysis, plotted with their p-value (on a $-\log_{10}$ scale) as a function of genomic position (NCBI Build 36). In each panel, the lead SNP is represented by the purple diamond. The colour coding of all other SNPs (circles) indicates LD with the lead SNP (estimated by CEU r^2 from the 1000 Genomes Project June 2010 release): 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. Recombination rates are estimated from the International HapMap Project and gene annotations are taken from the University of California Santa Cruz genome browser.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rs780094
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rs243088
rs7569522
rs13389219
rs2943640
rs1801282
rs1496653
rs12497268
rs6795735
−log10(p−value)
Recombination rate (cM/Mb)
Position on chr1 (Mb)
Position on chr2 (Mb)
Position on chr3 (Mb)
TBX15 HAO2 ZNF697 NOTCH2 FAM72B EMBP1
WARS2 HSD3B2 PHGDH HIST2H2BA
VASH2 LOC100505832 SMYD2 CENPF
ANGEL2 PROX1 PTPN14 MIR548F3
OTOF DPYSL5 SLC5A6 GCKR MRPL33 LOC100505716
C2orf70 MAPRE3 TRIM54 C2orf16 RBKS FOSL2
KCNG3 THADA PPM1B
MTA3 LOC100129726 LOC728819 SLC3A1
MIR4432 PAPOLG KIAA1841
BCL11A FLJ16341 C2orf74
BAZ2B LY75 ITGB6 TANK
MARCH7 RBMS1 PSMD14
FIGN GRB14 SLC38A11 SCN2A
COBLL1 SCN3A CSRNP3
KIAA1486 IRS1 COL4A4
RHBDD1
ATG7 TAMM41 SYN2 PPARG RAF1 IQSEC1
VGLL4 TIMP4 TSEN2 CAND2 NUP210
UBE2E2 UBE2E1 THRB
NKIRAS1
LOC285401 SNTN PSMD6 ADAMTS9
SYNPR C3orf49 PRICKLE2
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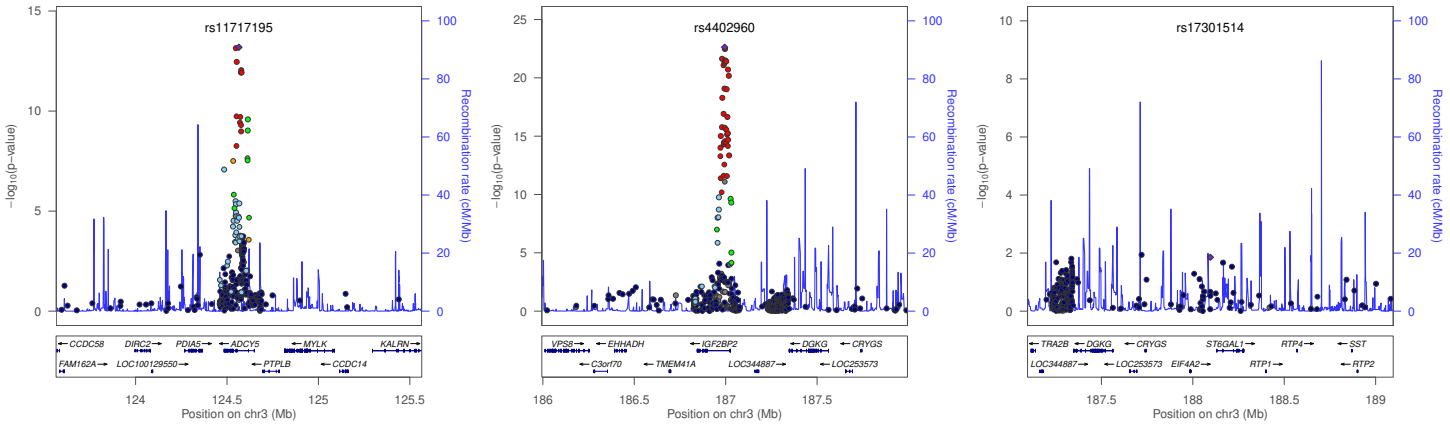
THOC7 ADAMTS9-AS2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Recombination rate (cM/Mb)
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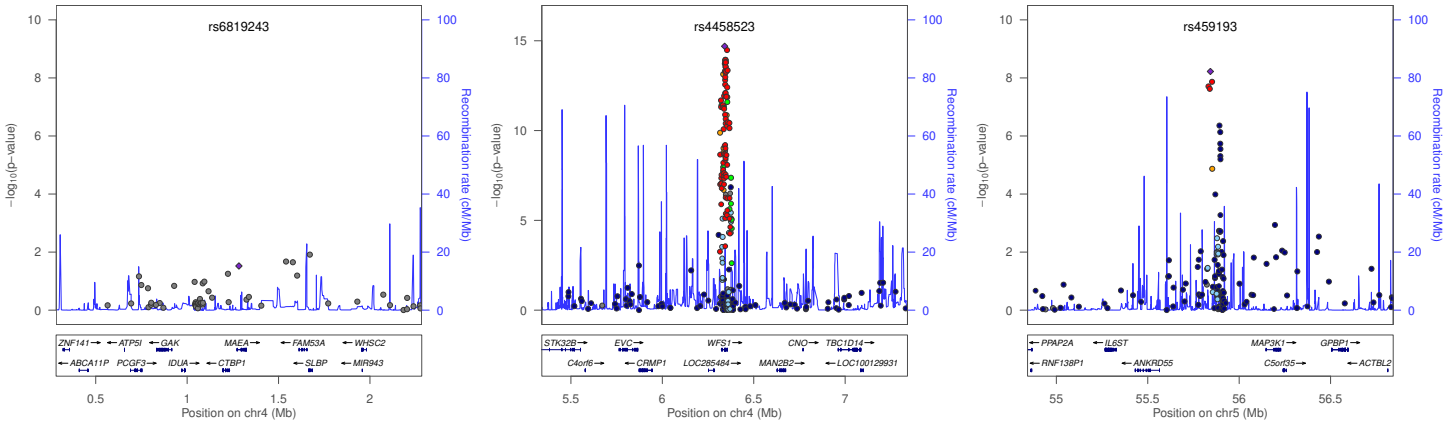
FAM162A LOC100129550 PTPLB CCDC14
VPS8 EHHADH IGF2BP2 DGKG CRYGS
C3orf70 TMEM41A LOC344887 LOC253573
TRA2B DGKG CRYGS ST6GAL1 RTP4 SST
LOC344887 LOC253573 EIF4A2 RTP1 RTP2
Position on chr3 (Mb)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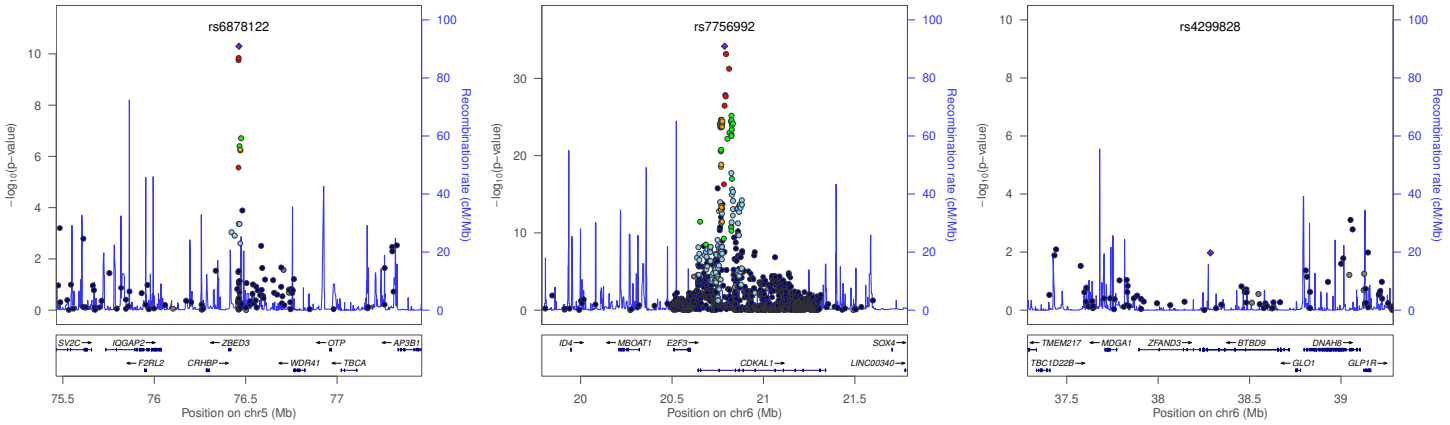
rs4458523
rs459193
−log10(p−value)
Recombination rate (cM/Mb)
ZNF141 ATP5I GAK MAEA FAM53A WHSC2
ABCA11P PCGF3 IDUA CTBP1 SLBP MIR943
STK32B EVC WFS1 CNO TBC1D14
C4orf6 CRMP1 LOC285484 MAN2B2 LOC100129931
PPAP2A IL6ST MAP3K1 GPBP1
RNF138P1 ANKRD55 C5orf35 ACTBL2
Position on chr4 (Mb)
Position on chr5 (Mb)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rs7756992
rs4299828
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Recombination rate (cM/Mb)
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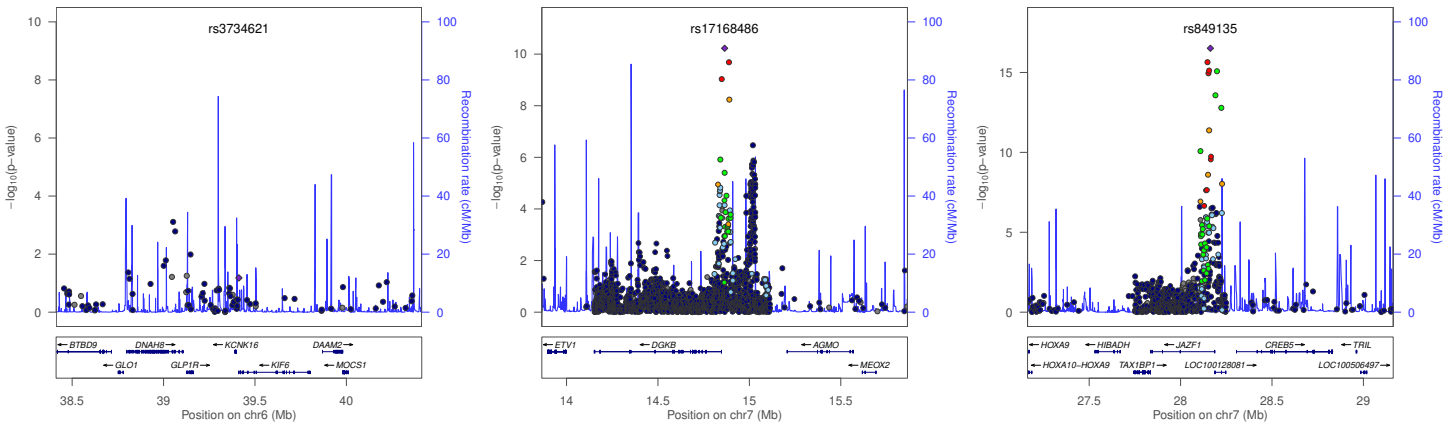
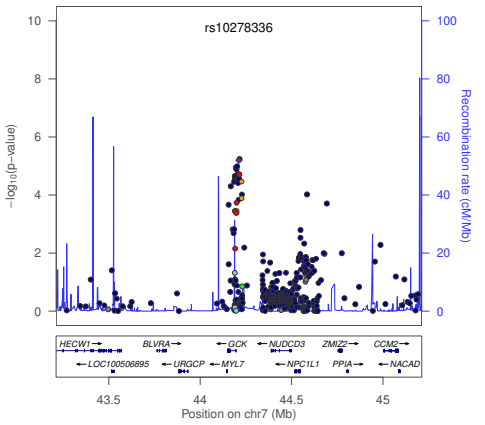
F2RL2 CRHBP WDR41 TBCA
ID4 MBOAT1 E2F3 SOX4
CDKAL1 LINC00340
TMEM217 MOGA1 ZFAND3 BTBD9 DNAH8
TBC1D22B GLO1 GLP1R
Position on chr5 (Mb)
Position on chr6 (Mb)


rs3734621
rs17168486
rs849135
−log10(p−value)
Recombination rate (cM/Mb)
BTBD9 DNAH8 KCNK16 DAAM2
GLO1 GLP1R KIF6 MOCS1
ETV1 DGKB AGMO
MECX2
HOXA9 HIBADH JAZF1 CREB5 TRIL
HOXA10-HOXA9 TAX1BP1 LOC100128081 LOC100506497
Position on chr6 (Mb)
Position on chr7 (Mb)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Recombination rate (cM/Mb)
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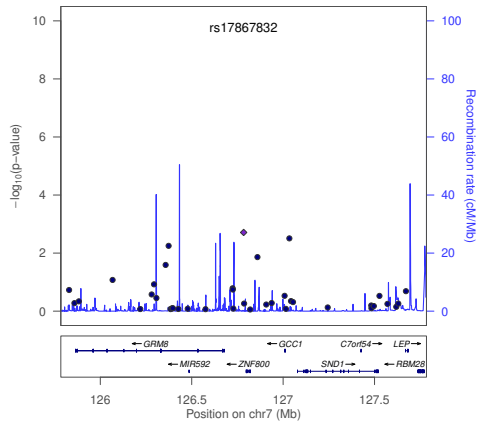
LOC100506895 UBQCP MYL7 NPC1L1 PPIA NACAD
Position on chr7 (Mb)


rs17867832
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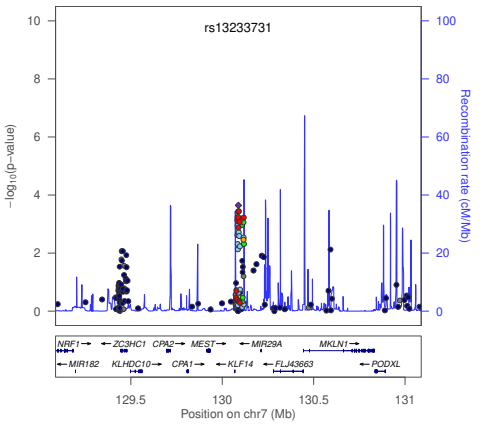
Recombination rate (cM/Mb)
GRM8 GCC1 C7orf54 LEP
MIR592 ZNF800 SND1 RBM28
Position on chr7 (Mb)


rs13233731
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Recombination rate (cM/Mb)
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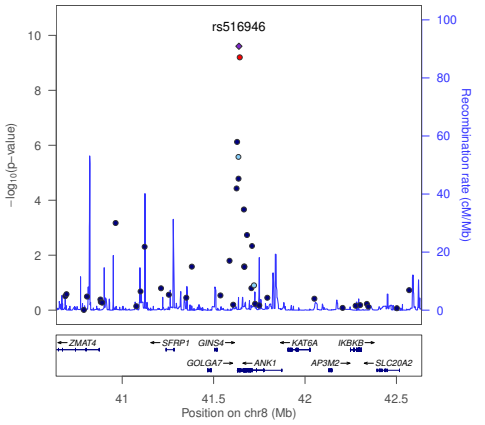
MIR182 KLHDC10 CPA1 KLF14 FLJ43663 PODXL
Position on chr7 (Mb)


rs516946
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Recombination rate (cM/Mb)
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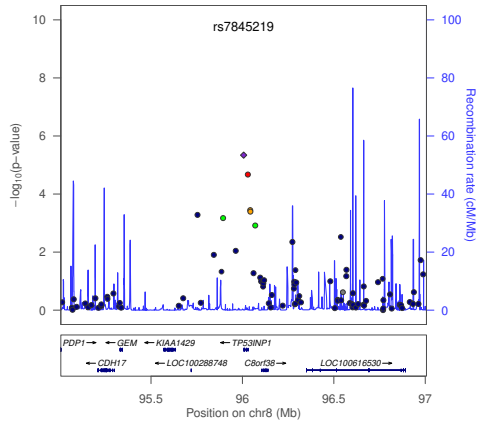
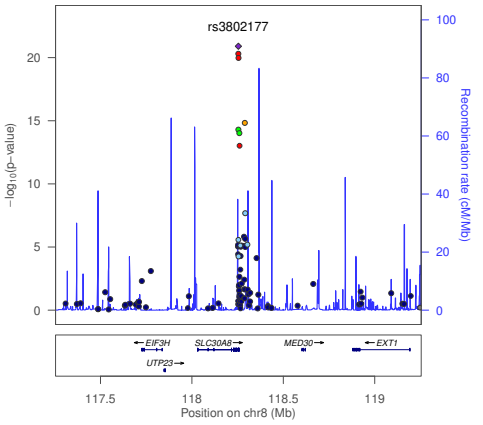
GOLGA7 ANK1 AP3M2 SLC20A2
Position on chr8 (Mb)


rs7845219
−log10(p-value)
Recombination rate (cM/Mb)
PDP1 GEM KIAA1429 TPS3INP1
CDH17 LOC100288748 C8orf38 LOC100616530
Position on chr8 (Mb)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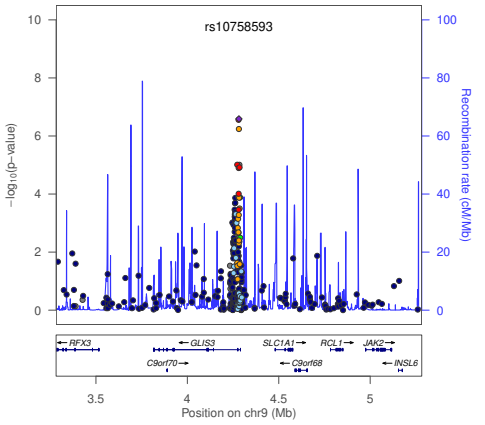
EIF3H SLC30A8 MED30 EXT1
UTP23
Position on chr8 (Mb)


rs10758593
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Recombination rate (cM/Mb)
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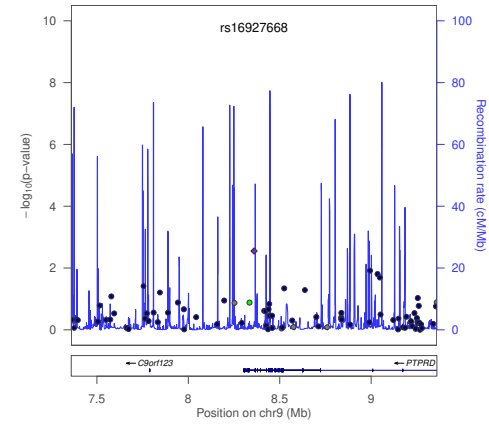
C9orf70 C9orf68 INSL6
Position on chr9 (Mb)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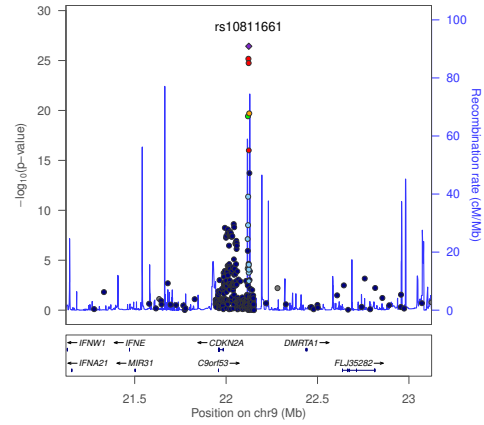
Recombination rate (cM/Mb)
C9orf123 PTPRD
Position on chr9 (Mb)


rs10811661
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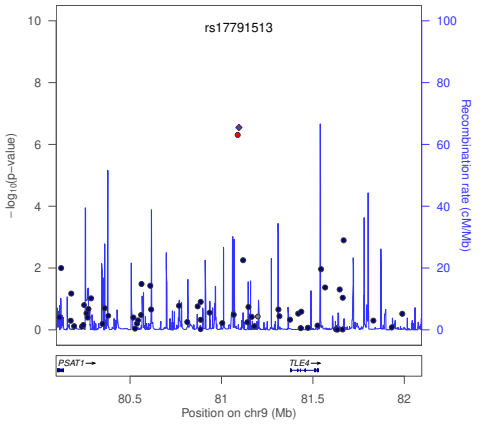
IFNA21 MIR31 C9orf53 FLJ35282
Position on chr9 (Mb)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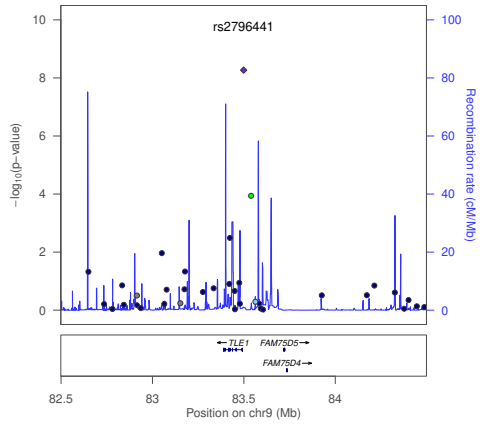
Recombination rate (cM/Mb)
PSAT1 TLE4
Position on chr9 (Mb)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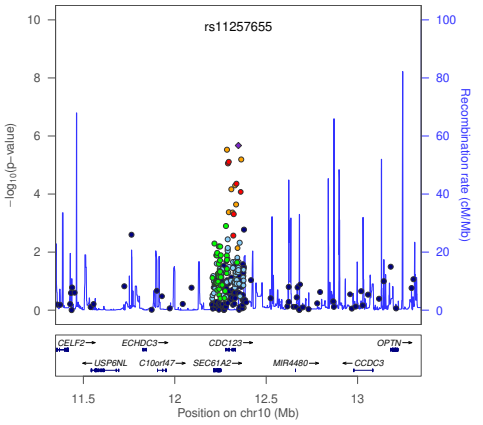
TLE1 FAM75D5
FAM75D4
Position on chr9 (Mb)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Recombination rate (cM/Mb)
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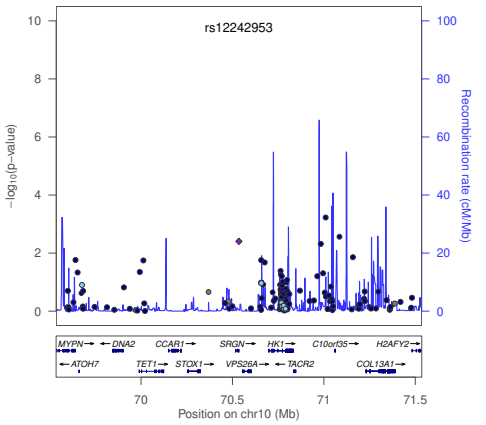
USP6NL C10orf47 SEC61A2 MIR4480 CCDC3
Position on chr10 (Mb)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Recombination rate (cM/Mb)
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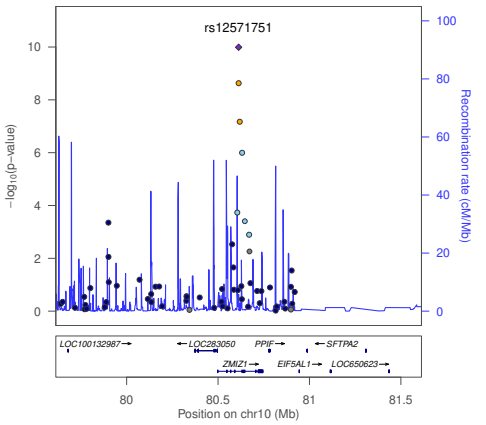
ATOH7 TET1 STOX1 VPS26A TACR2 COL13A1
Position on chr10 (Mb)


rs12571751
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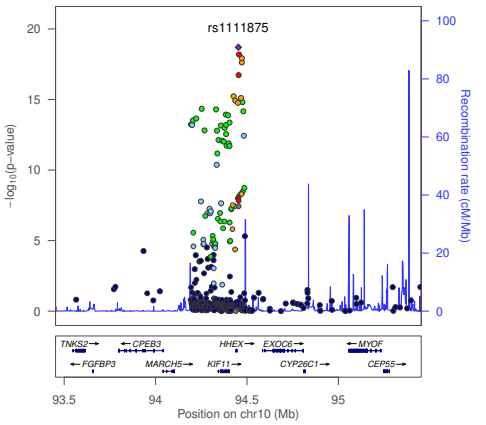
Recombination rate (cM/Mb)
LOC100132987 LOC283050 PPIF SFTPA2
ZMIZ1 EIF5AL1 LOC650623
Position on chr10 (Mb)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Recombination rate (cM/Mb)
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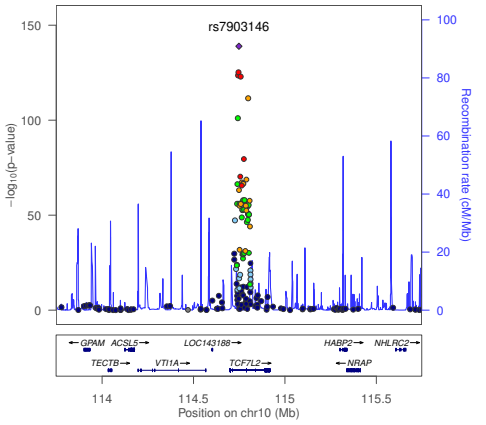
FGFBP3 MARCH5 KIF11 CYP26C1 CEP55
Position on chr10 (Mb)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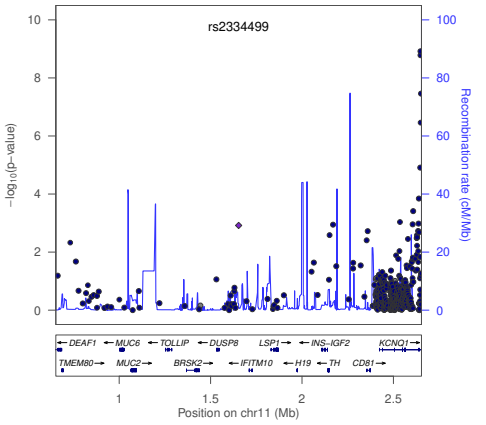
TECTB VTI1A TCF7L2 NRAP
Position on chr10 (Mb)


rs2334499
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Recombination rate (cM/Mb)
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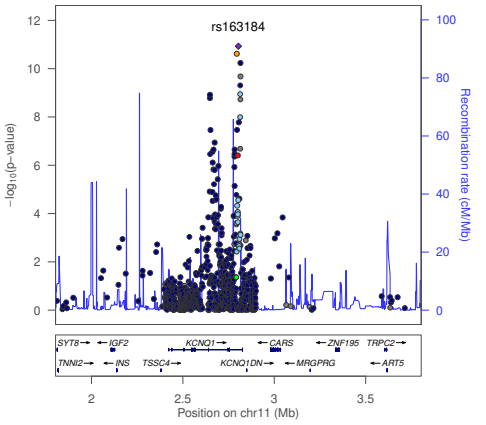
TMEM80 MUC2 BRSK2 IFITM10 H19 TH CD81
Position on chr11 (Mb)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Recombination rate (cM/Mb)
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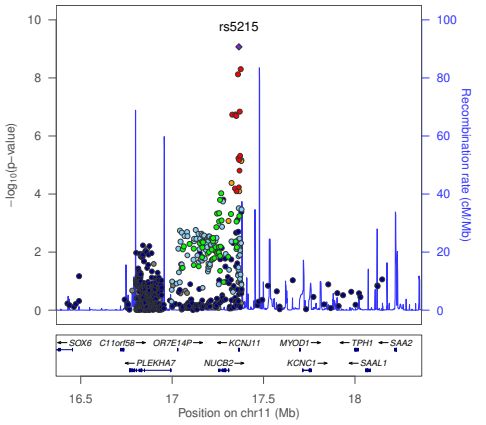
TNNI2 INS TSSC4 KCNQ1DN MRGPRG ART5
Position on chr11 (Mb)


rs5215
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Recombination rate (cM/Mb)
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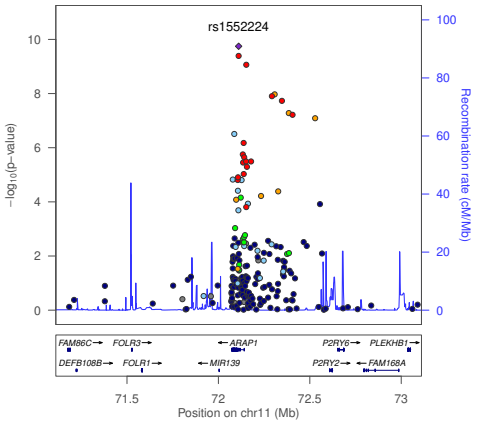
PLEKHA7 NUCB2 KCNC1 SAAL1
Position on chr11 (Mb)


rs1552224
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Recombination rate (cM/Mb)
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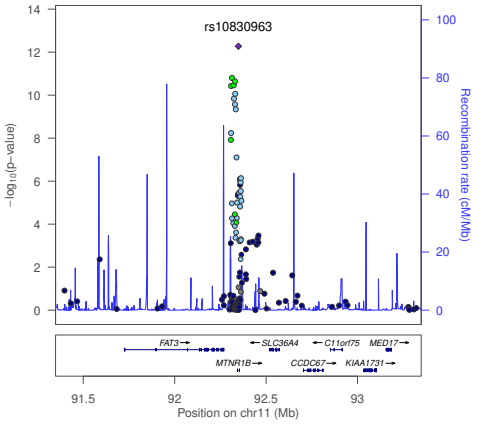
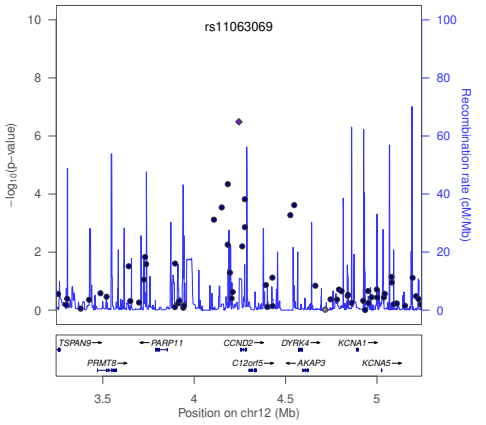
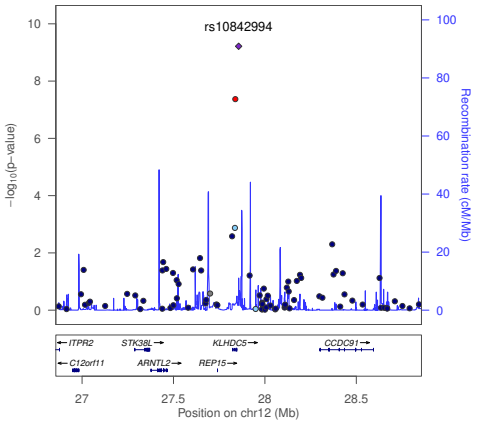
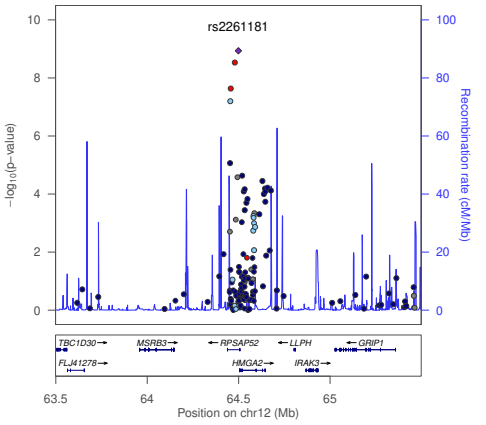
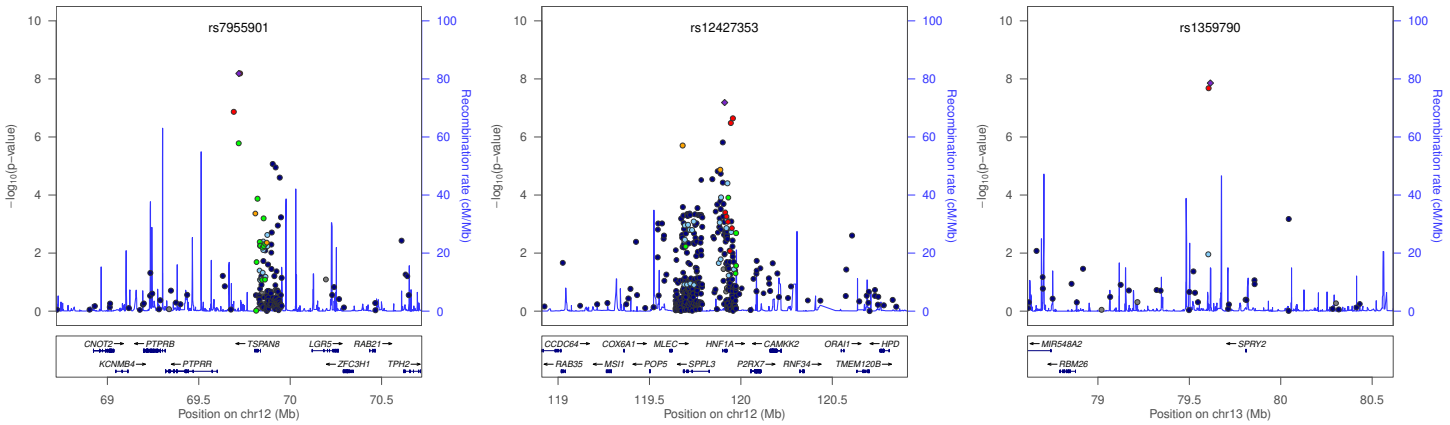
DEFB108B FOLR1 MIR139 P2RY2 FAM168A
Position on chr11 (Mb)

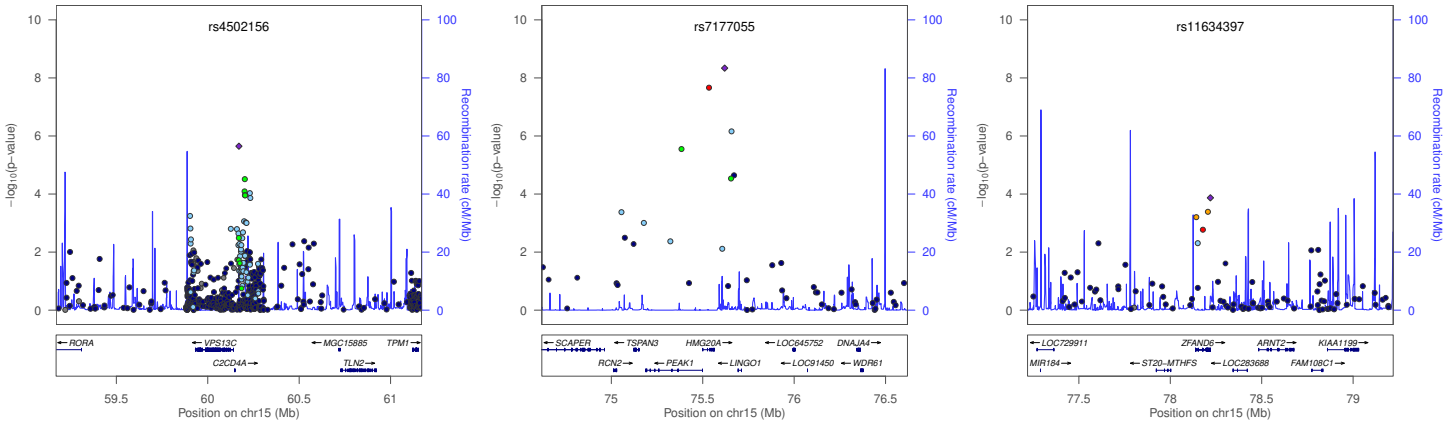

rs10830963
−log10(p−value)
Recombination rate (cM/Mb)
FAT3 SLC36A4 C11orf75 MED17
MTNR1B CCDC67 KIAA1731
Position on chr11 (Mb)

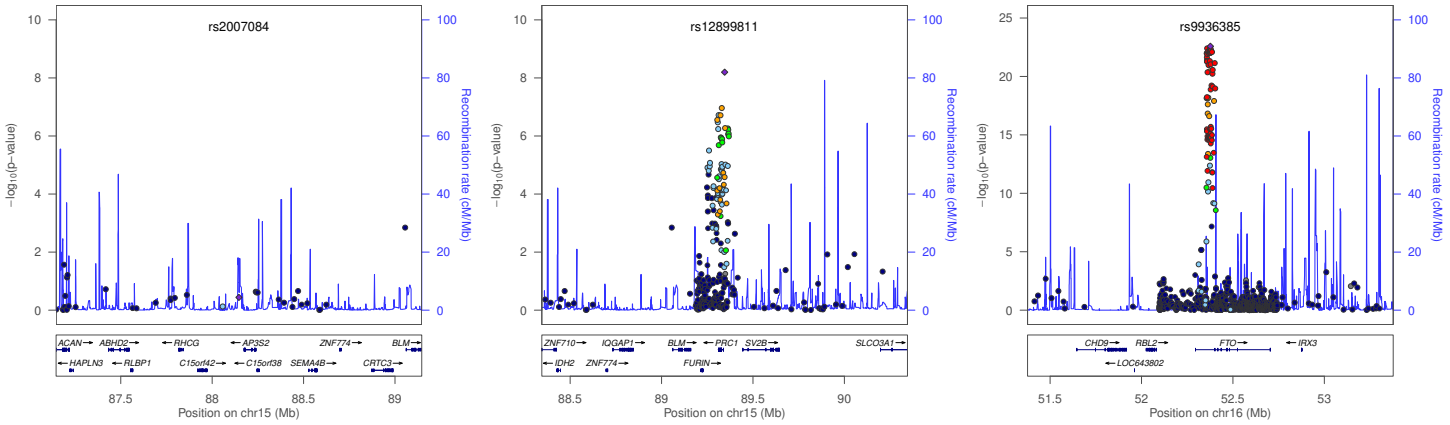

rs11063069
−log10(p−value)
Recombination rate (cM/Mb)
TSPAN9 PARP11 CCND2 DYRK4 KCNA1
PRMT8 C12orf5 AKAP3 KCNA5
Position on chr12 (Mb)

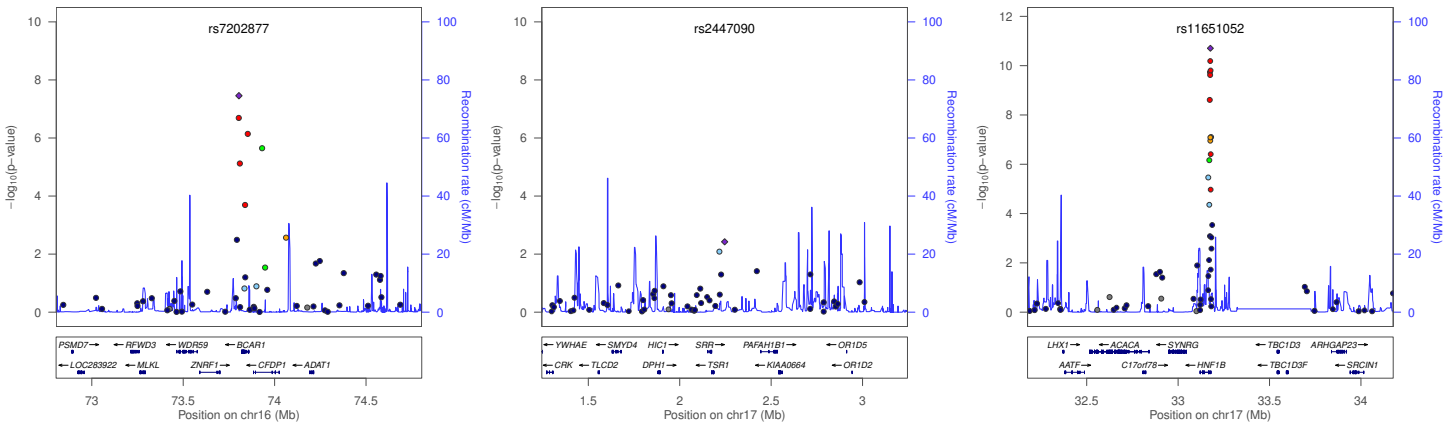

rs10842994
−log10(p−value)
Recombination rate (cM/Mb)
ITPR2 STK38L KLHDC5 CCDC91
C12orf11 ARNTL2 REP15
Position on chr12 (Mb)

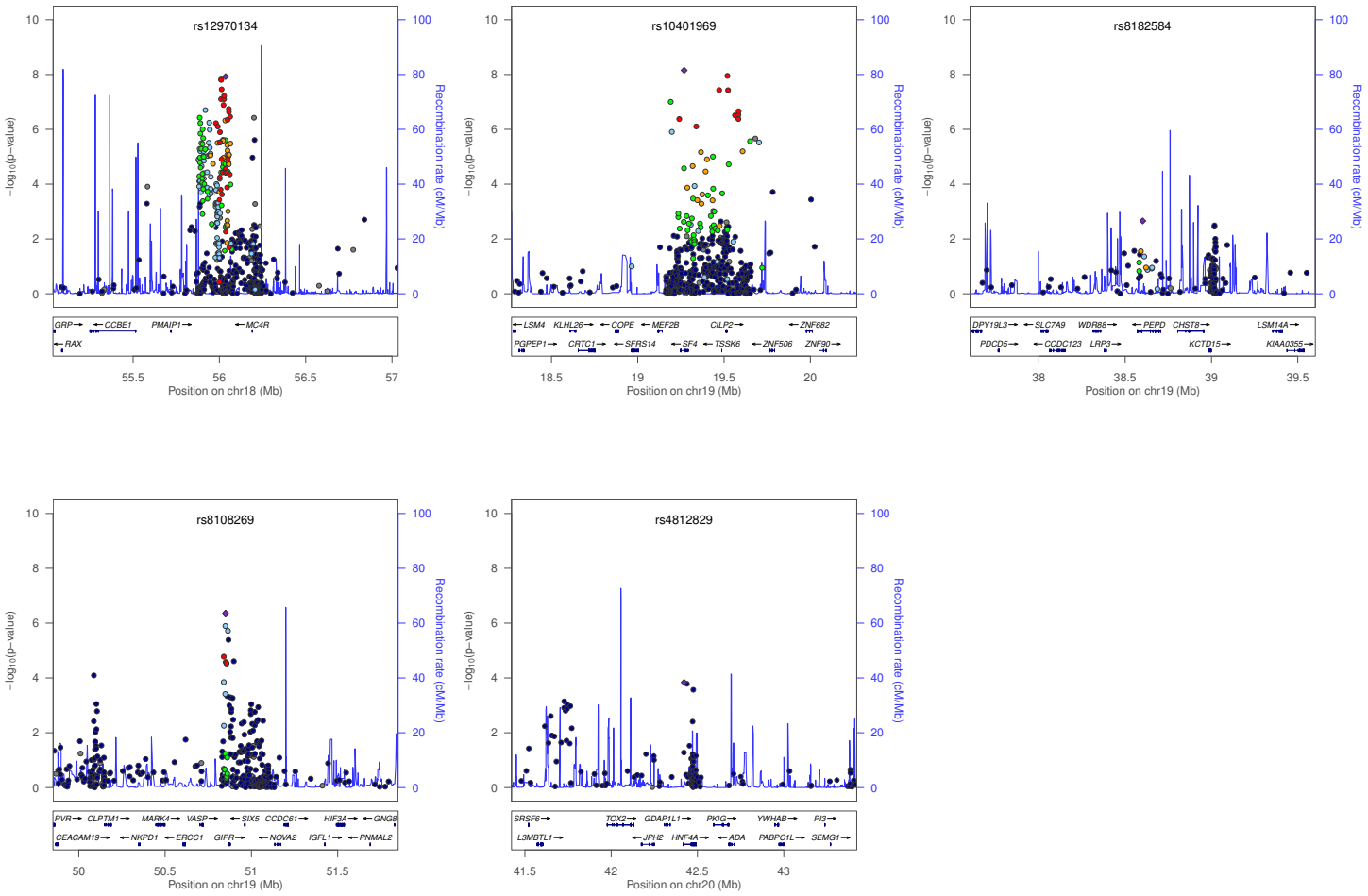

rs2261181
−log10(p−value)
Recombination rate (cM/Mb)
TBC1D30 MSRB3 RPSAP52 LLPH GRIP1
FLJ41278 HMGA2 IRAK3
Position on chr12 (Mb)


rs7955901
rs12427353
rs1359790
−log10(p−value)
Recombination rate (cM/Mb)
CNOT2 PTPRB TSPAN8 LGR5 RAB21
KCNMB4 PTPRR ZFC3H1 TPH2
Position on chr12 (Mb)
CCDC64 COX6A1 MLEC HNF1A CAMKK2 ORAI1 HPD
RAB35 MSI1 POP5 SPPL3 P2RX7 RNF34 TMEM120B
Position on chr12 (Mb)
MIR548A2 SPRY2
RBM26
Position on chr13 (Mb)


rs4502156
rs7177055
rs11634397
−log10(p−value)
Recombination rate (cM/Mb)
RORA VPS13C MGC15885 TPM1
C2CD4A TLN2
Position on chr15 (Mb)
SCAPER TSPAN3 HMG20A LOC645752 DNAJA4
RCN2 PEAK1 LINGO1 LOC91450 WDR61
Position on chr15 (Mb)
LOC729911 ZFAND6 ARNT2 KIAA1199
MIR184 ST20-MTHFS LOC283688 FAM108C1
Position on chr15 (Mb)


rs2007084
rs12899811
rs9936385
−log10(p−value)
Recombination rate (cM/Mb)
ACAN ABHD2 RHCG AP3S2 ZNF774 BLM
HAPLN3 RLBP1 C15orf42 C15orf38 SEMA4B CRTC3
Position on chr15 (Mb)
ZNF710 IQGAP1 BLM PRC1 SV2B SLCO3A1
IDH2 ZNF774 FURIN
Position on chr15 (Mb)
CHD9 RBL2 FTO IRX3
LOC643802
Position on chr16 (Mb)


rs7202877
rs2447090
rs11651052
−log10(p−value)
Recombination rate (cM/Mb)
PSMD7 RFWD3 WDR59 BCAR1
LOC283922 MLKL ZNRF1 CFDP1 ADAT1
Position on chr16 (Mb)
YWHAE SMYD4 HIC1 SRR PAFAH1B1 OR1D5
CRK TLCD2 DPH1 TSR1 KIAA0664 OR1D2
Position on chr17 (Mb)
LHX1 ACACA SYNRG TBC1D3 ARHGAP23
AATF C17orf78 HNF1B TBC1D3F SRCIN1
Position on chr17 (Mb)


rs12970134
rs10401969
rs8182584
rs8108269
rs4812829
−log10(p−value)
Recombination rate (cM/Mb)
Position on chr18 (Mb)
Position on chr19 (Mb)
Position on chr19 (Mb)
Position on chr19 (Mb)
Position on chr20 (Mb)
GRP
CCBE1
PMAIP1
MC4R
RAX
LSM4
KLHL26
COPE
MEF2B
CILP2
ZNF682
PQPEP1
CRTC1
SFRS14
SF4
TSSK6
ZNF506
ZNF90
DPY19L3
SLC7A9
WDR88
PEPD
CHST8
LSM14A
PDCD5
CCDC123
LRP3
KCTD15
KIAA0355
PVR
CLPTM1
MARK4
VASP
SIX5
CCDC61
HIF3A
GNG8
CEACAM19
NKPD1
ERCC1
GIPR
NOVA2
IGFL1
PNMAL2
SRSF6
TOX2
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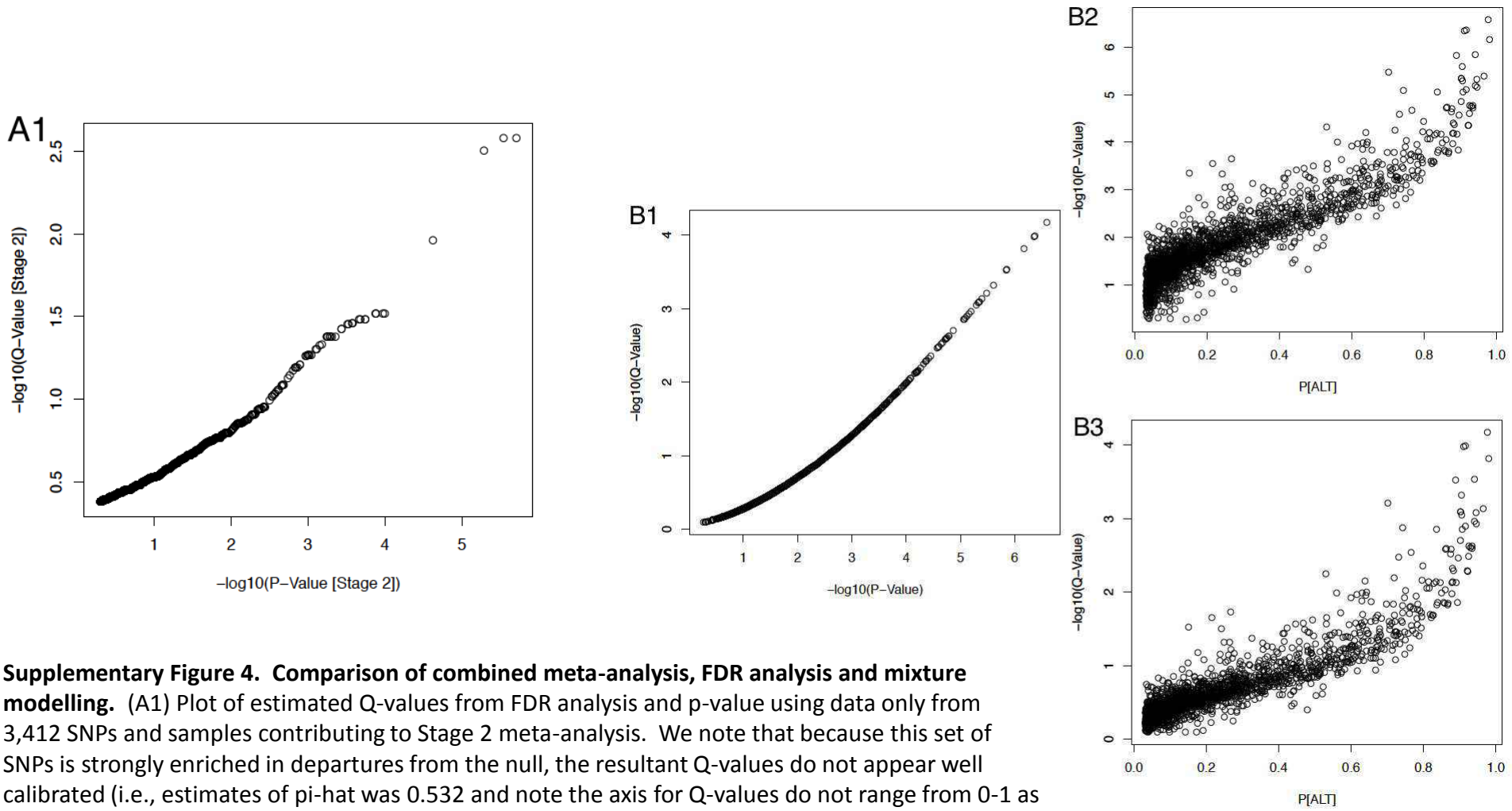
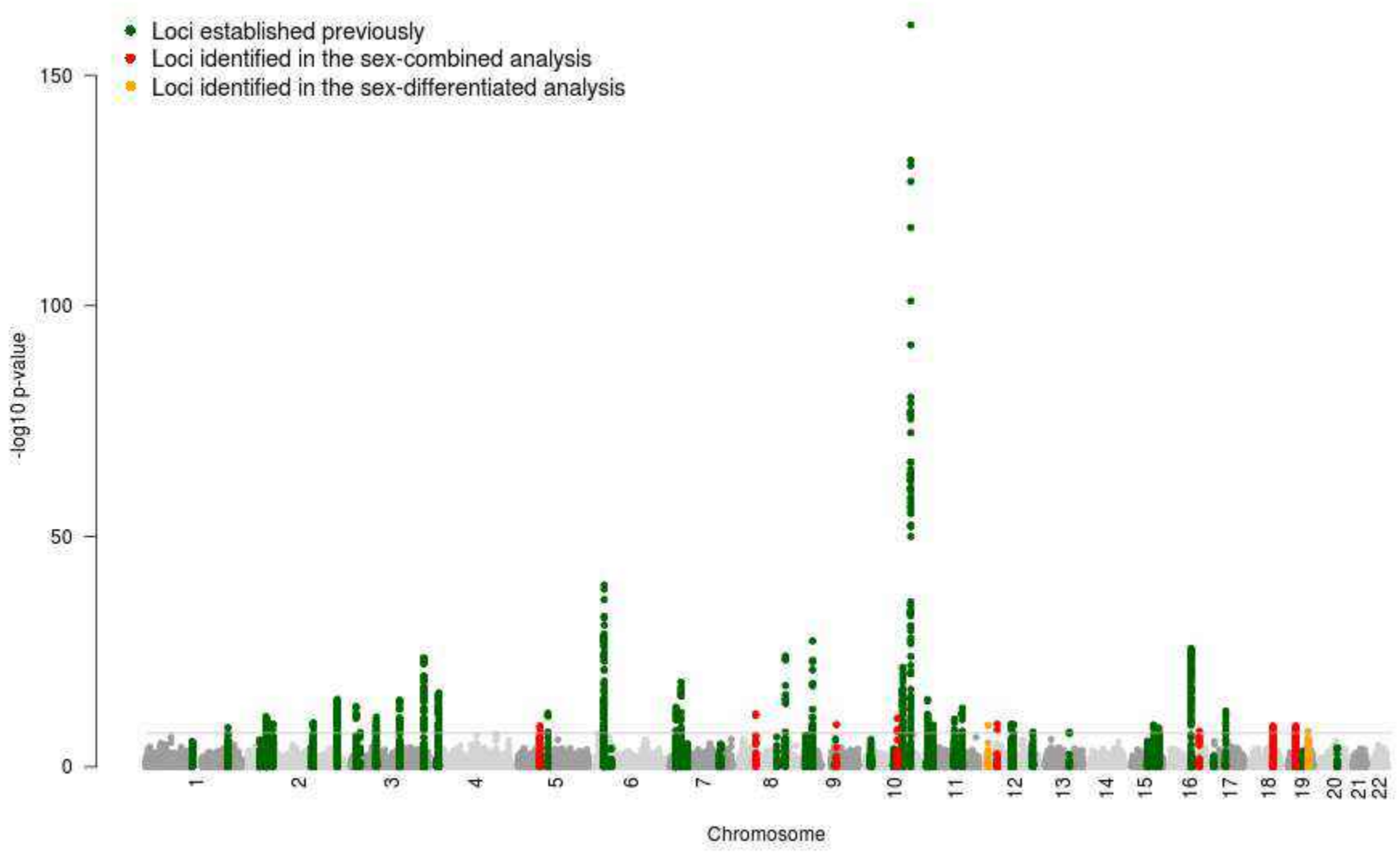
PKIG
YWHAB
PIG
L3MBTL1
JPH2
HNF4A
ADA
PABPC1L
SEMG1

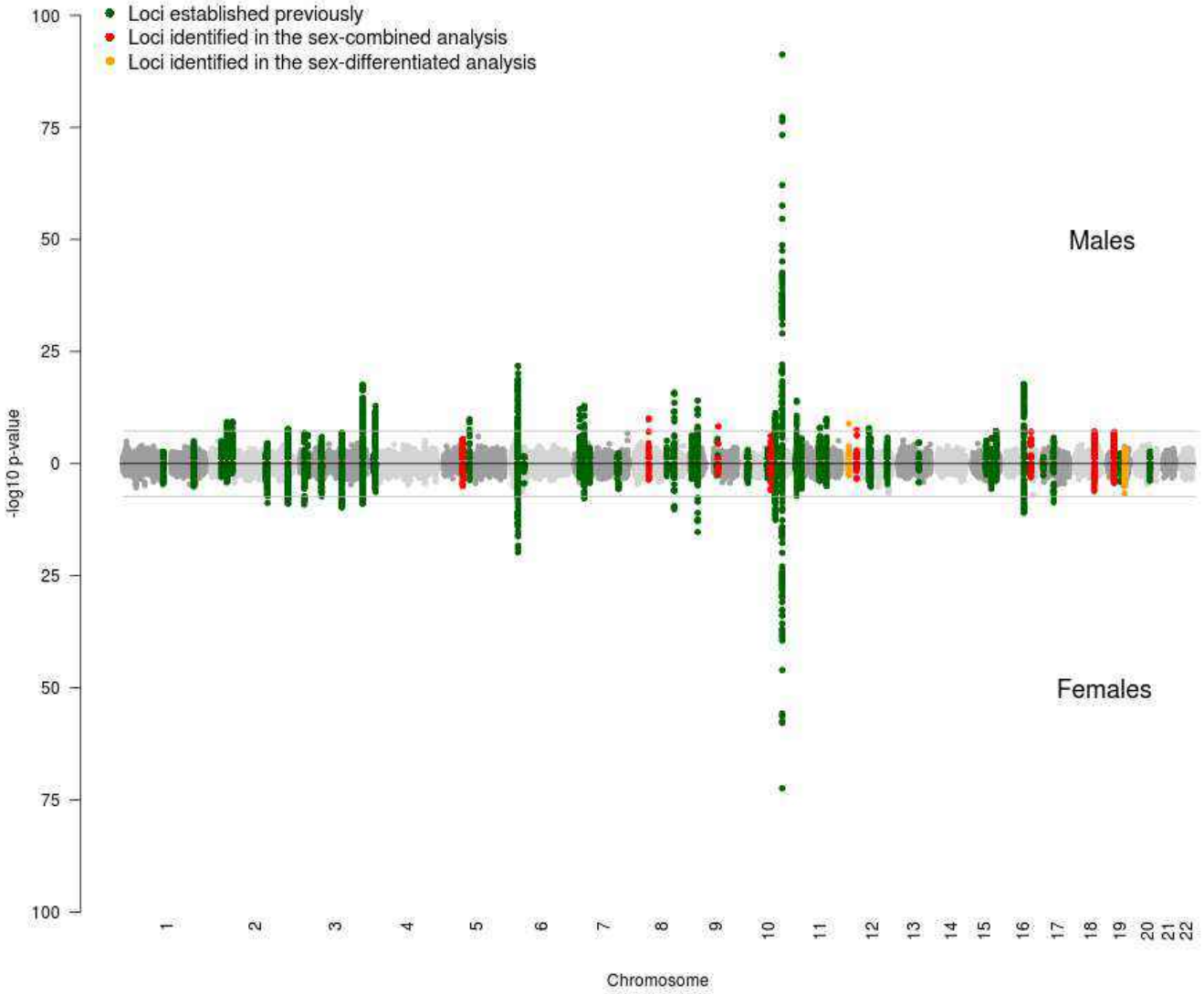


Supplementary Figure 4. Comparison of combined meta-analysis, FDR analysis and mixture modelling. (A1) Plot of estimated Q-values from FDR analysis and p-value using data only from 3,412 SNPs and samples contributing to Stage 2 meta-analysis. We note that because this set of SNPs is strongly enriched in departures from the null, the resultant Q-values do not appear well calibrated (i.e., estimates of pi-hat was 0.532 and note the axis for Q-values do not range from 0-1 as expected with significant constraint in the range). Given this, we do not advocate this strategy for SNP and sample selection for FDR analysis on these data. (B1-B3) Plotted are pair-wise comparisons between combined meta-analysis p-value, estimated Q-value from FDR analysis using combined meta-analysis data, and probability of membership to the alternative distribution from mixture modelling of Stage 2 meta-analysis data alone (P[ALT]). Results are plotted for 2,172 T2D replication SNPs with consistent direction of effect between Stage 1 and 2 meta-analyses. In these figures, FDR Q-values were estimated using the set of 64,646 replication SNPs for all traits on Metabochip.

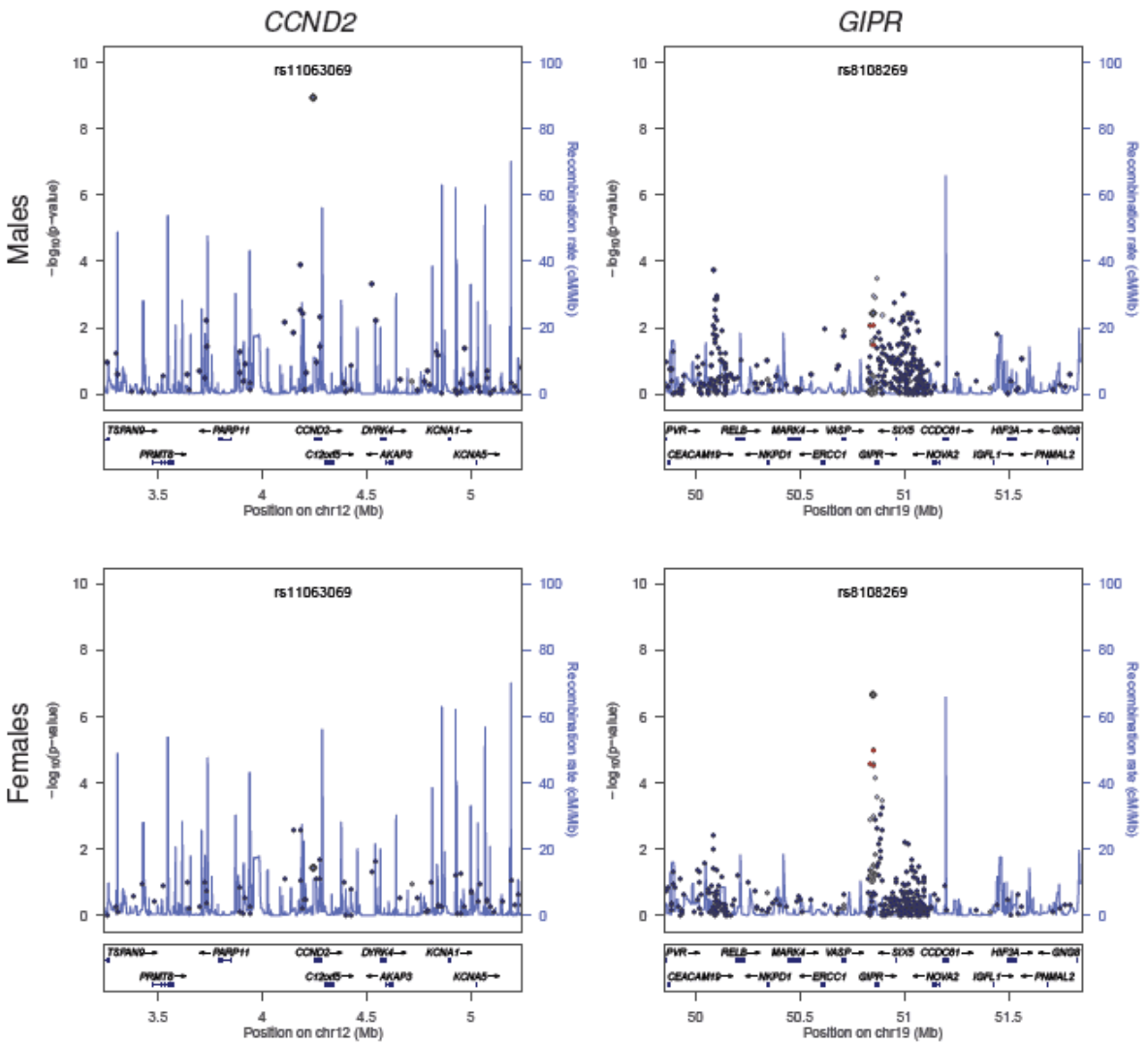
Supplementary Figure 5. Manhattan plot for the sex-differentiated meta-analysis. Previously established loci are highlighted in green. Novel loci achieving genome-wide significance in the sex-combined meta-analysis are highlighted in red. Novel loci achieving genome-wide significance in the sex-differentiated meta-analysis are highlighted in gold.



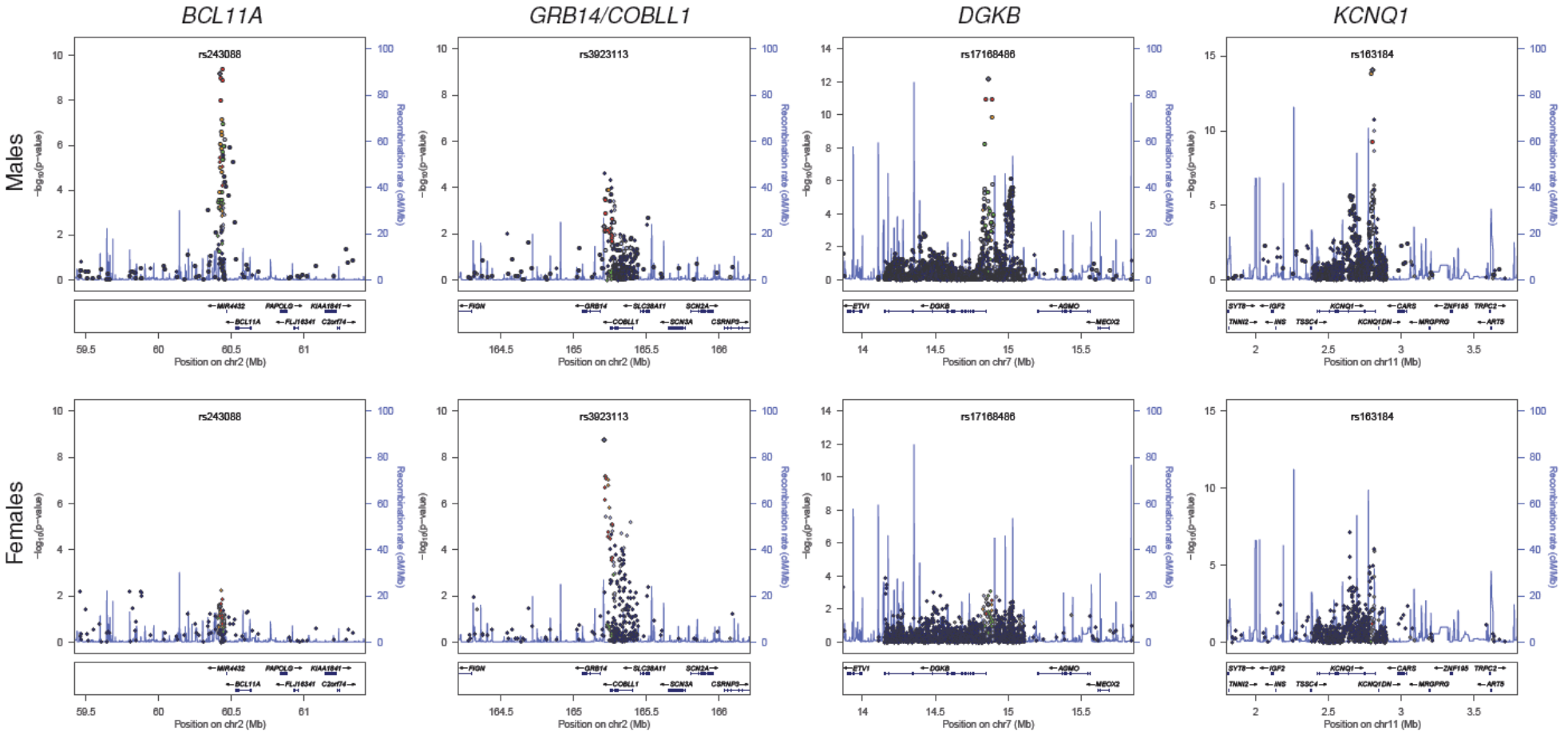
Supplementary Figure 6. Miami plot for the sex-specific meta-analyses. The top and bottom panels summarise the results of the male- and female-specific meta-analyses. Previously established loci are highlighted in green. Novel loci achieving genome-wide significance in the sex-combined meta-analysis are highlighted in red. Novel loci achieving genome-wide significance in the sex-differentiated meta-analysis are highlighted in gold.



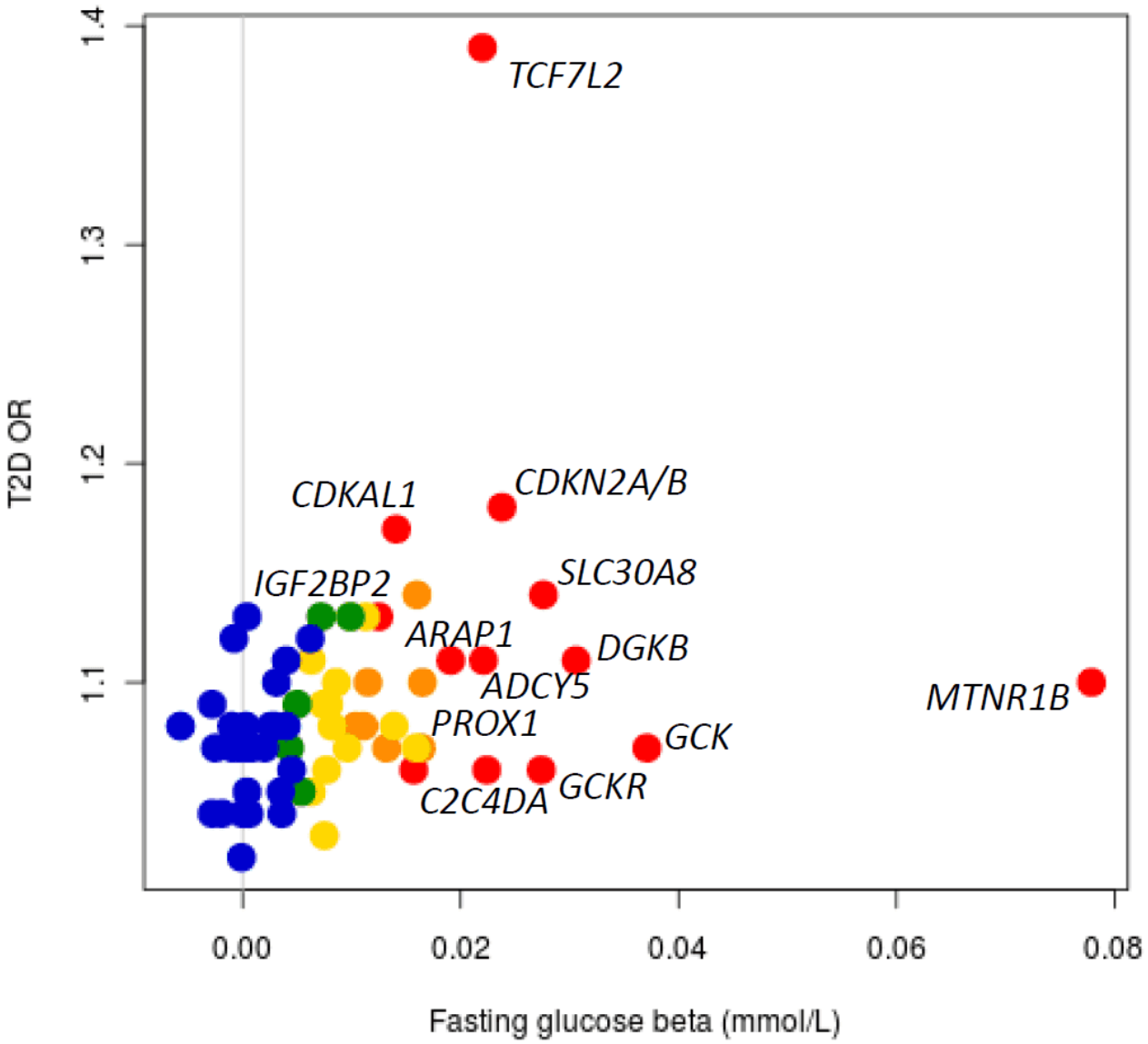
Supplementary Figure 7. Regional plots of novel T2D susceptibility loci identified through sex-differentiated meta-analysis. Each point represents a Metabochip SNP passing quality control in our combined meta-analysis, plotted with their p-value (on a $-\log_{10}$ scale) as a function of genomic position (NCBI Build 36). In each panel, the lead sex-differentiated SNP is represented by the purple diamond. The colour coding of all other SNPs (circles) indicates LD with the lead SNP (estimated by CEU r^2 from the 1000 Genomes Project June 2010 release): 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. Recombination rates are estimated from the International HapMap Project and gene annotations are taken from the University of California Santa Cruz genome browser.



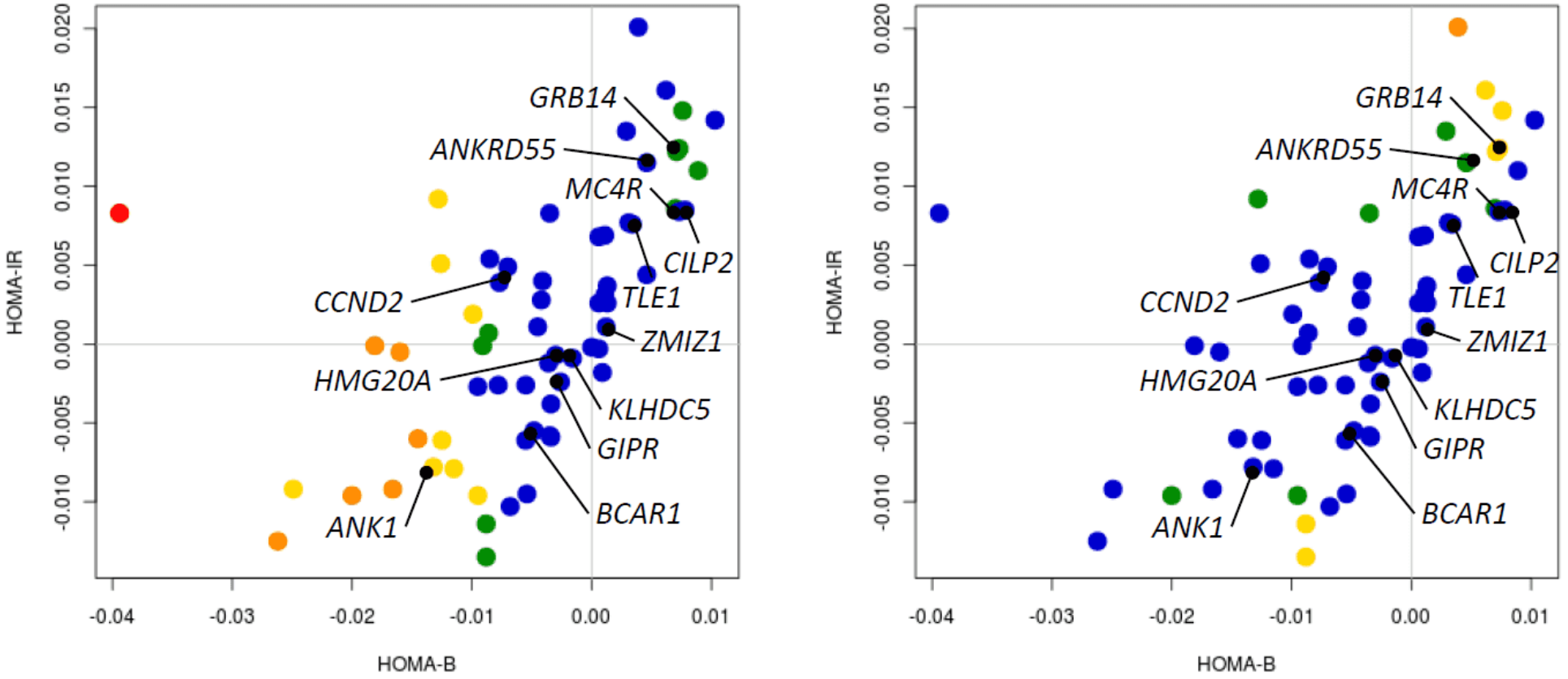
Supplementary Figure 8. Regional plots of T2D susceptibility loci demonstrating nominal heterogeneity in allelic effects between sexes. Each point represents a Metabochip SNP passing quality control in our combined meta-analysis, plotted with their p-value (on a $-\log_{10}$ scale) as a function of genomic position (NCBI Build 36). In each panel, the lead sex-differentiated SNP is represented by the purple diamond. The colour coding of all other SNPs (circles) indicates LD with the lead SNP (estimated by CEU r^2 from the 1000 Genomes Project June 2010 release): 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. Recombination rates are estimated from the International HapMap Project and gene annotations are taken from the University of California Santa Cruz genome browser.



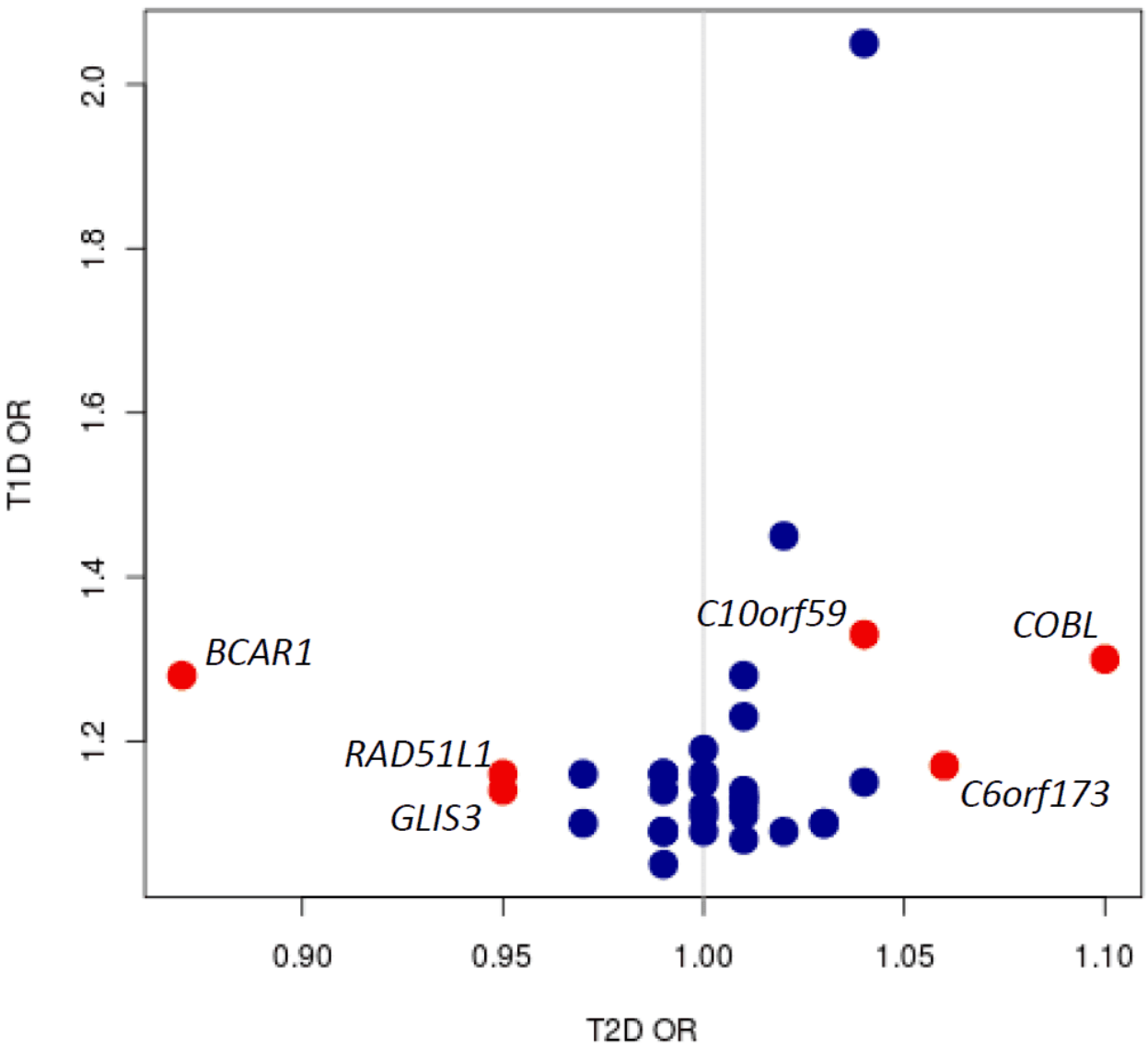
Supplementary Figure 9. Plot of FG and T2D risk at novel and established T2D susceptibility loci obtained from the present meta-analysis and up to 133,010 non-diabetic individuals from the MAGIC Investigators. Each point represents a lead T2D SNP, aligned to the risk allele, coloured according to the significance of association with FG: red $p<5x10^{-8}$; orange $5x10^{-8}\leq p<10^{-4}$; yellow $10^{-4}\leq p<0.01$; green $0.01\leq p<0.05$; blue $p\geq 0.05$.



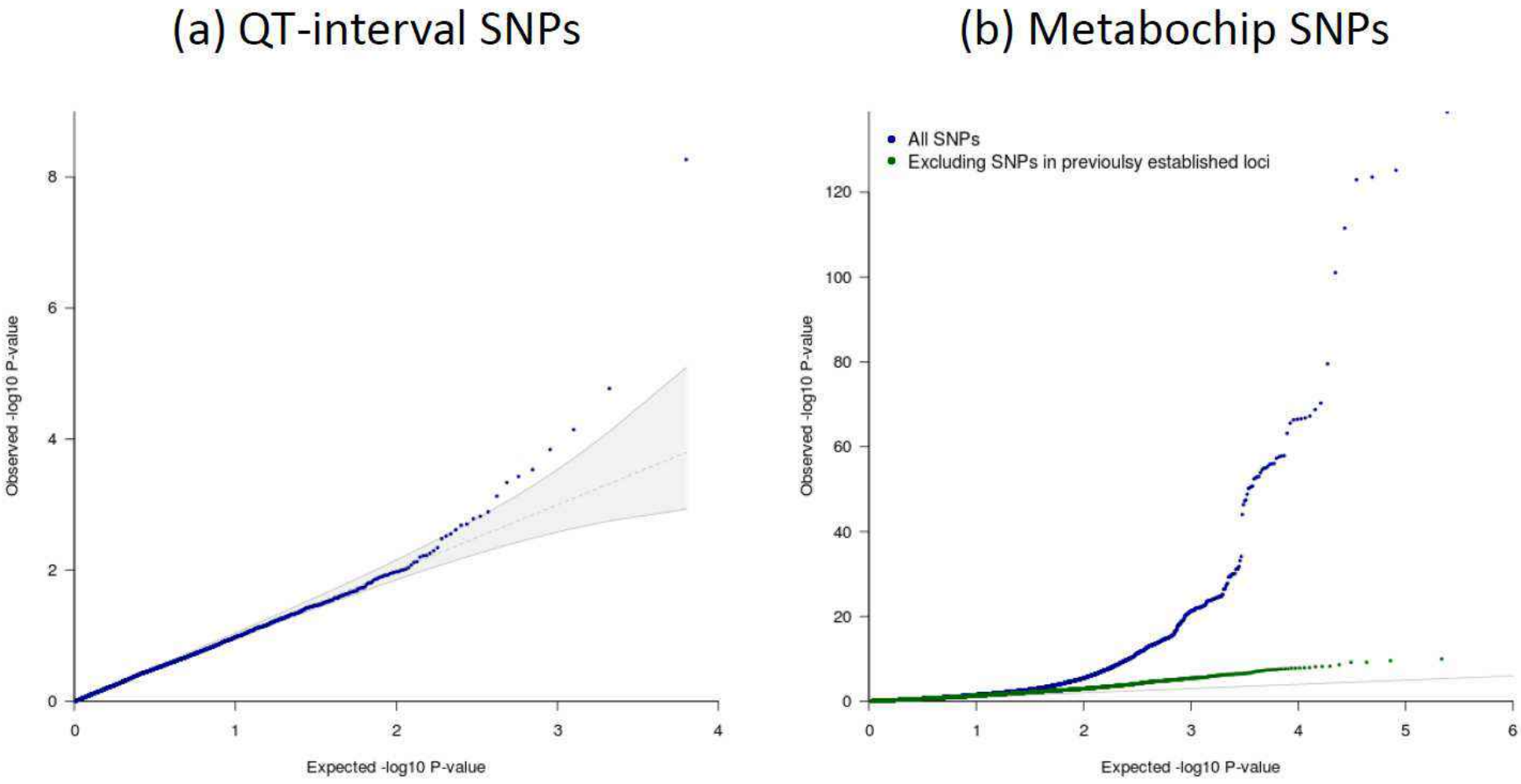
Supplementary Figure 10. Plots of indices of beta-cell function (HOMA-B) and insulin sensitivity (HOMA-IR) at novel and established T2D susceptibility loci obtained from up to 37,037 individuals from the MAGIC Investigators. Each point represents a lead T2D SNP, aligned to the risk allele, coloured according to the significance of association with HOMA-B (left panel) and HOMA-IR (right panel): red $p<5\times10^{-8}$; orange $5\times10^{-8}\leq p<10^{-4}$; yellow $10^{-4}\leq p<0.01$; green $0.01\leq p<0.05$; blue $p\geq0.05$.



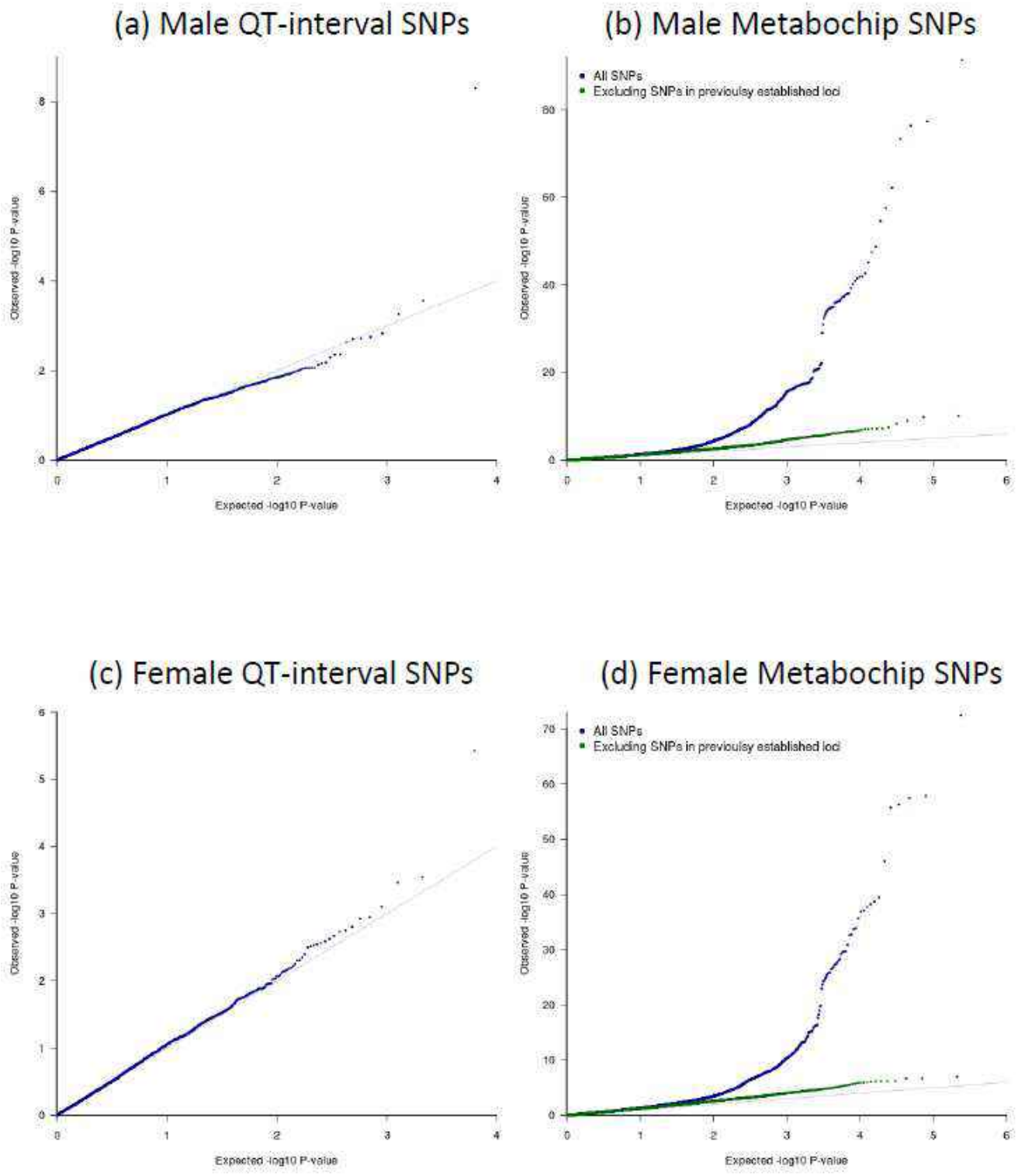
Supplementary Figure 11. Plot of T2D and T1D risk at 37 established T1D susceptibility loci obtained from the present meta-analysis and up to 7,514 T1D cases and 9,045 population controls from the Type 1 Diabetes Genetics Consortium. Each point represents a lead T1D SNP, aligned to the risk allele, coloured according to the significance of association with T2D: red p<0.05; blue p≥0.05.



Supplementary Figure 12. QQ-plots of association statistics from the combined meta-analysis. Each point represents a Metabochip SNP passing quality control in the combined meta-analysis. The y-axis corresponds to the observed $\log_{10}$ p-value for association from the meta-analysis. The x-axis corresponds to the corresponding expected $\log_{10}$ p-value under the null hypothesis of no association with T2D. The grey funnel represents 95% confidence limits for the expected p-values. Panel (a) includes 3,155 QT-interval replication SNPs, not expected to be associated with T2D, used for genomic control correction. Panel (b) includes all Metabochip SNPs (in blue) and after excluding established T2D loci (in green).



Supplementary Figure 13. QQ-plots of association statistics from sex-specific meta-analyses. Each point represents a Metabochip SNP passing quality control in the sex-differentiated meta-analysis. The y-axis corresponds to the observed $\log_{10}$ p-value for association from the meta-analysis. The x-axis corresponds to the corresponding expected $\log_{10}$ p-value under the null hypothesis of no association with T2D. The grey funnel represents 95% confidence limits for the expected p-values. Results are presented for the male-specific meta-analysis in panels (a) and (b), whilst those for the female-specific meta-analysis are presented in panels (c) and (d). Panels (a) and (c) include 3,155 QT-interval replication SNPs, not expected to be associated with T2D, used for genomic control correction. Panels (b) and (d) include all Metabochip SNPs (in blue) and after excluding established T2D loci (in green).



Supplementary Table 1. Study sample characteristics, genotyping, quality control and association analysis.

Study	Ethnic group (origin)	Disease status	Sample characteristics: Sample size (males/females)	Age (years) mean (SD)	Age at onset (years) mean (SD)	Fasting glucose (mmol/l) mean (SD)	BMI (kg/m2) mean (SD)	Genotyping platform	Sample QC: Call rate	Sample QC: Exclusion criteria	SNP QC: Call rate	SNP QC: HWE	SNP QC: MAF	SNP QC: Imputation	Association analysis: SNPs	Association analysis: Analysis software	Association analysis: Covariates	Association analysis: Genomic control
Stage 1																		
ARIC	European	Cases Controls	775 (416/359) 7,159 (3,167/3,992)	56.1 (5.6) 54.0 (5.7)	50.9 (10.4) -	9.3 (3.6) 5.4 (0.4)	30.4 (5.4) 26.4 (4.5)	Affymetrix Human SNP Array 6.0	≥0.95	Relatedness and duplicates	≥0.90	$p>10^{-6}$	≥0.01	$r^2>0.3$	2,443,161	ProbABEL	Age, sex, and study centre	1.01 (G) 1.01 (I)
deCODE	European (Iceland)	Cases Controls	1,465 (868/597) 23,194 (7,316/15,878)	68.4 (10.1) 59.7 (18.1)	55.1 (12.7) -	8.5 (2.7) 5.3 (0.7)	30.1 (5.4) 26.8 (5.0)	Illumina HumanHap 300/370	≥0.98	Duplicates	≥0.96	$p>10^{-6}$	≥0.01	proper-info>0.5	2,338,113	SNPTEST	-	1.31 (G) 1.31 (I)
DGDG	European (France)	Cases Controls	679 (413/266) 697 (281/416)	59.5 (10.1) 53.9 (5.6)	45.1 (8.4) -	9.2 (3.1) 5.1 (0.4)	25.9 (2.8) 23.2 (1.8)	Illumina HumanHap 300	≥0.95	Duplicates	≥0.95	$p>10^{-4}$	≥0.01	proper-info>0.5	2,051,387	SNPTEST	-	1.10 (G) 1.10 (I)
DGI	European (Sweden/Finland)	Cases Controls	1,022 (529/493) 1,075 (540/535)	65.9 (10.0) 58.0 (10.0)	58.0 (10.0) -	9.5 (3.1) 5.3 (0.5)	28.1 (4.1) 27.6 (3.7)	Affymetrix GeneChip 500K	≥0.95	Duplicates	≥0.95	$p>10^{-6}$	≥0.01	proper-info>0.5	2,230,032	PLINK and SNPTEST	Age, sex, BMI, and study centre	1.05 (G) 1.06 (I)
EUROSPAN	European	Cases Controls	269 (127/142) 3,710 (1,557/2,153)	62.9 49.9	- -	8.0 4.8	29.8 26.5	Illumina HumanHap 300/370	≥0.98	Duplicates	≥0.98	$p>10^{-6}$	≥0.01	$r^2>0.5$	2,359,525	GenABEL and SNPTEST	Age and sex	0.97 (G) 0.98 (I)
FHS	European (USA)	Cases Controls	674 (386/288) 7,664 (3,443/4,221)	63.7 (12.4) 52.3 (16.0)	- -	8.6 (2.8) 5.3 (0.5)	31.4 (6.5) 27.0 (5.1)	Affymetrix GeneChip 500K & MIPS 50K	≥0.95	Duplicates	≥0.95	$p>10^{-6}$	≥0.01	$r^2>0.3$	2,389,929	R (GEE correction for relatedness)	Age, sex, and cohort	1.02 (G) 1.02 (I)
FUSION	European	Cases Controls	1,161 (653/508) 1,174 (574/600)	62.9 (7.6) 63.6 (7.4)	53.7 (9.1) -	9.4 (3.1) 5.3 (0.5)	30.2 (4.7) 27.1 (3.9)	Illumina HumanHap 300	≥0.975	Duplicates	≥0.90	$p>10^{-6}$	≥0.01	$r^2>0.3$	2,413,085	MACH2DAT	Age, sex, and birth province	1.03 (G) 1.04 (I)
HPFS	European (USA)	Cases Controls	1,124 (1,124/0) 1,298 (1,298/0)	55.0 (8.6) 55.0 (8.4)	64.0 (8.4) -	- -	27.8 (4.0) 25.0 (2.9)	Affymetrix Human SNP Array 6.0	≥0.95	Relatedness and duplicates	≥0.95	$p>10^{-6}$	≥0.01	-	622,575	PLINK	Age and BMI	1.03 (G)
KORAGen	European (Germany)	Cases Controls	433 (255/178) 1,438 (693/745)	65.2 (8.3) 61.9 (7.4)	58.2 (10.3) -	- -	30.9 (5.0) 27.7 (4.3)	Affymetrix GeneChip 500K	≥0.93	Duplicates	≥0.95	$p>10^{-6}$	≥0.01	proper-info>0.5	2,325,232	SNPTEST	Age and sex	1.04 (G) 1.04 (I)
NHS	European (USA)	Cases Controls	1,467 (0/1,467) 1,754 (0/1,754)	43.5 (6.7) 43.1 (6.8)	58.7 (10.6) -	- -	27.4 (0.1) 23.5 (0.1)	Affymetrix Human SNP Array 6.0	≥0.98	Relatedness and duplicates	≥0.98	$p>10^{-6}$	≥0.02	-	615,391	PLINK	Age and BMI	0.98 (G)
RS1	European (Netherlands)	Cases Controls	1,178 (488/690) 4,761 (1,928/2,833)	71.7 (8.9) 69.0 (9.1)	71.5 (8.9) -	- -	27.4 (4.0) 26.0 (3.6)	Illumina HumanHap 550	≥0.975	Duplicates	≥0.98	$p>10^{-6}$	≥0.01	$r^2>0.5$	2,439,672	GenABEL and SNPTEST	-	1.01 (G) 1.01 (I)
WTCCC	European (UK)	Cases Controls	1,924 (1,118/806) 2,938 (1,446/1,492)	58.6 (9.2) -	50.3 (9.2) -	- -	30.7 (6.1) -	Affymetrix GeneChip 500K	≥0.97	Duplicates	≥0.95 (≥0.99 for MAF<0.05)	$p>10^{-3}$	≥0.01	proper-info>0.5	2,308,535	PLINK and SNPTEST	-	1.06 (G) 1.08 (I)
Stage 2																		
AMC-PAS	European (Netherlands)	Cases Controls	48 (35/13) 442 (333/109)	44.0 (4.7) 43.2 (5.3)	- -	8.6 (3.2) 5.3 (0.6)	29.3 (4.4) 26.6 (4.1)	Metabochip	≥0.95	Duplicates and non-European descent	≥0.98	$p>10^{-4}$	≥0.01	-	109,525	PLINK	Age and sex	1.00 (QT)
BHS	European	Cases Controls	51 (38/13) 359 (224/135)	72.3 (7.8) 70.0 (9.6)	- -	7.8 (4.0) 5.1 (0.9)	27.2 (3.9) 26.6 (3.9)	Metabochip	≥0.95	Ambiguous sex and relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	119,893	PLINK	Age and sex	0.96 (QT)
deCODE-Stage2	European (Iceland)	Cases Controls	722 (433/289) 10,153 (6,604/3,549)	67.3 (13.6) 44.3 (26.5)	- -	- -	31.2 (6.3) -	Metabochip	-	-	-	-	≥0.01	-	125,236	SNPTEST	Sex	0.95 (QT)
DILGOM	European (Finland)	Cases Controls	541 (298/243) 3,357 (1,480/1,877)	60.5 (10.3) 50.9 (13.5)	- -	- -	30.1 (5.6) 26.5 (4.5)	Metabochip	≥0.95	Ambiguous sex and relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	116,634	PLINK	Age, sex, and population structure	0.93 (QT)
DUNDEE	European (UK)	Cases Controls	3,298 (1,940/1,358) 3,708 (1,918/1,790)	63.5 (9.6) 59.1 (11.3)	55.9 (8.9) -	- 4.9 (0.5)	31.9 (6.3) 27.0 (4.5)	Metabochip	≥0.95	Duplicates, ambiguous sex, and non-European descent	≥0.95 (≥0.99 for MAF<0.05)	$p>5.7x10^{-7}$ ($p>10^{-4}$ for MAF<0.05)	≥0.01	-	121,365	PLINK	Population structure	1.07 (QT)
EAS	European	Cases Controls	110 (64/46) 641 (301/340)	64.0 (5.6) 64.5 (5.6)	- -	- -	25.9 (3.3) 25.5 (3.9)	Metabochip	≥0.95	Gender check and ambiguous sex	≥0.95	$p>10^{-6}$	≥0.01	-	119,523	PLINK	Age and sex	1.00 (QT)
EGCUT	European (Estonia)	Cases Controls	938 (342/596) 915 (326/589)	64.1 (10.5) 51.7 (10.7)	- -	- -	33.4 (5.4) 22.3 (2.5)	Metabochip	≥0.95	Ambiguous sex, relatedness, and non-European descent	≥0.95	$p>10^{-6}$	≥0.01	-	120,720	SNPTEST	Age, sex, and population structure	1.00 (QT)
EMIL-ULM	European	Cases Controls	755 (510/245) 1,632 (765/867)	48.7 (12.0) 45.1 (10.9)	45.5 (10.8) -	- -	28.6 (7.1) 26.7 (5.0)	Metabochip	≥0.95	Ambiguous sex and cryptic relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	121,684	PLINK	Age and sex	1.14 (QT)
EPIC	European (UK)	Cases Controls	727 (432/295) 927 (393/534)	61.8 (8.2) 58.8 (9.4)	- -	- -	29.5 (4.4) 26.1 (3.7)	Metabochip	≥0.95	Gender check and duplicates	≥0.90	$p>10^{-6}$	≥0.01	-	120,527	PLINK	Age and sex	0.97 (QT)
FUSION-Stage2	European (Finland)	Cases Controls	1,037 (584/453) 1,157 (691/466)	59.7 (8.4) 59.0 (7.6)	- -	7.7 (2.3) 5.4 (0.4)	30.8 (5.4) 26.9 (3.9)	Metabochip	≥0.98	Relatedness and ambiguous sex	≥0.98	$p>10^{-5}$	≥0.01	-	123,853	PLINK	Age and sex	0.97 (QT)
FUSION-D2D2007	European (Finland)	Cases Controls	454 (269/185) 1,229 (455/774)	63.4 (7.6) 58.1 (8.2)	- -	7.7 (1.8) 5.6 (0.3)	30.6 (5.6) 26.2 (4.3)	Metabochip	≥0.98	Relatedness and ambiguous sex	≥0.98	$p>10^{-5}$	≥0.01	-	123,461	PLINK	Age and sex	0.96 (QT)
FUSION-DRExtra	European (Finland)	Cases Controls	110 (53/57) 785 (341/444)	68.4 (5.8) 66.0 (5.3)	- -	6.6 (0.8) 5.4 (0.3)	30.9 (5.6) 26.7 (4.0)	Metabochip	≥0.98	Relatedness and ambiguous sex	≥0.98	$p>10^{-5}$	≥0.01	-	120,746	PLINK	Age and sex	0.94 (QT)
FUSION-HUNT	European (Norway)	Cases Controls	1,239 (628/611) 1,375 (691/684)	64.0 (12.9) 63.5 (13.9)	61.9 (11.9) -	- -	29.2 (4.8) 26.5 (4.0)	Metabochip	≥0.98	Relatedness and ambiguous sex	≥0.98	$p>10^{-5}$	≥0.01	-	125,644	PLINK	Age, sex and collection site	1.10 (QT)
FUSION-METSIM	European (Finland)	Cases Controls	1,169 (1,169/0) 651 (651/0)	60.5 (6.6) 53.8 (5.0)	57.0 (8.0) -	7.5 (2.0) 5.5 (0.3)	30.2 (5.2) 25.9 (3.1)	Metabochip	≥0.98	Relatedness and ambiguous sex	≥0.98	$p>10^{-5}$	≥0.01	-	122,600	PLINK	Age and sex	1.01 (QT)
GMetS	European (France)	Cases Controls	507 (334/173) 2,553 (1,134/1,419)	55.9 (9.9) 47.3 (11.1)	- -	- -	28.5 (3.9) 24.8 (3.8)	Metabochip	≥0.95	Gender check, duplicates, and ambigous sex	≥0.95	$p>10^{-4}$	≥0.01	-	123,359	PLINK	Age, sex, and BMI	1.11 (QT)
HNR	European	Cases Controls	520 (315/205) 3,932 (1,911/2,021)	62.6 (7.2) 59.2 (7.8)	- -	- -	30.4 (5.2) 27.5 (4.4)	Metabochip	≥0.97	Ambiguous sex, relatedness, and non-European descent	≥0.95	$p>10^{-6}$	≥0.01	-	126,675	PLINK	Age and sex	1.00 (QT)
IMPROVE	European	Cases Controls	898 (513/385) 2,521 (1,134/1,387)	64.3 (5.6) 64.2 (5.3)	- -	7.7 (2.2) 5.3 (0.7)	29.2 (4.6) 26.5 (3.9)	Metabochip	≥0.95	Ambiguous sex, cryptic relatedness, non-European descent	≥0.95	$p>10^{-6}$	≥0.01	-	122,320	PLINK	Age, sex and population structure	1.13 (QT)
KORAGen-Stage2	European (Germany)	Cases Controls	940 (504/436) 4,209 (2,000/2,209)	61.6 (10.0) 53.8 (13.2)	- -	- -	30.8 (5.4) 27.2 (4.6)	Metabochip	≥0.95	Ambiguous sex and relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	120,547	PLINK	Age and sex	1.02 (QT)
PIVUS	European (Sweden)	Cases Controls	113 (70/43) 864 (419/445)	70.2 (0.2) 70.2 (0.2)	- -	- -	29.5 (5.1) 26.8 (4.2)	Metabochip	≥0.95	Relatedness and ambiguous sex	≥0.95	$p>10^{-6}$	≥0.01	-	120,892	PLINK	Age and sex	0.97 (QT)
PMB	European (Sweden/Finland)	Cases Controls	4,976 (2,911/2,065) 3,500 (1,700/1,800)	58.8 (12.5) 58.3 (8.4)	- -	- -	28.2 (8.7) 26.4 (4.4)	Metabochip	≥0.95	Outlying heterozygosity, relatedness and non-European descent	≥0.95	$p>10^{-6}$	≥0.01	-	119,674	PLINK	Population structure	1.05 (QT)
PROMIS	South Asian (Pakistan)	Cases Controls	1,178 (904/274) 2,472 (2,088/384)	53.5 (9.1) 52.1 (10.2)	- -	- -	- -	Metabochip	≥0.95	Ambiguous sex and relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	121,792	PLINK	Age, sex, population structure and MI status	1.00 (QT)
SCARFSHEEP	European (Sweden)	Cases Controls	341 (246/95) 3,073 (2,211/862)	59.6 (7.0) 57.9 (7.3)	- -	8.12(5.4) 4.0 (3.8)	27.4 (8.4) 25.4 (6.1)	Metabochip	≥0.95	Ambiguous sex and relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	119,375	PLINK	Age, sex, population structure and CAD status	0.98 (QT)
STR	European (Sweden)	Cases Controls	320 (141/179) 1,318 (612/706)	71.5 (9.3) 74.3 (10.5)	- -	- -	27.0 (4.1) 24.9 (3.8)	Metabochip	≥0.95	-	≥0.95	$p>10^{-6}$	≥0.01	-	120,509	PLINK	Age and sex	0.99 (QT)
THISEAS	European (Greece)	Cases Controls	327 (229/98) 1,180 (643/537)	63.6 (10.6) 58.2 (13.6)	- -	8.0 (2.6) 5.3 (0.6)	29.4 (4.8) 28.3 (5.0)	Metabochip	≥0.95	Duplicates, ambiguous sex, and non-European descent	≥0.98	$p>10^{-4}$	≥0.01	-	108,868	PLINK	Age and sex	1.00 (QT)
ULSAM	European (Sweden)	Cases Controls	233 (233/0) 942 (942/0)	71.0 (0.6) 71.0 (0.6)	- -	- -	27.7 (3.8) 25.9 (3.2)	Metabochip	≥0.95	Relatedness	≥0.95	$p>10^{-6}$	≥0.01	-	119,018	PLINK	Age and sex	0.95 (QT)
WARREN2	European (UK)	Cases Controls	1,117 (647/470) 4,224 (2,394/1,830)	- -	45.5 (11.0) -	- -	32.2 (6.6) -	Metabochip	≥0.95	Duplicates, ambiguous sex, and non-European descent	≥0.95 (≥0.99 for MAF<0.05)	$p>10^{-6}$	≥0.01	-	120,521	PLINK	-	1.07 (QT)

Supplementary Table 2. Summary of combined meta-analysis for 65 novel and established T2D susceptibility loci.

Please see attached spreadsheet.

Supplementary Table 3. Summary statistics for lead SNPs at novel loci in meta-analyses of: (i) 5,561 T2D cases and 14,458 controls from GWAS of South Asian descent populations, excluding 1,958 overlapping samples from PROMIS; and (ii) 6,952 T2D cases and 11,865 controls from GWAS of East Asian descent populations.

SNP	Chr	Position (Build 36 bp)	Alleles[a]		Locus	South Asian meta-analysis			East Asian meta-analysis		
			Risk[b]	Other		Risk allele frequency	OR (95% CI)	*p* -value	Risk allele frequency	OR (95% CI)	*p* -value
rs13389219	2	165,237,122	C	T	*GRB14*	0.74	1.13 (1.06-1.20)	4.9E-05	0.86	1.02 (0.94-1.10)	6.6E-01
rs459193	5	55,842,508	G	A	*ANKRD55*	0.64	1.02 (0.97-1.08)	4.2E-01	0.49	1.04 (1.00-1.10)	7.3E-02
rs516946	8	41,638,405	C	T	*ANK1*	0.80	1.08 (1.02-1.15)	1.2E-02	0.86	1.04 (0.97-1.11)	2.8E-01
rs2796441	9	83,498,768	G	A	*TLE1*	0.52	1.05 (1.00-1.11)	6.2E-02	0.34	1.08 (1.02-1.15)	1.5E-02
rs12571751	10	80,612,637	A	G	*ZMIZ1*	0.57	1.07 (1.01-1.13)	1.3E-02	0.54	1.06 (1.00-1.12)	4.8E-02
rs10842994	12	27,856,417	C	T	*KLHDC5*	0.88	1.11 (1.02-1.20)	1.2E-02	0.75	1.02 (0.95-1.11)	5.4E-01
rs7177055	15	75,619,817	A	G	*HMG20A*	0.53	1.10 (1.05-1.16)	2.0E-04	0.38	1.06 (1.01-1.12)	2.6E-02
rs7202877	16	73,804,746	T	G	*BCAR1*	0.93	1.09 (0.99-1.20)	7.4E-02	0.79	0.99 (0.93-1.05)	7.3E-01
rs12970134	18	56,035,730	A	G	*MC4R*	0.36	1.08 (1.03-1.14)	3.8E-03	0.17	1.11 (1.05-1.18)	2.9E-04
rs10401969	19	19,268,718	C	T	*CILP2*	0.09	1.01 (0.92-1.10)	8.8E-01	0.06	0.98 (0.88-1.08)	6.6E-01

Chr: chromosome. OR: odds-ratio. CI: confidence interval.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele for T2D from our primarily European descent meta-analysis combined meta-analysis.

Supplementary Table 4. Overlap of novel T2D susceptibility loci with related metabolic traits.

Locus	Trait	Lead SNP	CEU r^2 with lead T2D SNP	Reference
GRB14	Waist-hip ratio	rs10195252	0.933	Heid et al. (2010)
	Triglycerides	rs10195252	0.933	Teslovich et al. (2010)
	High-density lipoprotein cholesterol	rs12328675	0.163	Teslovich et al. (2010)
ANK1	Hemoglobin A_{1C}	rs6474359	0.006	Soranzo et al. (2010)
	Hemoglobin A_{1C}	rs4737009	0.004	Soranzo et al. (2010)
MC4R	Body mass index	rs17782313	0.802	Loos et al. (2008)
	High-density lipoprotein cholesterol	rs12967135	0.840	Teslovich et al. (2010)
	Waist circumference	rs12970134[a]	1.000	Chambers et al. (2008)
	Insulin resistance	rs12970134[a]	1.000	Chambers et al. (2008)
CILP2	Total cholesterol	rs10401969[a]	1.000	Teslovich et al. (2010)
	Triglycerides	rs10401969[a]	1.000	Teslovich et al. (2010)
	Low-density lipoprotein cholesterol	rs10401969[a]	1.000	Teslovich et al. (2010)
GIPR	2-hour glucose	rs10423928	0.069	Saxena et al. (2010)
	Body mass index	rs2287019	0.064	Speliotes et al. (2010)

[a]Same lead SNP for T2D and trait

Supplementary Table 5. Contribution of lead SNPs at novel and established T2D susceptibility loci to the sibling relative risk and explained liability-scale variance explained.

Locus	Lead SNP	Chr	Position (Build 36 bp)	Combined meta-analysis p-value	Stage 2 risk allele frequency	Stage 2 OR (95% CI)	Sibling relative risk[a]	Explained liability-scale variance (%)[b]
Previously established susceptibility loci								
TCF7L2	rs7903146	10	114,748,339	1.2E-139	0.27	1.38 (1.34-1.42)	1.023	1.351
CDKAL1	rs7756992	6	20,787,688	7.0E-35	0.29	1.15 (1.11-1.18)	1.004	0.247
CDKN2A/B	rs10811661	9	22,124,094	3.7E-27	0.82	1.19 (1.14-1.23)	1.004	0.226
IGF2BP2	rs4402960	3	186,994,381	2.4E-23	0.33	1.13 (1.10-1.17)	1.003	0.198
FTO	rs9936385	16	52,376,670	2.6E-23	0.41	1.13 (1.10-1.16)	1.004	0.213
SLC30A8	rs3802177	8	118,254,206	1.3E-21	0.66	1.13 (1.09-1.16)	1.003	0.185
HHEX/IDE	rs1111875	10	94,452,862	2.0E-19	0.58	1.09 (1.06-1.12)	1.002	0.103
JAZF1	rs849135	7	28,162,938	3.1E-17	0.52	1.10 (1.07-1.13)	1.002	0.131
WFS1	rs4458523	4	6,340,887	2.0E-15	0.57	1.10 (1.07-1.13)	1.002	0.127
IRS1	rs2943640	2	226,801,829	2.7E-14	0.63	1.10 (1.07-1.13)	1.002	0.119
ADCY5	rs11717195	3	124,565,088	6.5E-14	0.77	1.12 (1.09-1.16)	1.002	0.123
MTNR1B	rs10830963	11	92,348,358	5.3E-13	0.31	1.10 (1.06-1.13)	1.002	0.116
PPARG	rs1801282	3	12,368,125	1.1E-12	0.86	1.11 (1.07-1.16)	1.001	0.073
THADA	rs10203174	2	43,543,534	9.5E-12	0.89	1.14 (1.09-1.20)	1.001	0.085
KCNQ1	rs163184	11	2,803,645	1.2E-11	0.50	1.09 (1.06-1.12)	1.002	0.107
HNF1B (TCF2)	rs11651052	17	33,176,494	2.0E-11	0.44	1.10 (1.07-1.13)	1.002	0.131
ZBED3	rs6878122	5	76,463,067	5.0E-11	0.28	1.09 (1.05-1.12)	1.002	0.090
DGKB	rs17168486	7	14,864,807	5.9E-11	0.19	1.09 (1.06-1.13)	1.001	0.071
ADAMTS9	rs6795735	3	64,680,405	7.4E-11	0.59	1.09 (1.06-1.12)	1.002	0.102
ARAP1 (CENTD2)	rs1552224	11	72,110,746	1.8E-10	0.81	1.09 (1.06-1.13)	1.001	0.062
KCNJ11	rs5215	11	17,365,206	8.5E-10	0.41	1.07 (1.04-1.10)	1.001	0.065
HMGA2	rs2261181	12	64,498,585	1.2E-09	0.10	1.10 (1.05-1.16)	1.001	0.052
UBE2E2	rs1496653	3	23,429,794	3.6E-09	0.75	1.09 (1.05-1.12)	1.001	0.077
HMG20A	rs7177055	15	75,619,817	4.6E-09	0.68	1.08 (1.05-1.11)	1.001	0.073
PRC1	rs12899811	15	89,345,080	6.3E-09	0.31	1.07 (1.04-1.10)	1.001	0.058
TSPAN8/LGR5	rs7955901	12	69,719,560	6.5E-09	0.45	1.06 (1.03-1.09)	1.001	0.049
PROX1	rs2075423	1	212,221,342	8.1E-09	0.62	1.07 (1.04-1.10)	1.001	0.061
GRB14	rs13389219	2	165,237,122	1.0E-08	0.60	1.09 (1.06-1.12)	1.002	0.101
SPRY2	rs1359790	13	79,615,157	1.4E-08	0.72	1.06 (1.03-1.10)	1.001	0.039
BCL11A	rs243088	2	60,422,249	1.8E-08	0.45	1.06 (1.03-1.09)	1.001	0.049
HNF1A (TCF1)	rs12427353	12	119,911,284	6.5E-08	0.79	1.07 (1.03-1.10)	1.001	0.042
TLE4	rs17791513	9	81,095,410	2.8E-07	0.91	1.08 (1.03-1.14)	1.000	0.026
GCKR	rs780094	2	27,594,741	5.4E-07	0.61	1.08 (1.05-1.11)	1.001	0.080
CDC123/CAMK1D	rs11257655	10	12,347,900	2.1E-06	0.23	1.08 (1.04-1.11)	1.001	0.064
C2CD4A	rs4502156	15	60,170,447	2.3E-06	0.52	1.05 (1.03-1.08)	1.001	0.034

TP53INP1	rs7845219	8	96,006,678	4.6E-06	0.52	1.04 (1.02-1.07)	1.000	0.022
GCK	rs10278336	7	44,211,888	6.4E-06	0.50	1.09 (1.05-1.13)	1.002	0.107
GLIS3	rs10758593	9	4,282,083	1.0E-05	0.42	1.06 (1.04-1.09)	1.001	0.048
NOTCH2	rs10923931	1	120,319,482	1.3E-05	0.12	1.07 (1.03-1.12)	1.001	0.030
RBMS1	rs7569522	2	161,054,693	4.1E-05	0.44	1.03 (1.01-1.06)	1.000	0.013
ZFAND6	rs11634397	15	78,219,277	1.4E-04	0.64	1.03 (1.00-1.06)	1.000	0.012
FTITM2/R3HDML/HNF4A	rs4812829	20	42,422,681	1.5E-04	0.19	1.06 (1.02-1.10)	1.001	0.032
KLF14	rs13233731	7	130,088,229	2.3E-04	0.51	1.01 (0.98-1.04)	1.000	0.001
PEPD	rs8182584	19	38,601,550	4.8E-04	0.38	1.05 (1.02-1.09)	1.001	0.033
DUSP8	rs2334499	11	1,653,425	1.2E-03	0.43	1.03 (1.00-1.06)	1.000	0.012
PTPRD	rs16927668	9	8,359,533	2.8E-03	0.24	1.05 (1.01-1.08)	1.000	0.026
SRR	rs2447090	17	2,245,724	3.8E-03	0.62	1.04 (1.01-1.07)	1.000	0.021
VPS26A	rs12242953	10	70,535,348	3.9E-03	0.93	1.05 (0.99-1.11)	1.000	0.009
ST64GAL1	rs17301514	3	188,096,103	1.4E-02	0.13	1.03 (0.99-1.07)	1.000	0.006
MAEA	rs6819243	4	1,283,245	7.6E-02	0.96	1.07 (0.99-1.14)	1.000	0.011
GCC1	rs17867832	7	126,784,073	9.5E-02	0.91	1.07 (0.99-1.16)	1.000	0.021
PSMD6	rs12497268	3	64,065,403	9.8E-02	0.80	1.03 (0.99-1.07)	1.000	0.008
ZFAND3	rs4299828	6	38,285,645	1.4E-01	0.79	1.03 (0.99-1.06)	1.000	0.008
KCNK16	rs3734621	6	39,412,189	2.5E-01	0.03	1.05 (0.97-1.14)	1.000	0.004
AP3S2	rs2007084	15	88,146,339	3.6E-01	0.92	1.03 (0.98-1.09)	1.000	0.004
Total							**1.093**	**5.156**
Novel susceptibility loci achieving genome-wide significance in combined meta-analysis								
ZMIZ1	rs12571751	10	80,612,637	1.0E-10	0.52	1.07 (1.04-1.10)	1.001	0.066
ANK1	rs516946	8	41,638,405	2.5E-10	0.76	1.08 (1.05-1.12)	1.001	0.059
KLHDC5	rs10842994	12	27,856,417	6.1E-10	0.80	1.10 (1.07-1.14)	1.001	0.079
TLE1	rs2796441	9	83,498,768	5.4E-09	0.57	1.07 (1.04-1.10)	1.001	0.064
ANKRD55	rs459193	5	55,842,508	6.0E-09	0.70	1.10 (1.06-1.13)	1.002	0.106
CILP2	rs10401969	19	19,268,718	7.0E-09	0.08	1.14 (1.08-1.20)	1.001	0.082
MC4R	rs12970134	18	56,035,730	1.2E-08	0.27	1.08 (1.05-1.11)	1.001	0.070
BCAR1	rs7202877	16	73,804,746	3.5E-08	0.89	1.10 (1.05-1.15)	1.001	0.047
Total							**1.010**	**0.574**
Combined total							**1.104**	**5.730**

Chr: chromosome. OR: odds-ratio. CI: confidence interval.

[a]Assuming a multiplicative model across loci.

[b]Assuming a liability threshold model and a disease prevalence of 8%.

Supplementary Table 6. Previously reported lead SNPs from GWAS and lead Metabochip SNPs from Stage 2 meta-analysis in 36 fine-mapping regions.

		Previously reported lead GWAS SNP (*or best proxy on Metabochip): Stage 2 meta-analysis										Lead SNP from Stage 2 meta-analysis											
Locus	Fine-mapping trait	SNP	Chr	Position	Risk allele	Other allele	Risk allele frequency	Cases	Controls	p-value	OR (95% CI)	SNP	Chr	Position	Risk allele	Other allele	Risk allele frequency	Cases	Controls	p-value	OR (95% CI)	CEU r^2	Reference
NOTCH2	T2D	rs10923931	1	120,319,482	T	G	0.11	22,162	55,566	1.3E-03	1.07 (1.03-1.12)	rs835575	1	120,258,086	T	G	0.11	22,669	58,119	1.0E-03	1.07 (1.03-1.12)	1.00	Voight et al. (2010)
PROX1	FG	rs340874	1	212,225,879	C	T	0.52	22,669	58,119	1.4E-05	1.06 (1.03-1.09)	rs17712208	1	212,217,068	T	A	0.03	21,387	56,604	3.9E-06	1.20 (1.11-1.30)	0.06	Dupuis et al. (2010)
GCKR	TG	rs780094	2	27,594,741	C	T	0.62	22,669	58,119	3.3E-07	1.08 (1.05-1.11)	rs780094	2	27,594,741	C	T	0.62	22,669	58,119	3.3E-07	1.08 (1.05-1.11)	Same SNP	Dupuis et al. (2010)
THADA	T2D	rs11899863	2	43,472,323	C	T	0.92	22,669	58,119	6.6E-08	1.16 (1.10-1.22)	rs10203174	2	43,543,534	C	T	0.90	22,669	58,119	2.0E-08	1.14 (1.09-1.20)	0.90	Voight et al. (2010)
BCL11A	T2D	rs243019*	2	60,439,310	C	T	0.46	22,669	58,119	3.7E-05	1.06 (1.03-1.09)	rs243083	2	60,427,374	G	A	0.46	22,669	58,119	1.1E-05	1.06 (1.03-1.09)	1.00	Voight et al. (2010)
GRB14	WHR and LDL-C	rs3923113	2	165,210,095	A	C	0.64	21,947	47,966	7.7E-09	1.09 (1.06-1.12)	rs1128249	2	165,236,870	G	T	0.61	22,669	58,119	1.7E-08	1.08 (1.05-1.12)	0.77	Kooner et al. (2011)
IRS1	T2D	rs7578326	2	226,728,897	A	G	0.64	22,669	58,119	8.4E-07	1.07 (1.04-1.11)	rs2943640	2	226,801,829	C	A	0.64	22,669	58,119	2.1E-11	1.10 (1.07-1.13)	0.65	Voight et al. (2010)
PPARG	T2D	rs13081389	3	12,264,800	A	G	0.93	22,669	58,119	2.0E-03	1.09 (1.03-1.15)	rs1899951	3	12,369,840	C	T	0.86	22,669	58,119	3.7E-07	1.11 (1.07-1.15)	0.34	Voight et al. (2010)
ADAMTS9	T2D	rs6795735	3	64,680,405	C	T	0.60	22,669	58,119	1.7E-09	1.09 (1.06-1.12)	rs6795735	3	64,680,405	C	T	0.60	22,669	58,119	1.7E-09	1.09 (1.06-1.12)	Same SNP	Voight et al. (2010)
ADCY5	T2D	rs11708067	3	124,548,468	A	G	0.79	22,669	58,119	3.6E-11	1.12 (1.08-1.16)	rs11717195	3	124,565,088	T	C	0.78	22,669	58,119	1.2E-11	1.12 (1.09-1.16)	0.80	Dupuis et al. (2010)
IGF2BP2	T2D	rs6769511*	3	187,012,984	C	T	0.31	22,669	58,119	3.4E-16	1.13 (1.10-1.16)	rs4402960	3	186,994,381	T	G	0.31	21,942	57,192	4.8E-17	1.13 (1.10-1.17)	1.00	Voight et al. (2010)
WFS1	T2D	rs1801214	4	6,353,923	T	C	0.58	22,669	58,119	1.3E-10	1.09 (1.06-1.13)	rs4416547	4	6,344,868	A	G	0.59	22,669	58,119	9.6E-11	1.10 (1.07-1.13)	1.00	Voight et al. (2010)
ZBED3	T2D	rs4457053	5	76,460,705	G	A	0.27	22,669	58,119	5.0E-07	1.08 (1.05-1.11)	rs6878122	5	76,463,067	G	A	0.27	22,669	58,119	8.7E-08	1.09 (1.05-1.12)	1.00	Voight et al. (2010)
CDKAL1	T2D	rs9368222*	6	20,794,975	A	C	0.28	21,942	57,192	1.1E-18	1.14 (1.11-1.18)	rs7756992	6	20,787,688	G	A	0.28	22,669	58,119	9.9E-20	1.15 (1.11-1.18)	1.00	Voight et al. (2010)
DGKB	FG	rs2191349	7	15,030,834	T	G	0.52	22,669	58,119	3.9E-03	1.04 (1.01-1.07)	rs17168486	7	14,864,807	T	C	0.17	22,669	58,119	2.8E-07	1.09 (1.06-1.13)	0.00	Dupuis et al. (2010)
JAZF1	T2D	rs849134	7	28,162,747	A	G	-	-	-	-	-	rs849135	7	28,162,938	G	A	0.52	22,669	58,119	1.7E-11	1.10 (1.07-1.13)	1.00	Voight et al. (2010)
GCKR	FG and HbA_{1C}	rs4607517	7	44,202,193	A	G	0.15	21,947	47,966	4.6E-06	1.09 (1.05-1.14)	rs6975024	7	44,198,411	C	T	0.15	22,669	58,119	6.6E-06	1.09 (1.05-1.13)	1.00	Dupuis et al. (2010)
KLF14	T2D	rs972283	7	130,117,394	G	A	0.52	22,669	58,119	3.3E-01	1.01 (0.99-1.04)	7-130116320	7	130,116,320	A	G	0.02	21,491	45,519	4.5E-02	1.10 (1.00-1.21)	0.15	Voight et al. (2010)
TP53INP1	T2D	rs896854	8	96,029,687	T	C	0.50	22,669	58,119	1.3E-02	1.03 (1.01-1.06)	rs7845219	8	96,006,678	T	C	0.51	22,669	58,119	2.3E-03	1.04 (1.02-1.07)	0.85	Voight et al. (2010)
SLC30A8	T2D	rs3802177	8	118,254,206	G	A	0.67	22,669	58,119	2.1E-15	1.13 (1.09-1.16)	rs11558471	8	118,254,914	A	G	0.66	22,669	58,119	1.1E-15	1.13 (1.09-1.16)	0.96	Voight et al. (2010)
GLIS3	FG	rs7041847	9	4,277,466	A	G	0.49	21,947	47,966	8.4E-03	1.04 (1.01-1.07)	9-4284707	9	4,284,707	G	T	0.36	22,669	58,119	3.0E-06	1.07 (1.04-1.10)	0.39	Cho et al. (2012)
CDKN2A/B	T2D	rs10965250	9	22,123,284	G	A	0.83	22,669	58,119	8.1E-19	1.18 (1.14-1.23)	rs10811661	9	22,124,094	T	C	0.83	22,669	58,119	3.0E-19	1.19 (1.14-1.23)	0.92	Voight et al. (2010)
CDC123/CAMK1D	T2D	rs12779790	10	12,368,016	G	A	-	-	-	-	-	rs11257655	10	12,347,900	T	C	0.22	22,669	58,119	7.9E-06	1.08 (1.04-1.11)	0.75	Voight et al. (2010)
HHEX/IDE	T2D	rs5015480	10	94,455,539	C	T	-	-	-	-	-	rs7923837	10	94,471,897	G	A	0.62	22,669	58,119	6.4E-10	1.09 (1.06-1.12)	0.66	Voight et al. (2010)
TCF7L2	T2D	rs7903146	10	114,748,339	T	C	0.25	22,669	58,119	2.6E-99	1.38 (1.34-1.42)	rs7903146	10	114,748,339	T	C	0.25	22,669	58,119	2.6E-99	1.38 (1.34-1.42)	Same SNP	Voight et al. (2010)
KCNQ1	T2D	rs231362	11	2,648,047	G	A	0.52	18,660	52,922	1.6E-05	1.07 (1.04-1.10)	rs2237896	11	2,815,016	G	A	0.95	22,618	57,760	4.7E-11	1.25 (1.17-1.34)	0.00	Voight et al. (2010)
KCNJ11	T2D	rs5215	11	17,365,206	C	T	0.40	22,669	58,119	1.2E-06	1.07 (1.04-1.10)	rs5215	11	17,365,206	C	T	0.40	22,669	58,119	1.2E-06	1.07 (1.04-1.10)	Same SNP	Voight et al. (2010)
ARAP1 (CENTD2)	T2D	rs1552224	11	72,110,746	A	C	0.82	22,669	58,119	9.5E-07	1.09 (1.06-1.13)	11-72138046	11	72,138,046	A	C	0.82	22,669	58,119	1.3E-07	1.10 (1.06-1.14)	0.95	Voight et al. (2010)
MTNR1B	T2D	rs1387153	11	92,313,476	T	C	0.29	22,669	58,119	9.7E-07	1.08 (1.05-1.11)	rs10830963	11	92,348,358	G	C	0.29	21,866	56,045	1.9E-09	1.10 (1.06-1.13)	0.56	Voight et al. (2010)
HMGA2	T2D	rs2612035*	12	64,478,934	G	A	0.09	22,669	58,119	1.5E-05	1.10 (1.06-1.16)	rs7134682	12	64,454,418	T	G	0.12	22,669	58,119	1.5E-06	1.10 (1.06-1.15)	0.29	Voight et al. (2010)
TSPAN8/LGR5	T2D	rs4760915*	12	69,920,379	T	C	0.27	22,669	58,119	5.4E-03	1.04 (1.01-1.08)	rs7955901	12	69,719,560	C	T	0.43	22,669	58,119	1.1E-05	1.06 (1.03-1.09)	0.13	Voight et al. (2010)
HNF1A (TCF1)	T2D	rs7957197	12	119,945,069	T	A	0.79	22,162	55,566	9.4E-04	1.06 (1.02-1.10)	rs1169288	12	119,901,033	C	A	0.33	21,334	54,628	2.4E-05	1.07 (1.03-1.10)	0.07	Voight et al. (2010)
C2CD4A	FG and 2 hour glucose	rs7163757	15	60,178,900	C	T	-	-	-	-	-	rs4502156	15	60,170,447	T	C	0.53	22,669	58,119	1.2E-04	1.05 (1.03-1.08)	1.00	Yamauchi et al. (2010)
PRC1	T2D	rs8042680	15	89,322,341	A	C	0.31	21,947	47,966	4.2E-05	1.06 (1.03-1.10)	rs12899811	15	89,345,080	G	A	0.31	22,669	58,119	2.1E-06	1.07 (1.04-1.10)	0.62	Voight et al. (2010)
FTO	BMI	rs11642841	16	52,402,988	A	C	0.40	22,669	58,119	1.6E-13	1.11 (1.08-1.14)	rs1121980	16	52,366,748	A	G	0.43	22,669	58,119	8.2E-18	1.13 (1.10-1.16)	0.78	Voight et al. (2010)
HNF1B (TCF2)	T2D	rs11651755*	17	33,173,953	C	T	0.45	22,669	58,119	2.0E-11	1.10 (1.07-1.13)	rs11263763	17	33,177,678	G	A	0.44	22,669	58,119	1.8E-11	1.10 (1.07-1.13)	0.87	Voight et al. (2010)

Chr: chromosome. OR: odds-ratio. CI: confidence interval.

Supplementary Table 7. Summary of sex-differentiated meta-analysis for loci demonstrating heterogeneity in allelic effects between males and females.

SNP	Chr	Position (Build 36 bp)	Alleles[a]		Sex	Stage 1 meta-analysis				Stage 2 meta-analysis				Combined meta-analysis				Sex-differentiated meta-analysis				Locus	Rationale for inclusion in this table
			Risk[b]	Other		Cases	Controls	*p* -value	OR (95% CI)	Cases	Controls	*p* -value	OR (95% CI)	Cases	Controls	*p* -value	OR (95% CI)	Cases	Controls	*p* -value	Heterogeneity *p* -value		
rs243088	2	60,422,249	T	A	Male	5,253	20,945	2.6E-05	1.11 (1.06-1.17)	13,842	32,361	3.1E-06	1.09 (1.05-1.13)	19,095	53,306	6.5E-10	1.10 (1.06-1.13)	32,249	111,929	4.7E-10	1.2E-02	*BCL11A*	Lead SNP from sex-differentiated meta-analysis
					Female	4,327	32,865	1.0E-01	1.04 (0.99-1.10)	8,827	25,758	9.6E-02	1.03 (0.99-1.07)	13,154	58,623	2.8E-02	1.04 (1.00-1.07)						
rs3923113	2	165,210,095	A	C	Male	5,253	20,945	5.5E-01	1.02 (0.96-1.07)	13,409	25,757	2.2E-03	1.06 (1.02-1.10)	18,662	46,702	4.9E-03	1.05 (1.01-1.08)	31,527	101,776	2.6E-10	8.0E-03	*GRB14*	Lead SNP from sex-differentiated meta-analysis
					Female	4,327	32,865	1.1E-02	1.07 (1.02-1.14)	8,538	22,209	2.9E-09	1.14 (1.09-1.19)	12,865	55,074	1.8E-09	1.11 (1.08-1.15)						
rs17168486	7	14,864,807	T	C	Male	5,253	20,945	5.8E-10	1.23 (1.16-1.32)	13,842	32,361	4.9E-06	1.11 (1.06-1.16)	19,095	53,306	6.5E-13	1.15 (1.11-1.19)	32,249	111,929	1.2E-13	6.8E-03	*DGKB*	Lead SNP from sex-differentiated meta-analysis
					Female	4,327	32,865	3.3E-01	1.03 (0.97-1.11)	8,827	25,758	3.9E-03	1.08 (1.02-1.13)	13,154	58,623	5.2E-03	1.06 (1.02-1.11)						
rs6960043	7	15,019,385	C	T	Male	6,377	22,243	2.6E-03	1.07 (1.03-1.13)	13,613	31,718	7.5E-05	1.08 (1.04-1.11)	19,990	53,961	7.9E-07	1.07 (1.04-1.11)	34,513	113,801	1.9E-07	1.2E-01		Lead SNP for putative secondary signal from sex-combined meta-analysis
					Female	5,794	34,619	7.2E-03	1.07 (1.02-1.12)	8,729	25,221	2.9E-01	1.02 (0.98-1.06)	14,523	59,840	1.5E-02	1.04 (1.01-1.07)						
rs163184	11	2,803,645	G	T	Male	5,253	20,945	2.3E-05	1.12 (1.06-1.18)	13,578	31,385	4.7E-11	1.13 (1.09-1.17)	18,831	52,330	8.5E-15	1.12 (1.09-1.16)	31,874	110,307	2.4E-15	1.3E-03	*KCNQ1*	Lead SNP from sex-differentiated meta-analysis
					Female	4,327	32,865	4.2E-02	1.06 (1.00-1.12)	8,716	25,112	5.0E-02	1.04 (1.00-1.08)	13,043	57,977	7.8E-03	1.05 (1.01-1.08)						
rs231361	11	2,648,076	A	G	Male	5,253	20,945	5.2E-03	1.09 (1.03-1.16)	13,842	32,361	1.4E-04	1.08 (1.04-1.12)	19,095	53,306	2.9E-06	1.08 (1.05-1.12)	32,249	111,929	1.8E-10	7.2E-01		Lead SNP for putative secondary signal from sex-combined meta-analysis
					Female	4,327	32,865	1.7E-03	1.11 (1.04-1.18)	8,827	25,758	1.8E-04	1.09 (1.04-1.13)	13,154	58,623	2.9E-06	1.09 (1.05-1.13)						
rs11063069	12	4,244,634	G	A	Male	5,096	14,646	3.0E-06	1.16 (1.09-1.24)	13,338	30,361	2.3E-05	1.10 (1.05-1.15)	18,434	45,007	1.1E-09	1.12 (1.08-1.16)	31,756	86,881	9.8E-10	1.3E-02	*CCND2*	Lead SNP from sex-differentiated meta-analysis
					Female	4,931	18,325	7.5E-02	1.06 (0.99-1.13)	8,391	23,549	1.7E-01	1.04 (0.99-1.09)	13,322	41,874	3.6E-02	1.04 (1.00-1.09)						
rs8108269	19	50,850,353	G	T	Male	6,377	22,243	8.8E-02	1.05 (0.99-1.11)	13,842	32,361	1.7E-02	1.05 (1.01-1.09)	20,219	54,604	3.7E-03	1.05 (1.02-1.08)	34,840	114,981	2.1E-08	5.7E-02	*GIPR*	Lead SNP from sex-differentiated meta-analysis
					Female	5,794	34,619	4.1E-03	1.09 (1.03-1.15)	8827	25758	4.7E-06	1.10 (1.06-1.15)	14,621	60,377	2.2E-07	1.10 (1.06-1.14)						

Chr: chromosome. OR: odds-ratio. CI: confidence interval.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele from sex-combined meta-analysis.

Supplementary Table 8. Lead SNPs from sex-differentiated meta-analysis for 65 novel and established T2D susceptibility loci.

			Alleles		Male-specific meta-analysis				Female-specific meta-analysis				Sex-differentiated meta-analysis					Sex-combined meta-analysis	
SNP	Chr	Position (Build 36 bp)	Risk	Other	Cases	Controls	*p* -value	OR (95% CI)	Cases	Controls	*p* -value	OR (95% CI)	Cases	Controls	*p* -value	Heterogeneity *p* -value	Locus	Lead SNP	CEU r^2
rs2641352	1	120,247,586	C	T	18,362	50,663	4.6E-03	1.07 (1.02-1.12)	12,718	56,414	3.1E-05	1.11 (1.06-1.17)	31,080	107,077	3.0E-06	2.2E-01	*NOTCH2*	rs10923931	1.00
rs2075423	1	212,221,342	G	T	20,219	54,604	9.3E-06	1.07 (1.04-1.10)	14,621	60,377	1.0E-05	1.08 (1.04-1.11)	34,840	114,981	3.2E-09	7.7E-01	*PROX1*	rs2075423	Same SNP
rs780094	2	27,594,741	C	T	20,219	54,604	4.7E-05	1.06 (1.03-1.09)	14,621	60,377	1.2E-03	1.05 (1.02-1.09)	34,840	114,981	1.3E-06	7.4E-01	*GCKR*	rs780094	Same SNP
rs13405158	2	43,558,790	T	C	20,219	54,604	5.2E-10	1.16 (1.11-1.22)	14,621	60,377	6.4E-04	1.10 (1.04-1.15)	34,840	114,981	1.2E-11	1.0E-01	*THADA*	rs10203174	1.00
rs243088	2	60,422,249	T	A	19,095	53,306	6.5E-10	1.10 (1.06-1.13)	13,154	58,623	2.8E-02	1.04 (1.00-1.07)	32,249	111,929	4.7E-10	1.2E-02	*BCL11A*	rs243088	Same SNP
rs7569522	2	161,054,693	A	G	20,219	54,604	3.1E-02	1.03 (1.00-1.06)	14,621	60,377	9.5E-05	1.06 (1.03-1.10)	34,840	114,981	4.8E-05	1.5E-01	*RBMS1*	rs7569522	Same SNP
rs3923113	2	165,210,095	A	C	18,662	46,702	4.9E-03	1.05 (1.01-1.08)	12,865	55,074	1.8E-09	1.11 (1.08-1.15)	31,527	101,776	2.6E-10	8.0E-03	*GRB14*	rs13389219	0.77
rs2943640	2	226,801,829	C	A	20,219	54,604	3.0E-08	1.09 (1.06-1.12)	14,621	60,377	1.3E-09	1.11 (1.07-1.14)	34,840	114,981	2.2E-15	4.5E-01	*IRS1*	rs2943640	Same SNP
rs11709077	3	12,311,507	G	A	20,219	54,604	1.5E-07	1.12 (1.07-1.17)	14,621	60,377	1.1E-08	1.14 (1.09-1.20)	34,840	114,981	8.7E-14	5.1E-01	*PPARG*	rs1801282	1.00
rs1496653	3	23,429,794	A	G	20,219	54,604	4.4E-07	1.09 (1.05-1.13)	14,621	60,377	3.3E-03	1.06 (1.02-1.10)	34,840	114,981	3.8E-08	2.3E-01	*UBE2E2*	rs1496653	Same SNP
rs12497268	3	64,065,403	G	C	20,219	54,604	6.9E-03	1.05 (1.01-1.09)	14,621	60,377	5.9E-01	1.01 (0.97-1.05)	34,840	114,981	2.2E-02	1.5E-01	*PSMD6*	rs12497268	Same SNP
rs4611812	3	64,674,485	C	T	19,095	53,306	1.1E-06	1.08 (1.05-1.11)	13,154	58,623	3.3E-07	1.09 (1.05-1.13)	32,249	111,929	1.6E-11	5.8E-01	*ADAMTS9*	rs6795735	0.94
rs11708067	3	124,548,468	A	G	20,219	54,604	4.1E-07	1.09 (1.06-1.13)	14,621	60,377	1.7E-10	1.13 (1.09-1.18)	34,840	114,981	3.8E-15	1.8E-01	*ADCY5*	rs11717195	0.80
rs7640539	3	186,995,990	A	T	18,866	52,663	1.5E-17	1.14 (1.11-1.18)	13,043	57,977	1.8E-09	1.11 (1.07-1.15)	31,909	110,640	2.3E-24	2.2E-01	*IGF2BP2*	rs4402960	1.00
rs17301514	3	188,096,103	A	G	18,227	45,990	1.9E-02	1.06 (1.01-1.11)	12,557	42,745	1.3E-01	1.04 (0.99-1.10)	30,784	88,735	2.0E-02	6.6E-01	*ST64GAL1*	rs17301514	Same SNP
rs2306248	4	850,146	G	A	19,095	53,306	2.0E-01	0.98 (0.95-1.01)	13,154	58,623	1.3E-02	1.04 (1.01-1.08)	32,249	111,929	2.0E-02	6.9E-03	*MAEA*	rs6819243	0.01
rs1801214	4	6,353,923	T	C	19,095	53,306	2.9E-12	1.11 (1.08-1.15)	13,154	58,623	5.0E-07	1.09 (1.05-1.13)	32,249	111,929	8.6E-17	3.6E-01	*WFS1*	rs4458523	1.00
rs459193	5	55,842,508	G	A	19,095	53,306	3.4E-06	1.08 (1.05-1.12)	13,154	58,623	1.1E-05	1.09 (1.05-1.13)	32,249	111,929	1.3E-09	8.4E-01	*ANKRD55*	rs459193	Same SNP
rs6878122	5	76,463,067	G	A	18,566	52,766	2.6E-10	1.12 (1.08-1.15)	12,661	58,088	2.3E-04	1.07 (1.03-1.12)	31,227	110,854	2.4E-12	1.4E-01	*ZBED3*	rs6878122	Same SNP
rs7756992	6	20,787,688	G	A	20,219	54,604	1.5E-22	1.17 (1.13-1.20)	14,621	60,377	1.9E-20	1.17 (1.14-1.22)	34,840	114,981	4.0E-40	7.7E-01	*CDKAL1*	rs7756992	Same SNP
rs4299828	6	38,285,645	A	G	20,219	54,604	1.9E-02	1.04 (1.01-1.08)	14,621	60,377	2.8E-01	1.02 (0.98-1.06)	34,840	114,981	3.5E-02	4.4E-01	*ZFAND3*	rs4299828	Same SNP
rs1537230	6	39,052,174	G	A	20,219	54,604	1.9E-01	1.02 (0.99-1.05)	14,621	60,377	3.8E-05	1.07 (1.04-1.11)	34,840	114,981	8.7E-05	3.0E-02	*KCNK16*	rs3734621	0.01
rs17168486	7	14,864,807	T	C	19,095	53,306	6.5E-13	1.15 (1.11-1.19)	13,154	58,623	5.2E-03	1.06 (1.02-1.11)	32,249	111,929	1.2E-13	6.8E-03	*DGKB*	rs17168486	Same SNP
rs849135	7	28,162,938	G	A	19,095	53,306	3.2E-13	1.11 (1.08-1.15)	13,154	58,623	2.0E-08	1.10 (1.06-1.13)	32,249	111,929	4.4E-19	4.7E-01	*JAZF1*	rs849135	Same SNP
rs4607517	7	44,202,193	A	G	18,662	46,702	9.2E-04	1.07 (1.03-1.11)	12,865	55,074	5.2E-04	1.08 (1.04-1.13)	31,527	101,776	9.9E-06	6.9E-01	*GCK*	rs10278336	0.18
rs17867832	7	126,784,073	T	G	11,770	32,695	1.8E-01	1.05 (0.98-1.12)	8,282	41,116	4.7E-04	1.14 (1.06-1.22)	20,052	73,811	8.8E-04	9.9E-02	*GCC1*	rs17867832	Same SNP
rs6467314	7	130,092,681	G	C	19,095	53,306	5.6E-01	1.01 (0.98-1.04)	13,154	58,623	2.2E-06	1.09 (1.05-1.13)	32,249	111,929	1.1E-05	1.8E-03	*KLF14*	rs13233731	0.32
rs516946	8	41,638,405	C	T	20,219	54,604	7.8E-11	1.12 (1.08-1.16)	14,621	60,377	1.1E-03	1.06 (1.03-1.10)	34,840	114,981	3.1E-12	5.2E-02	*ANK1*	rs516946	Same SNP
rs7845219	8	96,006,678	T	C	19,095	53,306	7.2E-06	1.07 (1.04-1.10)	13,154	58,623	1.8E-03	1.05 (1.02-1.09)	32,249	111,929	3.2E-07	5.0E-01	*TP53INP1*	rs7845219	Same SNP
rs3802177	8	118,254,206	G	A	18,840	52,613	1.4E-16	1.15 (1.11-1.18)	12,976	57,878	7.2E-11	1.13 (1.09-1.17)	31,816	110,491	9.2E-25	5.1E-01	*SLC30A8*	rs3802177	Same SNP
rs10758593	9	4,282,083	A	G	18,797	51,826	5.8E-07	1.08 (1.05-1.11)	12,911	56,746	1.0E-02	1.04 (1.01-1.08)	31,708	108,572	1.4E-07	1.6E-01	*GLIS3*	rs10758593	Same SNP
rs16927668	9	8,359,533	T	C	19,095	53,306	1.0E-02	1.05 (1.01-1.08)	13,154	58,623	1.7E-02	1.05 (1.01-1.09)	32,249	111,929	2.1E-03	9.3E-01	*PTPRD*	rs16927668	Same SNP
rs10965250	9	22,123,284	G	A	19,095	53,306	8.5E-15	1.17 (1.13-1.22)	13,154	58,623	5.7E-16	1.20 (1.15-1.26)	32,249	111,929	4.9E-28	4.1E-01	*CDKN2A/B*	rs10811661	0.92
rs17791513	9	81,095,410	A	G	19,095	53,306	2.8E-06	1.14 (1.08-1.20)	13,108	58,283	1.5E-02	1.08 (1.02-1.15)	32,203	111,589	8.8E-07	2.1E-01	*TLE4*	rs17791513	Same SNP
rs2796441	9	83,498,768	G	A	19,690	54,064	4.9E-09	1.09 (1.06-1.13)	14,128	59,842	5.0E-03	1.05 (1.01-1.08)	33,818	113,906	7.2E-10	6.4E-02	*TLE1*	rs2796441	Same SNP
rs11257655	10	12,347,900	T	C	18,761	52,172	8.3E-04	1.06 (1.02-1.10)	13,154	58,623	5.9E-05	1.08 (1.04-1.13)	31,915	110,795	1.2E-06	4.5E-01	*CDC123/CAMK1D*	rs11257655	Same SNP
rs5030913	10	70,676,137	T	G	20,219	54,604	6.7E-01	1.01 (0.98-1.04)	14,621	60,377	1.1E-03	1.06 (1.02-1.10)	34,840	114,981	4.4E-03	3.4E-02	*VPS26A*	rs12242953	0.02
rs12571751	10	80,612,637	A	G	20,219	54,604	6.4E-07	1.07 (1.04-1.11)	14,621	60,377	1.2E-06	1.08 (1.05-1.12)	34,840	114,981	3.1E-11	7.8E-01	*ZMIZ1*	rs12571751	Same SNP
rs1111875	10	94,452,862	C	T	20,219	54,604	4.9E-12	1.11 (1.07-1.14)	14,621	60,377	6.7E-13	1.12 (1.09-1.16)	34,840	114,981	2.7E-22	4.9E-01	*HHEX/IDE*	rs1111875	Same SNP
rs7903146	10	114,748,339	T	C	19,095	53,306	5.6E-92	1.39 (1.35-1.44)	13,154	58,623	4.0E-73	1.39 (1.34-1.44)	32,249	111,929	1.3E-161	8.7E-01	*TCF7L2*	rs7903146	Same SNP
rs2334499	11	1,653,425	T	C	19,095	53,306	8.5E-04	1.05 (1.02-1.08)	13,154	58,623	1.1E-01	1.03 (0.99-1.06)	32,249	111,929	1.1E-03	2.9E-01	*DUSP8*	rs2334499	Same SNP
rs163184	11	2,803,645	G	T	18,831	52,330	8.5E-15	1.12 (1.09-1.16)	13,043	57,977	7.8E-03	1.05 (1.01-1.08)	31,874	110,307	2.4E-15	1.3E-03	*KCNQ1*	rs163184	Same SNP
rs757110	11	17,375,053	C	A	19,095	53,306	2.5E-06	1.07 (1.04-1.11)	13,154	58,623	9.7E-06	1.08 (1.04-1.11)	32,249	111,929	8.6E-10	8.9E-01	*KCNJ11*	rs5215	0.87
rs1552224	11	72,110,746	A	C	19,095	53,306	8.7E-09	1.12 (1.08-1.16)	13,154	58,623	1.3E-04	1.09 (1.04-1.14)	32,249	111,929	4.4E-11	3.3E-01	*ARAP1 (CENTD2)*	rs1552224	Same SNP
rs10830963	11	92,348,358	G	C	19,955	53,628	2.7E-10	1.11 (1.07-1.14)	13,141	58,514	1.4E-05	1.08 (1.05-1.12)	33,096	112,142	1.8E-13	3.7E-01	*MTNR1B*	rs10830963	Same SNP
rs11063069	12	4,244,634	G	A	19,715	52,604	1.1E-09	1.12 (1.08-1.16)	14,185	58,168	3.6E-02	1.04 (1.00-1.09)	33,900	110,772	9.8E-10	1.3E-02	*CCND2*	rs11063069	Same SNP
rs10842994	12	27,856,417	C	T	20,219	54,604	3.2E-08	1.11 (1.07-1.15)	14,621	60,377	5.3E-04	1.07 (1.03-1.12)	34,840	114,981	5.6E-10	2.4E-01	*KLHDC5*	rs10842994	Same SNP
rs2261181	12	64,498,585	T	C	19,955	53,628	1.1E-07	1.14 (1.09-1.19)	14,510	59,731	1.3E-04	1.11 (1.05-1.17)	34,465	113,359	5.1E-10	4.7E-01	*HMGA2*	rs2261181	Same SNP
rs7138300	12	69,725,856	C	T	20,219	54,604	1.8E-06	1.07 (1.04-1.10)	14,621	60,377	1.0E-05	1.07 (1.04-1.11)	34,840	114,981	6.8E-10	9.7E-01	*TSPAN8/LGR5*	rs7955901	0.90
rs12427353	12	119,911,284	G	C	19,095	53,306	3.5E-05	1.08 (1.04-1.12)	13,154	58,623	2.5E-05	1.09 (1.05-1.14)	32,249	111,929	2.7E-08	7.6E-01	*HNF1A (TCF1)*	rs12427353	Same SNP
rs1359790	13	79,615,157	G	A	19,885	53,470	1.6E-05	1.07 (1.04-1.11)	14,448	58,958	6.7E-05	1.07 (1.04-1.11)	34,333	112,428	3.3E-08	9.6E-01	*SPRY2*	rs1359790	Same SNP
rs4502156	15	60,170,447	T	C	19,095	53,306	3.3E-05	1.06 (1.03-1.10)	13,154	58,623	3.7E-03	1.05 (1.02-1.08)	32,249	111,929	2.7E-06	5.4E-01	*C2CD4A*	rs4502156	Same SNP
rs7177055	15	75,619,817	A	G	20,219	54,604	1.8E-06	1.08 (1.05-1.11)	14,621	60,377	1.3E-05	1.08 (1.04-1.12)	34,840	114,981	8.1E-10	9.8E-01	*HMG20A*	rs7177055	Same SNP
rs1415571	15	77,606,926	G	T	19,095	53,306	8.4E-01	1.00 (0.97-1.03)	13,154	58,623	1.6E-05	1.08 (1.04-1.11)	32,249	111,929	8.9E-05	2.1E-03	*ZFAND6*	rs11634387	N/A
rs2007084	15	88,146,339	G	A	16,929	49,651	9.7E-01	1.00 (0.94-1.06)	11,566	55,205	1.1E-01	1.06 (0.99-1.13)	28,495	104,856	2.7E-01	2.2E-01	AP3S2	rs2007084	Same SNP
rs12899811	15	89,345,080	G	A	19,095	53,306	8.4E-08	1.09 (1.05-1.12)	13,154	58,623	1.5E-03	1.06 (1.02-1.09)	32,249	111,929	3.7E-09	2.3E-01	*PRC1*	rs12899811	Same SNP
rs9936385	16	52,376,670	C	T	19,095	53,306	3.2E-18	1.14 (1.11-1.17)	13,154	58,623	6.4E-11	1.12 (1.08-1.15)	32,249	111,929	1.9E-26	3.6E-01	*FTO*	rs9936385	Same SNP
rs7202877	16	73,804,746	T	G	19,095	53,306	7.0E-08	1.15 (1.09-1.20)	13,141	58,514	1.1E-02	1.07 (1.02-1.13)	32,236	111,820	1.9E-08	8.5E-02	*BCAR1*	rs7202877	Same SNP
rs7209945	17	2,421,679	A	G	20,219	54,604	2.7E-01	1.02 (0.99-1.05)	14,621	60,377	2.2E-03	1.05 (1.02-1.08)	34,840	114,981	5.0E-03	1.3E-01	*SRR*	rs2447090	0.06
rs11651052	17	33,176,494	A	G	13,842	32,361	6.6E-06	1.09 (1.05-1.12)	8,827	25,758	2.7E-09	1.13 (1.09-1.18)	22,669	58,119	8.2E-13	1.4E-01	*HNF1B (TCF2)*	rs11651052	Same SNP
rs8089364	18	56,009,809	C	T	19,095	53,306	6.0E-08	1.09 (1.06-1.13)	13,154	58,623	8.2E-04	1.06 (1.03-1.10)	32,249	111,929	1.6E-09	2.7E-01	*MC4R*	rs12970134	0.92
rs10401969	19	19,268,718	C	T	20,219	54,604	2.9E-07	1.15 (1.09-1.21)	14,621	60,377	1.4E-04	1.12 (1.06-1.19)	34,840	114,981	1.4E-09	5.7E-01	*CILP2*	rs10401969	Same SNP
rs552523	19	39,017,610	A	G	13,842	32,361	4.8E-01	1.02 (0.97-1.06)	8,827	25,758	8.7E-05	1.10 (1.05-1.15)	22,669	58,119	3.5E-04	1.3E-02	*PEPD*	rs8182584	0.09
rs8108269	19	50,850,353	G	T	20,219	54,604	3.7E-03	1.05 (1.02-1.08)	14,621	60,377	2.2E-07	1.10 (1.06-1.14)	34,840	114,981	2.1E-08	5.7E-02	*GIPR*	rs8108269	Same SNP
rs1800961	20	42,475,778	T	C	18,050	51,058	3.3E-02	1.09 (1.01-1.18)	13,033	56,933	1.5E-04	1.18 (1.08-1.29)	31,083	107,991	7.7E-05	1.8E-01	*HNF4A*	rs4812829	0.02

Chr: chromosome. OR: odds-ratio. CI: confidence interval.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele from sex-combined meta-analysis.

Supplementary Table 9. Meta-analysis summary statistics for loci demonstrating genome-wide significant evidence (p <5x10^{-8}) of association for both T2D and FG (or FG adjusted for BMI) in (i): the present study for T2D; and (ii) up to 133,010 non-diabetic individuals of European descent from the MAGIC Investigators for FG.

Locus	Lead SNP for FG	Chr	Position	Alleles[a]		Combined meta-analysis (T2D)					MAGIC meta-analysis (FG or FG adjusted for BMI)				
				Risk[b]	Other	Risk allele frequency	Cases	Controls	p -value	OR (95% CI)	Risk allele frequency	Sample size	p -value	Beta	SE
Previously reported loci for both T2D and FG															
MTNR1B	rs10830963	11	92,348,358	G	C	0.29	21,866	56,045	5.3E-13	1.10 (1.07-1.13)	0.29	124,513	1.1E-215	0.078	0.002
GCK	rs2908289	7	44,190,467	A	G	0.15	22,669	58,119	2.2E-05	1.07 (1.04-1.10)	0.16	128,047	3.3E-88	0.057	0.003
DGKB	rs2191349	7	15,030,834	T	G	0.52	22,669	58,119	3.0E-05	1.05 (1.03-1.08)	0.53	123,378	1.3E-42	0.029	0.002
GCKR	rs780094	2	27,594,741	C	T	0.62	22,669	58,119	5.4E-07	1.06 (1.04-1.09)	0.61	127,460	2.6E-37	0.027	0.002
SLC30A8	rs11558471	8	118,254,914	A	G	0.66	22,669	58,119	1.1E-20	1.13 (1.10-1.16)	0.68	127,858	7.8E-37	0.029	0.002
C2CD4A	rs4502156	15	60,170,447	T	C	0.53	22,669	58,119	2.3E-06	1.06 (1.03-1.08)	0.55	128,155	1.4E-25	0.022	0.002
TCF7L2	rs7903146	10	114,748,339	T	C	0.25	22,669	58,119	1.2E-139	1.39 (1.35-1.42)	0.28	127,477	2.7E-20	0.022	0.002
ADCY5	rs11708067	3	124,548,468	A	G	0.79	22,669	58,119	7.2E-14	1.11 (1.08-1.14)	0.79	128,599	1.3E-18	0.023	0.003
PROX1	rs340874	1	212,225,879	C	T	0.52	22,669	58,119	1.1E-07	1.07 (1.04-1.09)	0.52	127,021	4.1E-10	0.013	0.002
Novel loci for both T2D and FG															
CDKN2A/B	rs10811661	9	22,124,094	T	C	0.83	22,669	58,119	3.7E-27	1.18 (1.15-1.22)	0.82	128,488	5.7E-18	0.024	0.003
ARAP1 (CENTD2)	rs1783598	11	72,529,111	T	C	0.76	22,669	58,119	8.2E-08	1.08 (1.05-1.11)	0.79	127,480	1.2E-10	0.017	0.003
IGF2BP2	rs7651090	3	186,996,086	G	A	0.31	22,669	58,119	3.4E-23	1.13 (1.10-1.16)	0.31	128,548	1.8E-08	0.013	0.002
CDKAL1	rs2328548	6	20,824,937	A	G	0.18	22,669	58,119	1.9E-23	1.16 (1.13-1.20)	0.18	123,391	2.0E-08	0.015	0.003
Novel loci for both T2D and FG adjusted for BMI															
ZBED3	rs7708285	5	76,461,623	G	A	0.27	22,342	56,939	1.5E-10	1.10 (1.07-1.13)	0.27	117,931	1.2E-08	0.015	0.003

Chr: chromosome. OR: odds-ratio. CI: confidence interval. SE: standard error.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele for T2D from our combined meta-analysis.

Supplementary Table 10. Summary statistics for lead SNPs at novel and established T2D susceptibility loci in a meta-analysis of glycaemic traits in up to 133,010 non-diabetic individuals of European descent from the MAGIC Investigators.

			Alleles[a]			Fasting glucose				Fasting insulin				HOMA-IR				HOMA-B			
SNP	Chr	Position (Build 36 bp)	Risk[b]	Other	Locus	Beta	SE	p-value	Sample size	Beta	SE	p-value	Sample size	Beta	SE	p-value	Sample size	Beta	SE	p-value	Sample size
rs10923931	1	120,319,482	T	G	*NOTCH2*	0.0139	0.0053	8.7E-03	53,569	0.0018	0.0057	7.5E-01	42,854	0.0011	0.0064	8.7E-01	36,848	-0.0045	0.0052	3.8E-01	36,277
rs2075423	1	212,221,342	G	T	*PROX1*	0.0164	0.0036	7.1E-06	52,627	-0.0108	0.0039	5.8E-03	41,998	-0.0061	0.0044	1.6E-01	35,895	-0.0125	0.0035	3.9E-04	35,429
rs780094	2	27,594,741	C	T	*GCKR*	0.0274	0.0021	2.6E-37	127,460	0.0187	0.0025	7.1E-14	103,026	0.0201	0.0041	7.6E-07	35,899	0.0039	0.0034	2.5E-01	35,433
rs10203174	2	43,543,534	C	T	*THADA*	0.0160	0.0036	8.7E-06	128,571	-0.0109	0.0043	1.1E-02	104,031	-0.0125	0.0070	7.5E-02	37,020	-0.0262	0.0059	9.8E-06	36,449
rs243088	2	60,422,249	T	A	*BCL11A*	0.0096	0.0034	4.4E-03	53,312	0.0040	0.0036	2.6E-01	42,608	0.0026	0.0040	5.1E-01	36,602	0.0006	0.0033	8.6E-01	36,031
rs7569522	2	161,054,693	A	G	*RBMS1*	0.0063	0.0021	2.4E-03	132,848	0.0068	0.0024	4.7E-03	108,413	0.0068	0.0041	9.3E-02	36,933	0.0006	0.0034	8.6E-01	36,362
rs13389219	2	165,237,122	C	T	*GRB14*	0.0002	0.0034	9.4E-01	53,754	0.0133	0.0036	2.7E-04	43,028	0.0124	0.0041	2.2E-03	37,021	0.0073	0.0034	3.0E-02	36,451
rs2943640	2	226,801,829	C	A	*IRS1*	0.0031	0.0022	1.5E-01	128,565	0.0134	0.0025	1.4E-07	104,040	0.0086	0.0041	3.6E-02	37,022	0.0070	0.0034	3.7E-02	36,451
rs1801282	3	12,368,125	C	G	*PPARG*	0.0099	0.0049	4.2E-02	53,770	0.0185	0.0051	3.3E-04	43,043	0.0161	0.0058	5.6E-03	37,037	0.0062	0.0047	1.8E-01	36,466
rs1496653	3	23,429,794	A	G	*UBE2E2*	0.0050	0.0024	3.7E-02	131,768	-0.0120	0.0028	1.7E-05	103,956	-0.0135	0.0047	3.8E-03	35,839	-0.0088	0.0038	1.9E-02	35,373
rs12497268	3	64,065,403	G	C	*PSMD6*	0.0075	0.0027	4.9E-03	132,966	0.0032	0.0031	2.9E-01	108,517	0.0040	0.0052	4.5E-01	37,034	-0.0041	0.0042	3.3E-01	36,463
rs6795735	3	64,680,405	C	T	*ADAMTS9*	0.0040	0.0021	6.0E-02	127,473	0.0000	0.0025	1.0E+00	103,032	0.0069	0.0040	8.6E-02	35,910	0.0011	0.0033	7.5E-01	35,444
rs11717195	3	124,565,088	T	C	*ADCY5*	0.0221	0.0026	1.7E-17	125,481	-0.0129	0.0030	1.8E-05	102,796	-0.0001	0.0051	9.8E-01	35,808	-0.0181	0.0043	2.7E-05	35,238
rs4402960	3	186,994,381	T	G	*IGF2BP2*	0.0125	0.0023	4.4E-08	127,307	-0.0009	0.0026	7.4E-01	102,883	-0.0079	0.0043	6.9E-02	35,770	-0.0115	0.0036	1.2E-03	35,304
rs17301514	3	188,096,103	A	G	*ST64GAL1*	0.0035	0.0036	3.3E-01	118,929	-0.0055	0.0041	1.9E-01	98,708	-0.0027	0.0078	7.3E-01	32,209	-0.0095	0.0065	1.4E-01	32,937
rs6819243	4	1,283,245	T	C	*MAEA*	0.0159	0.0060	8.4E-03	118,285	-0.0055	0.0062	3.8E-01	97,518	-0.0092	0.0121	4.4E-01	30,623	-0.0249	0.0096	9.5E-03	30,068
rs4458523	4	6,340,887	G	T	*WFS1*	0.0165	0.0034	1.0E-06	53,717	0.0021	0.0036	5.7E-01	42,993	0.0083	0.0041	4.2E-02	36,987	-0.0035	0.0034	3.0E-01	36,416
rs459193	5	55,842,508	G	A	*ANKRD55*	0.0111	0.0023	1.6E-06	132,989	0.0144	0.0027	6.6E-08	108,537	0.0115	0.0045	1.1E-02	37,034	0.0046	0.0037	2.1E-01	36,463
rs6878122	5	76,463,067	G	A	*ZBED3*	0.0115	0.0025	3.3E-06	128,033	0.0021	0.0029	4.7E-01	103,526	0.0049	0.0048	3.0E-01	32,498	-0.0070	0.0040	7.6E-02	31,945
rs7756992	6	20,787,688	G	A	*CDKAL1*	0.0141	0.0023	1.8E-09	127,467	-0.0095	0.0027	5.1E-04	99,562	-0.0096	0.0044	2.9E-02	35,896	-0.0095	0.0036	7.5E-03	35,430
rs4299828	6	38,285,645	A	G	*ZFAND3*	-0.0028	0.0026	2.8E-01	131,875	-0.0020	0.0030	4.9E-01	107,522	-0.0095	0.0050	5.6E-02	35,912	-0.0054	0.0041	1.8E-01	35,446
rs3734621	6	39,412,189	C	A	*KCNK16*	0.0020	0.0062	7.5E-01	130,537	-0.0002	0.0071	9.7E-01	105,934	0.0044	0.0122	7.2E-01	35,966	0.0046	0.0100	6.5E-01	35,454
rs17168486	7	14,864,807	T	C	*DGKB*	0.0306	0.0028	3.2E-28	127,472	0.0016	0.0032	6.3E-01	103,034	0.0051	0.0053	3.4E-01	35,902	-0.0126	0.0043	3.0E-03	35,436
rs849135	7	28,162,938	G	A	*JAZF1*	0.0063	0.0021	2.6E-03	128,602	-0.0021	0.0025	3.9E-01	100,600	-0.0012	0.0040	7.7E-01	37,032	-0.0036	0.0033	2.7E-01	36,461
rs10278336	7	44,211,888	A	G	*GCK*	0.0371	0.0035	1.9E-26	53,080	0.0074	0.0037	4.8E-02	42,388	0.0092	0.0042	2.7E-02	36,382	-0.0128	0.0034	2.1E-04	35,811
rs17867832	7	126,784,073	T	G	*GCC1*	-0.0028	0.0044	5.3E-01	82,995	-0.0063	0.0050	2.0E-01	72,577	-0.0103	0.0069	1.4E-01	37,026	-0.0068	0.0057	2.3E-01	36,455
rs13233731	7	130,088,229	G	A	*KLF14*	0.0054	0.0022	1.2E-02	122,723	0.0049	0.0025	5.0E-02	98,823	0.0077	0.0040	5.1E-02	37,022	0.0031	0.0033	3.5E-01	36,451
rs516946	8	41,638,405	C	T	*ANK1*	0.0074	0.0024	1.7E-03	132,954	-0.0051	0.0028	6.3E-02	105,035	-0.0078	0.0045	8.6E-02	37,033	-0.0132	0.0038	5.3E-04	36,462
rs7845219	8	96,006,678	T	C	*TP53INP1*	0.0077	0.0020	1.8E-04	132,999	-0.0013	0.0024	6.0E-01	108,541	-0.0026	0.0040	5.2E-01	37,034	-0.0055	0.0033	9.4E-02	36,463
rs3802177	8	118,254,206	G	A	*SLC30A8*	0.0276	0.0023	1.8E-32	128,022	-0.0070	0.0027	1.1E-02	103,485	-0.0005	0.0047	9.2E-01	37,025	-0.0160	0.0038	2.0E-05	36,454
rs10758593	9	4,282,083	A	G	*GLIS3*	0.0157	0.0022	1.2E-12	119,145	-0.0110	0.0026	1.9E-05	94,789	-0.0060	0.0040	1.4E-01	35,908	-0.0145	0.0033	1.3E-05	35,442
rs16927668	9	8,359,533	T	C	*PTPRD*	0.0006	0.0025	8.1E-01	132,990	0.0009	0.0029	7.5E-01	108,536	0.0037	0.0048	4.4E-01	37,024	0.0013	0.0040	7.4E-01	36,453
rs10811661	9	22,124,094	T	C	*CDKN2A/B*	0.0238	0.0028	5.7E-18	128,488	-0.0044	0.0032	1.8E-01	103,955	0.0054	0.0052	3.0E-01	36,988	-0.0085	0.0043	5.1E-02	36,417
rs17791513	9	81,095,410	A	G	*TLE4*	-0.0008	0.0038	8.4E-01	132,888	-0.0045	0.0043	3.0E-01	108,553	0.0026	0.0075	7.3E-01	33,028	0.0013	0.0059	8.3E-01	32,473
rs2796441	9	83,498,768	G	A	*TLE1*	-0.0002	0.0022	9.3E-01	132,285	0.0030	0.0025	2.3E-01	107,832	0.0076	0.0045	9.4E-02	36,328	0.0034	0.0037	3.5E-01	35,757
rs11257655	10	12,347,900	T	C	*CDC123/CAMK1D*	0.0132	0.0026	4.4E-07	127,025	0.0004	0.0030	8.9E-01	102,606	-0.0001	0.0050	9.9E-01	35,479	-0.0091	0.0041	2.5E-02	35,013
rs12242953	10	70,535,348	G	A	*VPS26A*	-0.0009	0.0043	8.4E-01	131,865	0.0016	0.0050	7.5E-01	107,335	-0.0026	0.0084	7.6E-01	35,914	-0.0078	0.0070	2.6E-01	35,448
rs12571751	10	80,612,637	A	G	*ZMIZ1*	0.0003	0.0021	8.9E-01	129,435	-0.0024	0.0024	3.1E-01	105,043	0.0011	0.0040	7.9E-01	37,035	0.0012	0.0033	7.2E-01	36,464
rs1111875	10	94,452,862	C	T	*HHEX/IDE*	0.0040	0.0021	6.2E-02	127,461	-0.0037	0.0025	1.4E-01	99,561	0.0028	0.0040	4.9E-01	35,912	-0.0042	0.0033	2.0E-01	35,446
rs7903146	10	114,748,339	T	C	*TCF7L2*	0.0220	0.0024	2.7E-20	127,477	-0.0181	0.0028	6.1E-11	103,037	-0.0096	0.0045	3.4E-02	35,903	-0.0200	0.0038	1.4E-07	35,437
rs2334499	11	1,653,425	T	C	*DUSP8*	0.0000	0.0021	9.9E-01	131,414	-0.0007	0.0025	7.7E-01	103,619	-0.0002	0.0042	9.7E-01	35,478	0.0000	0.0034	9.9E-01	35,012
rs163184	11	2,803,645	G	T	*KCNQ1*	0.0079	0.0022	3.5E-04	125,677	-0.0017	0.0026	5.2E-01	101,869	0.0007	0.0044	8.7E-01	35,476	-0.0086	0.0035	1.6E-02	35,010
rs5215	11	17,365,206	C	T	*KCNJ11*	-0.0025	0.0022	2.6E-01	121,160	-0.0056	0.0026	3.0E-02	97,873	-0.0018	0.0041	6.6E-01	35,882	0.0009	0.0033	7.8E-01	35,416
rs1552224	11	72,110,746	A	C	*ARAP1 (CENTD2)*	0.0191	0.0028	1.5E-11	127,016	-0.0123	0.0033	1.7E-04	102,607	-0.0092	0.0054	8.5E-02	35,479	-0.0166	0.0043	9.4E-05	35,013
rs10830963	11	92,348,358	G	C	*MTNR1B*	0.0779	0.0025	1.1E-215	124,513	-0.0013	0.0029	6.6E-01	100,402	0.0083	0.0049	9.1E-02	37,031	-0.0394	0.0040	8.6E-23	36,460
rs11063069	12	4,244,634	G	A	*CCND2*	0.0082	0.0027	2.7E-03	127,579	-0.0006	0.0031	8.4E-01	103,443	0.0039	0.0054	4.7E-01	37,031	-0.0077	0.0045	8.3E-02	36,460
rs10842994	12	27,856,417	C	T	*KLHDC5*	0.0086	0.0026	9.0E-04	132,994	0.0006	0.0030	8.4E-01	108,538	-0.0009	0.0052	8.6E-01	37,036	-0.0016	0.0044	7.2E-01	36,465
rs2261181	12	64,498,585	T	C	*HMGA2*	0.0072	0.0036	5.0E-02	126,156	0.0120	0.0043	5.4E-03	98,858	0.0135	0.0068	4.9E-02	35,903	0.0029	0.0058	6.1E-01	35,437
rs7955901	12	69,719,560	C	T	*TSPAN8/LGR5*	0.0043	0.0021	3.9E-02	131,877	-0.0036	0.0024	1.3E-01	107,523	-0.0055	0.0041	1.8E-01	35,912	-0.0048	0.0034	1.5E-01	35,446
rs12427353	12	119,911,284	G	C	*HNF1A (TCF1)*	-0.0057	0.0042	1.8E-01	53,751	-0.0084	0.0045	6.5E-02	43,024	-0.0058	0.0050	2.4E-01	37,018	-0.0035	0.0041	3.9E-01	36,447
rs1359790	13	79,615,157	G	A	*SPRY2*	0.0026	0.0023	2.6E-01	132,841	-0.0091	0.0026	4.7E-04	108,395	-0.0114	0.0044	9.7E-03	36,934	-0.0088	0.0036	1.6E-02	36,363
rs4502156	15	60,170,447	T	C	*C2CD4A*	0.0224	0.0021	1.4E-25	128,155	0.0019	0.0025	4.6E-01	103,638	0.0019	0.0041	6.5E-01	36,601	-0.0099	0.0034	3.6E-03	36,030
rs7177055	15	75,619,817	A	G	*HMG20A*	0.0104	0.0023	3.8E-06	131,868	0.0015	0.0026	5.7E-01	107,513	-0.0007	0.0044	8.7E-01	35,912	-0.0030	0.0036	4.0E-01	35,446
rs11634397	15	78,219,277	G	A	*ZFAND6*	0.0004	0.0022	8.7E-01	132,995	-0.0047	0.0025	6.7E-02	108,547	-0.0038	0.0043	3.8E-01	37,034	-0.0034	0.0035	3.3E-01	36,464
rs2007084	15	88,146,339	G	A	AP3S2	-0.0001	0.0042	9.8E-01	121,187	-0.0017	0.0049	7.3E-01	100,603	0.0142	0.0090	1.1E-01	30,461	0.0103	0.0071	1.5E-01	30,004
rs12899811	15	89,345,080	G	A	*PRC1*	0.0030	0.0023	1.9E-01	127,476	0.0001	0.0026	9.7E-01	103,040	0.0031	0.0044	4.8E-01	35,911	0.0011	0.0036	7.6E-01	35,446
rs9936385	16	52,376,670	C	T	*FTO*	0.0099	0.0035	5.1E-03	50,211	0.0150	0.0038	8.1E-05	39,557	0.0148	0.0041	3.3E-04	37,016	0.0076	0.0034	2.6E-02	36,445
rs7202877	16	73,804,746	T	G	*BCAR1*	0.0062	0.0033	6.2E-02	131,414	-0.0010	0.0039	8.0E-01	103,615	-0.0059	0.0065	3.7E-01	35,479	-0.0034	0.0053	5.2E-01	35,013
rs2447090	17	2,245,724	A	G	*SRR*	-0.0019	0.0022	3.9E-01	132,273	-0.0029	0.0025	2.4E-01	107,916	-0.0003	0.0044	9.5E-01	32,592	0.0006	0.0035	8.6E-01	32,037
rs4430796	17	33,176,494	A	G	*HNF1B (TCF2)*	0.0004	0.0044	9.2E-01	38,424	0.0079	0.0048	9.7E-02	28,921	0.0110	0.0057	5.5E-02	18,780	0.0089	0.0043	4.0E-02	18,662
rs12970134	18	56,035,730	A	G	*MC4R*	-0.0010	0.0038	8.0E-01	52,623	0.0106	0.0043	1.3E-02	38,530	0.0084	0.0047	7.6E-02	35,894	0.0073	0.0039	6.3E-02	35,428
rs10401969	19	19,268,718	C	T	*CILP2*	0.0113	0.0044	9.8E-03	128,495	0.0040	0.0052	4.3E-01	104,070	0.0085	0.0091	3.5E-01	37,037	0.0078	0.0076	3.1E-01	36,466
rs8182584	19	38,601,550	T	G	*PEPD*	0.0036	0.0022	1.0E-01	125,401	0.0125	0.0025	7.2E-07	101,687	0.0122	0.0042	3.9E-03	35,478	0.0071	0.0035	4.1E-02	35,012
rs8108269	19	50,850,353	G	T	*GIPR*	0.0008	0.0024	7.6E-01	127,565	-0.0016	0.0029	5.7E-01	99,539	-0.0024	0.0050	6.4E-01	37,027	-0.0026	0.0041	5.3E-01	36,457
rs4812829	20	42,422,681	A	G	*HNF4A*	0.0045	0.0027	9.5E-02	131,832	-0.0036	0.0032	2.5E-01	104,010	-0.0061	0.0053	2.5E-01	35,873	-0.0055	0.0043	2.0E-01	35,408

Chr: chromosome. SE: standard error.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele for T2D from our combined meta-analysis.

Supplementary Table 11. Summary statistics for lead SNPs at novel loci in a meta-analysis of BMI in up to 249,796 individuals of European descent, excluding T2D cohorts, from the GIANT Consortium.

SNP	Chr	Position (Build 36 bp)	Alleles[a]		Locus	Beta	SE	*p* -value	Sample size
			Risk[b]	Other					
rs13389219	2	165,237,122	C	T	*GRB14*	-0.0116	0.0049	1.8E-02	119,537
rs459193	5	55,842,508	G	A	*ANKRD55*	-0.0051	0.0055	3.5E-01	119,547
rs516946	8	41,638,405	C	T	*ANK1*	-0.0035	0.0056	5.3E-01	119,130
rs2796441	9	83,498,768	G	A	*TLE1*	-0.0005	0.0053	9.2E-01	119,538
rs12571751	10	80,612,637	A	G	*ZMIZ1*	0.0062	0.0048	2.0E-01	119,516
rs11063069	12	4,244,634	G	A	*CCND2*	-0.0090	0.0066	1.7E-01	119,532
rs10842994	12	27,856,417	C	T	*KLHDC5*	-0.0044	0.0061	4.7E-01	119,398
rs7177055	15	75,619,817	A	G	*HMG20A*	0.0102	0.0053	5.2E-02	119,548
rs7202877	16	73,804,746	T	G	*BCAR1*	-0.0102	0.0081	2.1E-01	119,554
rs12970134	18	56,035,730	A	G	*MC4R*	0.0483	0.0054	2.3E-19	119,529
rs10401969	19	19,268,718	C	T	*CILP2*	-0.0074	0.0101	4.6E-01	119,303
rs8108269	19	50,850,353	G	T	*GIPR*	0.0001	0.0057	9.9E-01	118,633

Chr: chromosome. SE: standard error.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele for T2D from our combined meta-analysis.

Supplementary Table 12. Summary statistics for lead SNPs at novel loci in a meta-analysis of lipid traits in up to 100,184 individuals of European descent from the Global Lipids Genetics Consortium.

			Alleles[a]			High-density lipoprotein cholesterol			Low-density lipoprotein cholesterol			Total cholesterol			Triglycerides		
SNP	Chr	Position (Build 36 bp)	Risk[b]	Other	Locus	Z-score	Sample size	*p* -value	Z-score	Sample size	*p* -value	Z-score	Sample size	*p* -value	Z-score	Sample size	*p* -value
rs13389219	2	165,237,122	C	T	*GRB14*	-5.20	99,892	2.0E-07	4.57	95,446	5.0E-06	4.14	100,176	3.4E-05	6.30	96,590	3.1E-10
rs459193	5	55,842,508	G	A	*ANKRD55*	-3.56	99,900	3.8E-04	-1.24	95,454	2.2E-01	-1.35	100,184	1.8E-01	4.07	96,598	4.7E-05
rs516946	8	41,638,405	C	T	*ANK1*	0.98	96,841	3.3E-01	0.11	92,441	9.1E-01	-0.07	97,081	9.4E-01	-0.55	93,495	5.8E-01
rs2796441	9	83,498,768	G	A	*TLE1*	0.18	99,897	8.6E-01	1.95	95,451	5.1E-02	1.27	100,181	2.0E-01	-1.72	96,595	8.5E-02
rs12571751	10	80,612,637	A	G	*ZMIZ1*	-2.18	96,900	2.9E-02	0.31	92,495	7.6E-01	0.60	97,140	5.5E-01	2.73	93,554	6.4E-03
rs11063069	12	4,244,634	G	A	*CCND2*	-0.36	99,890	7.2E-01	2.25	95,444	2.4E-02	2.71	100,174	6.6E-03	2.61	96,588	9.0E-03
rs10842994	12	27,856,417	C	T	*KLHDC5*	-0.99	99,872	3.2E-01	1.57	95,427	1.2E-01	0.90	100,154	3.7E-01	-1.03	96,568	3.0E-01
rs7177055	15	75,619,817	A	G	*HMG20A*	-1.21	98,370	2.3E-01	0.32	93,962	7.5E-01	-0.24	98,617	8.1E-01	0.45	95,031	6.6E-01
rs7202877	16	73,804,746	T	G	*BCAR1*	-2.13	98,409	3.3E-02	-0.27	93,999	7.9E-01	-0.82	98,656	4.2E-01	0.48	95,070	6.3E-01
rs12970134	18	56,035,730	A	G	*MC4R*	-4.42	98,409	9.7E-06	-0.63	93,999	5.3E-01	-0.75	98,656	4.5E-01	4.51	95,070	6.4E-06
rs10401969	19	19,268,718	C	T	*CILP2*	0.56	98,393	5.8E-01	-9.62	93,983	6.7E-22	-12.93	98,640	2.9E-38	-11.28	95,054	1.6E-29
rs8108269	19	50,850,353	G	T	*GIPR*	-3.41	98,337	6.6E-04	-1.63	93,933	1.0E-01	-2.54	98,583	1.1E-02	-9.64	84,180	5.4E-22

Chr: chromosome.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele for T2D from our combined meta-analysis.

Supplementary Table 13. Evidence for *cis* -eQTL expression with lead T2D SNPs (and proxies) at novel T2D susceptibility loci in multiple tissues from public databases and unpublished resources.

Locus	SNP ID	Lead T2D SNP or proxy?	CEU r2 with lead SNP	Transcript	Tissue	*p* -value	Strongest association with expression		
							cis -eQTL SNP	CEU r2	*p* -value
GRB14	rs13389219	Lead	Same SNP	*GRB14*	Adipose	1.1E-10	rs10195252	0.93	6.8E-11
	rs10195252	Proxy	0.93	*GRB14*	Omental fat	4.2E-13	rs10195252	Same SNP	4.2E-13
ANK1	rs516946	Lead	Same SNP	*ANK1*	Subcutaneous fat	1.5E-21	rs516946	Same SNP	1.5E-21
	rs516946	Lead	Same SNP	*ANK1*	Omental fat	3.8E-09	rs6989203	1.00	1.9E-20
	rs516946	Lead	Same SNP	*ANK1*	Adipose	5.2E-34	rs6989203	1.00	1.9E-34
	rs515071	Proxy	1.00	*ANK1*	Liver	2.2E-02	rs515071	Same SNP	2.2E-02
	rs13266210	Proxy	0.80	*ANK1*	Prefrontal cortex	2.4E-06	rs13266210	Same SNP	2.4E-06
KLHDC5	rs3751235	Proxy	0.94	*KLHDC5*	Blood	3.2E-05	rs3751235	Same SNP	3.2E-05
	rs3751235	Proxy	0.94	*KLHDC5*	CD4+ lymphocytes	2.8E-05	rs3751235	Same SNP	2.8E-05
	rs12578595	Proxy	1.00	*KLHDC5*	T cells	4.0E-06	rs12578595	Same SNP	4.0E-06
HMG20A	rs7177055	Lead	Same SNP	*LINGO1*	Adipose	9.1E-06	rs907372	0.73	7.3E-09
	rs7178572	Proxy	0.89	*AL355738*	Liver	4.5E-05	rs7178572	Same SNP	4.5E-05
	rs7178572	Proxy	0.89	*HMG20A*	Liver	7.5E-05	rs7178572	Same SNP	7.5E-05
CILP2	rs16996185	Proxy	0.91	*ATP13A1*	Monocytes	2.9E-141	rs16996185	Same SNP	2.9E-141
	rs12610185	Proxy	0.91	*ATP13A1*	Blood	3.0E-05	rs2304130	0.55	1.1E-97
BCAR1	rs7202877	Lead	Same SNP	*BCAR1*	Blood	2.0E-70	rs13331385	1.00	6.1E-74

Supplementary Table 14. Evidence for *cis* -eQTL expression with lead T2D SNPs at novel T2D susceptibility loci in adipose tissue and blood in individuals from the Icelandic population.

T2D Lead SNP	Chr	Position (Build 36 bp)	Alleles[a]		Locus	Gene (transcript)	Tissue	Beta	SE	*p* -value	Adjusted *p* -value	Strongest association with expression			
			Risk[b]	Other								*cis* -eQTL SNP	CEU r^2	*p* -value	Conditional *p* -value
rs13389219	2	165,237,122	C	T	*GRB14*	*GRB14* (NM_004490)	Adipose	0.367	0.055	1.1E-10	8.6E-01	rs10195252	1.00	6.8E-11	3.5E-01
						SLC38A11 (NM_173512)	Adipose	-0.341	0.055	2.2E-09	3.7E-01	rs10184126	0.18	1.6E-92	1.2E-79
rs516946	8	41,638,405	C	T	*ANK1*	*ANK1* (NM_020475)	Adipose	0.491	0.075	3.1E-10	5.3E-01	rs6989203	1.00	2.6E-10	4.0E-01
						ANK1 (NM_020477)	Adipose	0.517	0.075	2.8E-11	9.8E-02	rs6989203	1.00	1.8E-11	5.8E-02
						ANK1 (NM_020481)	Adipose	0.850	0.068	5.2E-34	1.1E-01	rs6989203	1.00	1.9E-34	4.4E-02
						N/A (NM_152568)	Blood	0.327	0.070	6.2E-06	8.1E-03	rs10110166	0.00	1.6E-51	1.2E-47
rs7177055	15	75,619,817	A	G	*HMG20A*	*LINGO1* (NM_032808)	Adipose	0.311	0.068	9.1E-06	4.7E-01	rs907372	0.73	7.3E-09	2.0E-04
rs7202877	16	73,804,746	T	G	*BCAR1*	*CFDP1* (NM_006324)	Adipose	-0.470	0.098	3.4E-06	7.0E-03	rs4243111	0.18	4.6E-18	1.4E-14
						CFDP1 (NM_006324)	Blood	-0.408	0.093	2.2E-05	9.2E-01	rs4888396	0.42	1.9E-14	3.3E-10
						BCAR1 (NM_014567)	Blood	-1.390	0.076	2.0E-70	1.1E-03	rs13331385	1.00	6.1E-74	2.9E-06
						TMEM170A (NM_145254)	Adipose	-0.439	0.099	1.8E-05	1.7E-01	rs766522	0.43	1.3E-07	9.2E-04

Chr: chromosome. SE: standard error.

[a]Alleles are aligned to the forward strand of NCBI Build 36.

[b]Risk allele for T2D from our combined meta-analysis.

Supplementary Table 15. Primary and secondary lists of genes implicated in monogenic forms of T2D, and established and "probable" disease susceptibility loci, as used in pathway and protein-protein interaction analyses.

Category	(Nearest) Gene	Lead T2D SNP		
		SNP	Chr	Position (Build 36 bp)
Primary list				
Established locus	*NOTCH2*	rs10923931	1	120,319,482
Monogenic gene	*LMNA*			
Established locus	*PROX1*	rs2075423	1	212,221,342
Monogenic gene	*KLF11*			
Established locus	*GCKR*	rs780094	2	27,594,741
Established locus	*THADA*	rs10203174	2	43,543,534
Established locus	*BCL11A*	rs243088	2	60,422,249
Monogenic gene	*EIF2AK3*			
Established locus	*RBMS1*	rs7569522	2	161,054,693
Novel locus	*GRB14*	rs13389219	2	165,237,122
Monogenic gene	*NEUROD1*			
Established locus	*IRS1*	rs2943640	2	226,801,829
Monogenic gene and established locus	*PPARG*	rs1801282	3	12,368,125
Established locus	*UBE2E2*	rs1496653	3	23,429,794
Established locus	*ADAMTS9*	rs6795735	3	64,680,405
Established locus	*ADCY5*	rs11717195	3	124,565,088
Established locus	*IGF2BP2*	rs4402960	3	186,994,381
Monogenic gene and established locus	*WFS1*	rs4458523	4	6,340,887
Monogenic gene	*CISD2*			
Strongly associated locus	*TMEM154*	rs6813195	4	153,739,925
Novel locus	*ANKRD55*	rs459193	5	55,842,508
Established locus	*ZBED3*	rs6878122	5	76,463,067
Strongly associated locus	*SSR1*	rs9505118	6	7,235,436
Established locus	*CDKAL1*	rs7756992	6	20,787,688
Strongly associated locus	*POU5F1*	rs3130501	6	31,244,432
Monogenic gene	*PLAGL1*			
Monogenic gene	*HYMAI*			
Established locus	*DGKB*	rs17168486	7	14,864,807
Established locus	*JAZF1*	rs849135	7	28,162,938
Monogenic gene and established locus	*GCK*	rs10278336	7	44,211,888
Established locus	*KLF14*	rs13233731	7	130,088,229
Novel locus	*ANK1*	rs516946	8	41,638,405
Established locus	*TP53INP1*	rs7845219	8	96,006,678
Established locus	*SLC30A8*	rs3802177	8	118,254,206
Strongly associated locus	*GLIS3*	rs10758593	9	4,282,083
Established locus	*CDKN2B*	rs10811661	9	22,124,094
Established locus	*TLE4*	rs17791513	9	81,095,410
Novel locus	*TLE1*	rs2796441	9	83,498,768
Monogenic gene	*CEL*			
Monogenic gene	*AGPAT2*			
Established locus	*CDC123*	rs11257655	10	12,347,900
Monogenic gene	*PTF1A*			
Novel locus	*ZMIZ1*	rs12571751	10	80,612,637
Established locus	*HHEX*	rs1111875	10	94,452,862
Established locus	*TCF7L2*	rs7903146	10	114,748,339
Strongly associated locus	*PLEKHA1*	rs2421016	10	124,157,502
Established locus	*MOB2*	rs2334499	11	1,653,425

Monogenic gene	*INS*			
Established locus	*KCNQ1*	rs163184	11	2,803,645
Monogenic gene and established locus	*KCNJ11*	rs5215	11	17,365,206
Monogenic gene	*ABCC8*			
Monogenic gene	*BSCL2*			
Established locus	*ARAP1*	rs1552224	11	72,110,746
Established locus	*MTNR1B*	rs10830963	11	92,348,358
Strongly associated locus	*ETS1*	rs7931302	11	127,741,268
Novel locus	*CCND2*	rs11063069	12	4,244,634
Novel locus	*KLHDC5*	rs10842994	12	27,856,417
Established locus	*HMGA2*	rs2261181	12	64,498,585
Established locus	*TSPAN8*	rs7955901	12	69,719,560
Monogenic gene and established locus	*HNF1A*	rs12427353	12	119,911,284
Monogenic gene	*PDX1*			
Established locus	*SPRY2*	rs1359790	13	79,615,157
Established locus	*C2CD4A*	rs4502156	15	60,170,447
Novel locus	*HMG20A*	rs7177055	15	75,619,817
Established locus	*ZFAND6*	rs11634397	15	78,219,277
Established locus	*VPS33B*	rs12899811	15	89,345,080
Established locus	*FTO*	rs9936385	16	52,376,670
Novel locus	*CTRB1*	rs7202877	16	73,804,746
Monogenic gene and established locus	*HNF1B*	rs4430796	17	33,176,494
Novel locus	*MC4R*	rs12970134	18	56,035,730
Monogenic gene	*LMNB2*			
Monogenic gene	*INSR*			
Novel locus	*SUGP1*	rs10401969	19	19,268,718
Monogenic gene	*AKT2*			
Novel locus	*GIPR*	rs8108269	19	50,850,353
Monogenic gene	*HNF4A*			
Established locus	*DUSP9*			

Secondary list

Associated locus	*KLHL21*	rs1556036	1	6,574,315
Associated locus	*MACF1*	rs636083	1	39,594,268
Associated locus	*FAF1*	rs17106184	1	50,682,573
Associated locus	*LEPR*	rs11208660	1	65,756,214
Associated locus	*LRRC52*	rs169557	1	163,793,417
Associated locus	*LYPLAL1*	rs765751	1	217,735,849
Associated locus	*ABCB10*	rs927204	1	227,747,629
Associated locus	*BCL2L11*	rs11123406	2	111,667,012
Associated locus	*INHBB*	rs12617659	2	121,026,229
Associated locus	*TANC1*	rs17206971	2	159,636,566
Associated locus	*SLC38A11*	rs1869543	2	165,512,906
Associated locus	*PARD3B*	rs9288354	2	205,086,815
Associated locus	*ERBB4*	rs16825005	2	212,012,810
Associated locus	*EPHA4*	rs616355	2	221,481,792
Associated locus	*MINA*	rs17302349	3	99,117,155
Associated locus	*MECOM*	rs7635320	3	170,447,312
Associated locus	*LPP*	rs6808574	3	189,223,217
Associated locus	*FAM13A*	rs13147493	4	89,961,202
Associated locus	*UNC5C*	rs2241743	4	96,310,547
Associated locus	*NHEDC2*	rs7674212	4	104,208,348
Associated locus	*NDST3*	rs2389527	4	119,241,747
Associated locus	*TMEM155*	rs2706785	4	122,879,700
Associated locus	*PDGFC*	rs1464454	4	157,836,217
Associated locus	*ACSL1*	rs1996546	4	185,951,283

Associated locus	*ARL15*	rs702634	5	53,307,177
Associated locus	*MAP3K1*	rs3843467	5	55,892,132
Associated locus	*PDE4D*	rs986067	5	58,424,152
Associated locus	*MCC*	rs367943	5	112,837,627
Associated locus	*DTWD2*	rs6896169	5	118,041,959
Associated locus	*PHF15*	rs329122	5	133,892,498
Associated locus	*PHACTR1*	rs9349459	6	13,219,227
Associated locus	*MYLIP*	rs4716034	6	16,151,564
Associated locus	*C6orf204*	rs12199837	6	119,037,337
Associated locus	*CENPW*	rs4897182	6	126,797,335
Associated locus	*L3MBTL3*	rs6569648	6	130,390,812
Associated locus	*SNX13*	rs17138444	7	17,926,686
Associated locus	*POU6F2*	rs7779853	7	39,024,266
Associated locus	*OGDH*	rs6961567	7	44,692,594
Associated locus	*FAM185A*	rs10228495	7	102,227,420
Associated locus	*BRAF*	rs9648716	7	140,258,632
Associated locus	*PINX1*	rs6601534	8	10,729,403
Associated locus	*PURG*	rs2543622	8	30,983,146
Associated locus	*IL7*	rs2010128	8	79,922,054
Associated locus	*MYC*	rs1561927	8	129,637,260
Associated locus	*ZNF34*	rs2294120	8	145,974,371
Associated locus	*ELAVL2*	rs2150461	9	23,306,365
Associated locus	*PTPDC1*	rs10114341	9	95,959,003
Associated locus	*DNLZ*	rs10870149	9	138,374,718
Associated locus	*RPS24*	rs10824617	10	79,900,233
Associated locus	*APIP*	rs1326941	11	34,873,286
Associated locus	*MAP3K11*	rs11227234	11	65,121,747
Associated locus	*CACNA1C*	rs7306916	12	2,471,624
Associated locus	*CPNE8*	rs11170498	12	37,725,840
Associated locus	*SLC38A4*	rs17684703	12	45,510,592
Associated locus	*ANO4*	rs4764773	12	99,858,781
Associated locus	*SBNO1*	rs6488868	12	122,365,927
Associated locus	*ZNF664*	rs825461	12	123,127,756
Associated locus	*RNF6*	rs10507349	13	25,679,528
Associated locus	*OLFM4*	rs2039632	13	53,825,274
Associated locus	*DLL4*	rs4923889	15	39,022,224
Associated locus	*C16orf68*	rs8052543	16	8,405,759
Associated locus	*GRIN2A*	rs11645816	16	9,679,607
Associated locus	*IRX3*	rs9928968	16	53,010,700
Associated locus	*IRX6*	rs16954899	16	53,958,597
Associated locus	*RPL13*	rs12709089	16	88,157,812
Associated locus	*ZZEF1*	rs8068804	17	3,932,613
Associated locus	*RAI1*	rs1006656	17	17,623,209
Associated locus	*CBX1*	rs2240122	17	43,507,558
Associated locus	*GATA6*	rs2046058	18	17,891,792
Associated locus	*CCBE1*	rs17781351	18	55,583,528
Associated locus	*ZNF536*	rs7253628	19	35,739,109
Associated locus	*EIF2S2*	rs6059662	20	32,139,388
Associated locus	*PROCR*	rs6087685	20	33,241,273
Associated locus	*ZHX3*	rs17265513	20	39,266,042
Associated locus	*R3HDML*	rs4812829	20	42,422,681
Associated locus	*URB1*	rs11702306	21	32,687,431
Associated locus	*ASCC2*	rs5997539	22	28,567,706

Chr: chromosome.

Supplementary Table 16. Biological processes with most significant enrichment from modified two-step gene set enrichment analysis.

Resource	Biological process	Number of genes	MAGENTA applied to Stage 1 meta-analysis		Modified GSEA of primary T2D susceptibility loci using Stage 2 meta-analysis[a]		Modified GSEA of primary and secondary T2D susceptibility loci using Stage 2 meta-anlysis[a]		Genes
			Enrichment *p* -value	FDR	Nearest gene	LD region	Nearest gene	LD region	
KEGG	Adipocytokine signalling pathway	67	6.2E-05	1.6E-03	1.4E-02	6.0E-02	7.0E-04	1.6E-04	*LEPR* , *RELA* , *RXRG* , *ACSL1* , *IRS1* , *NFKB1* , *CAMKK1* , *AKT2*
KEGG, REACTOME, BioCarta	Cell cycle regulation	40	1.1E-02	4.5E-02	4.0E-03	7.0E-04	5.0E-02	7.0E-04	*CDKN2B* , *CCND2* , *CDKN1C* , *CDKN2C* , *CCNA2* , *CCNE2*
Gene ontology	G1 phase of mitotic cell cycle	10	2.0E-04	1.0E-04	1.0E+00	3.0E-03	6.0E-02	3.0E-03	*MAP3K11* , *CDC123* , *CDKN1C*
REACTOME	G1 phase	16	4.4E-02	1.0E-01	1.0E+00	1.1E-02	1.0E+00	4.0E-02	*CCND2* , *E2F3*
KEGG	PPAR signalling pathway	69	4.2E-02	1.7E-01	1.0E+00	1.0E+00	3.0E-02	3.4E-01	*RXRG* , *PPARG* , *ACSL1*
MitoCarta	Oxidative phosphorylation	106	3.6E-02	1.6E-01	-	3.5E-01	-	1.0E-01	*ATPAF2* , *NDUFA13* , *UQCR10* , *NDUFS5* , *C8orf38* , *NDUFB2*
KEGG	Biosynthesis of unsaturated fatty acids	22	3.0E-03	1.4E-02	-	-	-	-	
Gene ontology	Negative regulation of inflammatory response	22	4.4E-03	1.9E-02	-	-	-	-	
Gene ontology	Positive regulation of inflammatory response	20	1.2E-02	3.5E-02	-	-	-	-	

[a]Bonferroni corrected cutoff for modified GSEA of Stage 2 meta-analysis: $p < 0.0014$.
"-" indicates that there was no transcript in the gene-set.