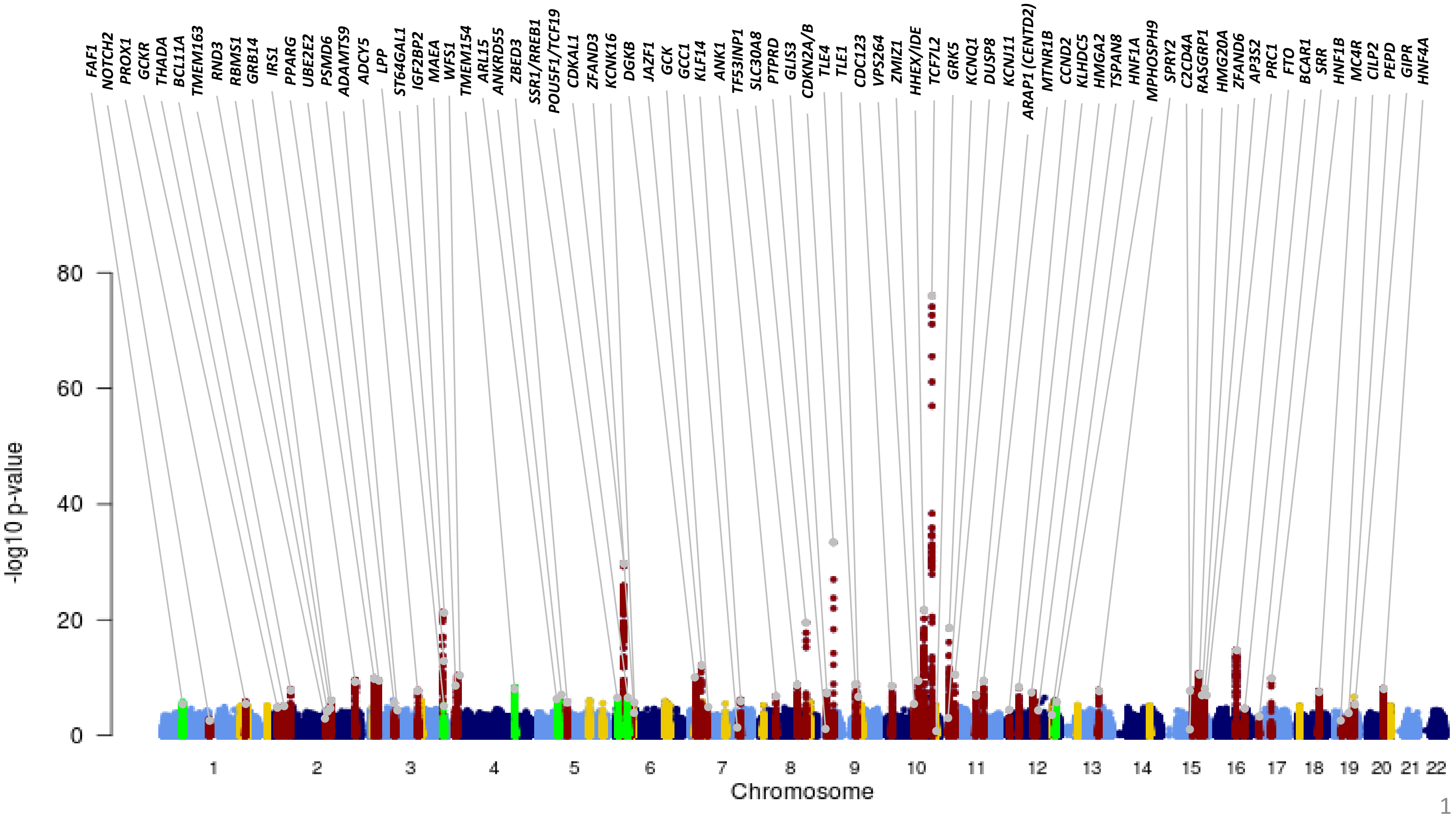
Genome-wide trans-ethnic meta-analysis reveals novel insights into the genetic architecture of type 2 diabetes susceptibility

DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) Consortium, Asian Genetic Epidemiology Network Type 2 Diabetes (AGEN-T2D) Consortium, South Asian Type 2 Diabetes (SAT2D) Consortium, Mexican American Type 2 Diabetes (MAT2D) Consortium and Type 2 Diabetes Genetic Exploration by Next-generation sequencing in multi-Ethnic Samples (T2D-GENES) Consortium

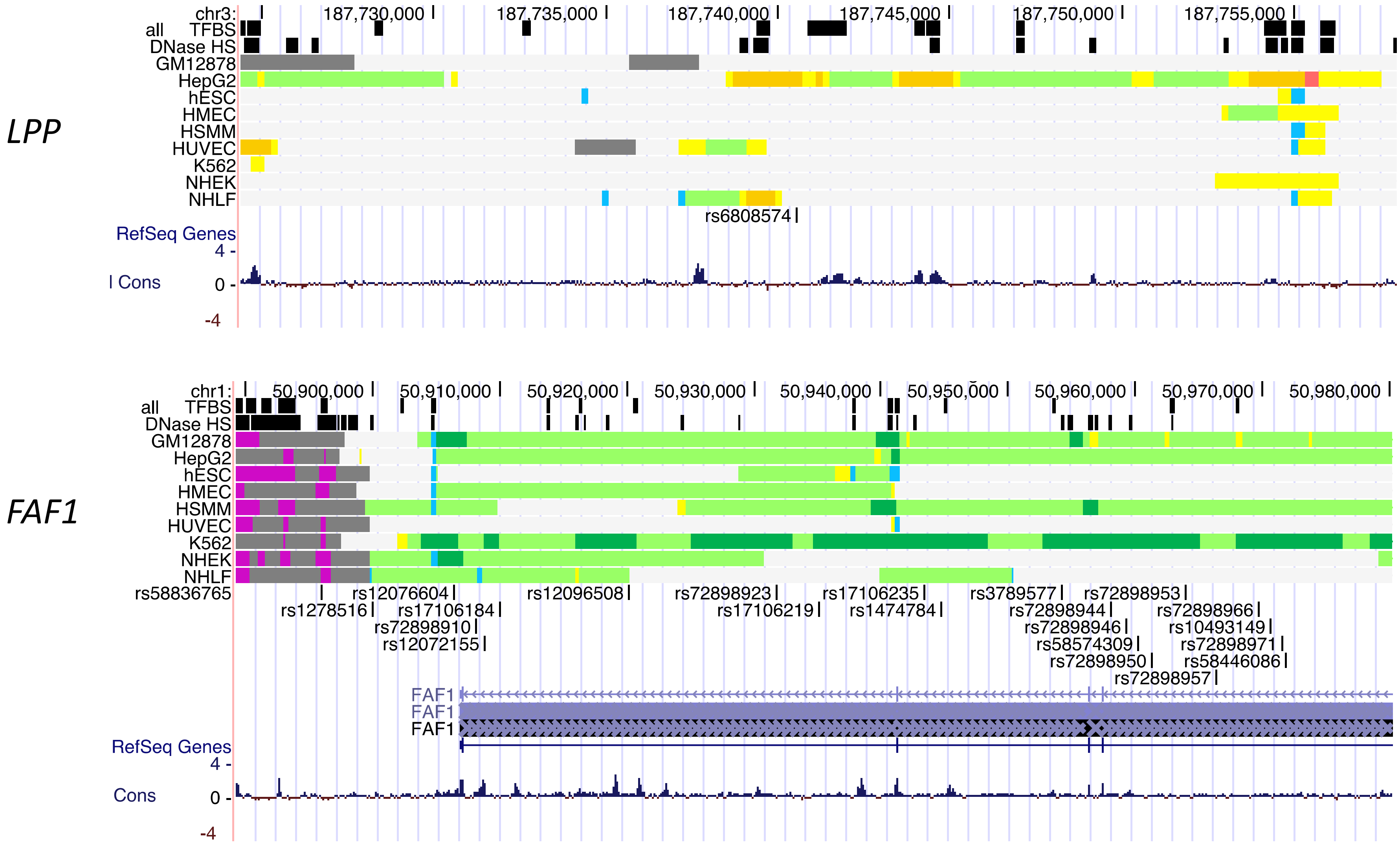
SUPPLEMENTARY INFORMATION

Contents

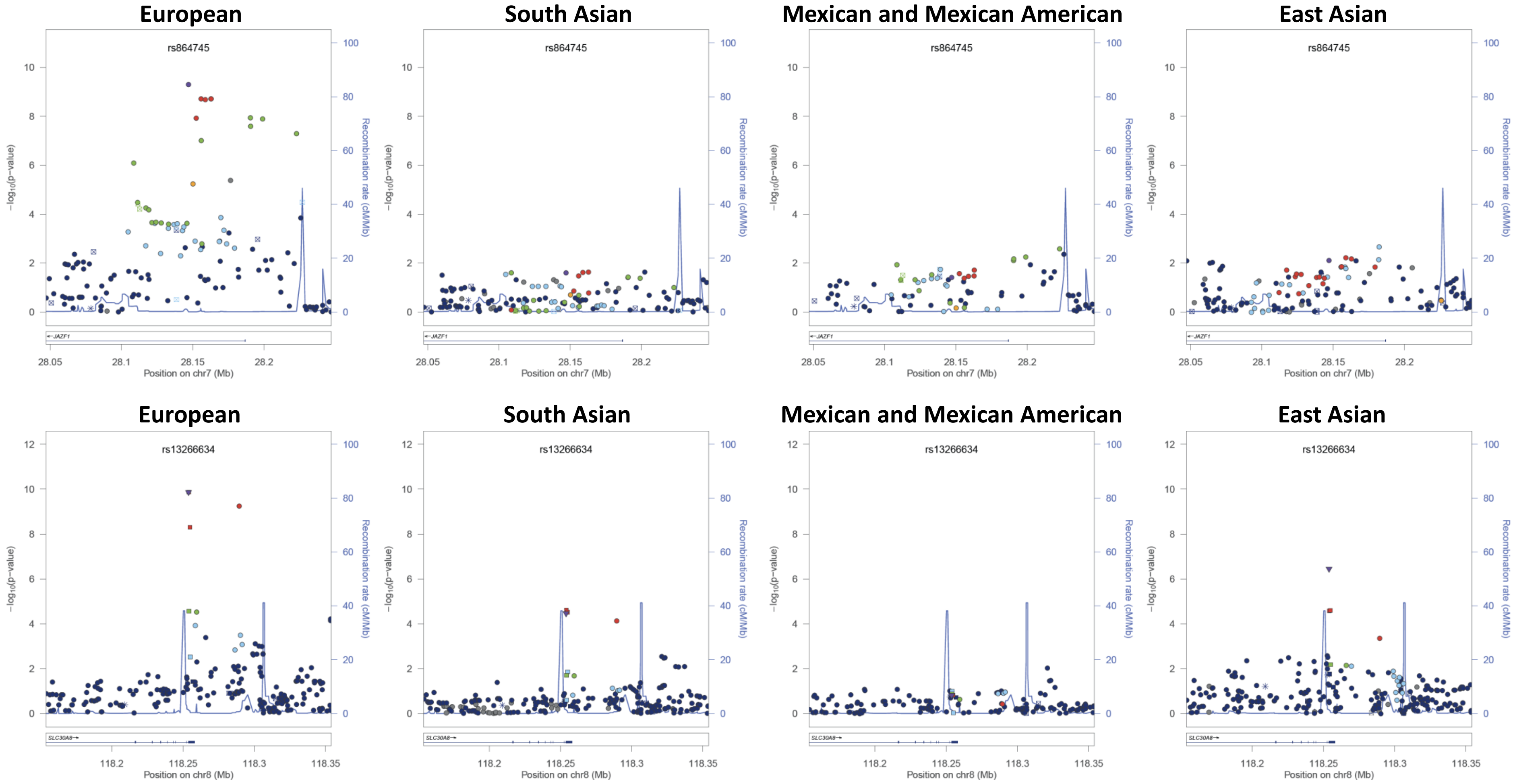
Supplementary Figure 1. Manhattan plot of trans-ethnic "discovery" GWAS meta-analysis. The trans-ethnic meta-analysis comprises 26,488 T2D cases and 83,964 controls from populations of European, East Asian, South Asian, and Mexican and Mexican American ancestry, imputed up to 2.5 million Phase II/III HapMap autosomal SNPs. Previously established T2D susceptibility loci are highlighted in red. Novel loci achieving nominal significance ($p<10^{-5}$) in the stage 1 meta-analysis, and genome-wide significance ($p<5\text{x}10^{-8}$) after the addition of the "validation" meta-analysis of 21,491 cases and 55,647 controls of European ancestry, are highlighted in green. Loci achieving nominal significance in the discovery meta-analysis, but not achieving genome-wide significance after the addition of the validation meta-analysis are highlighted in yellow.



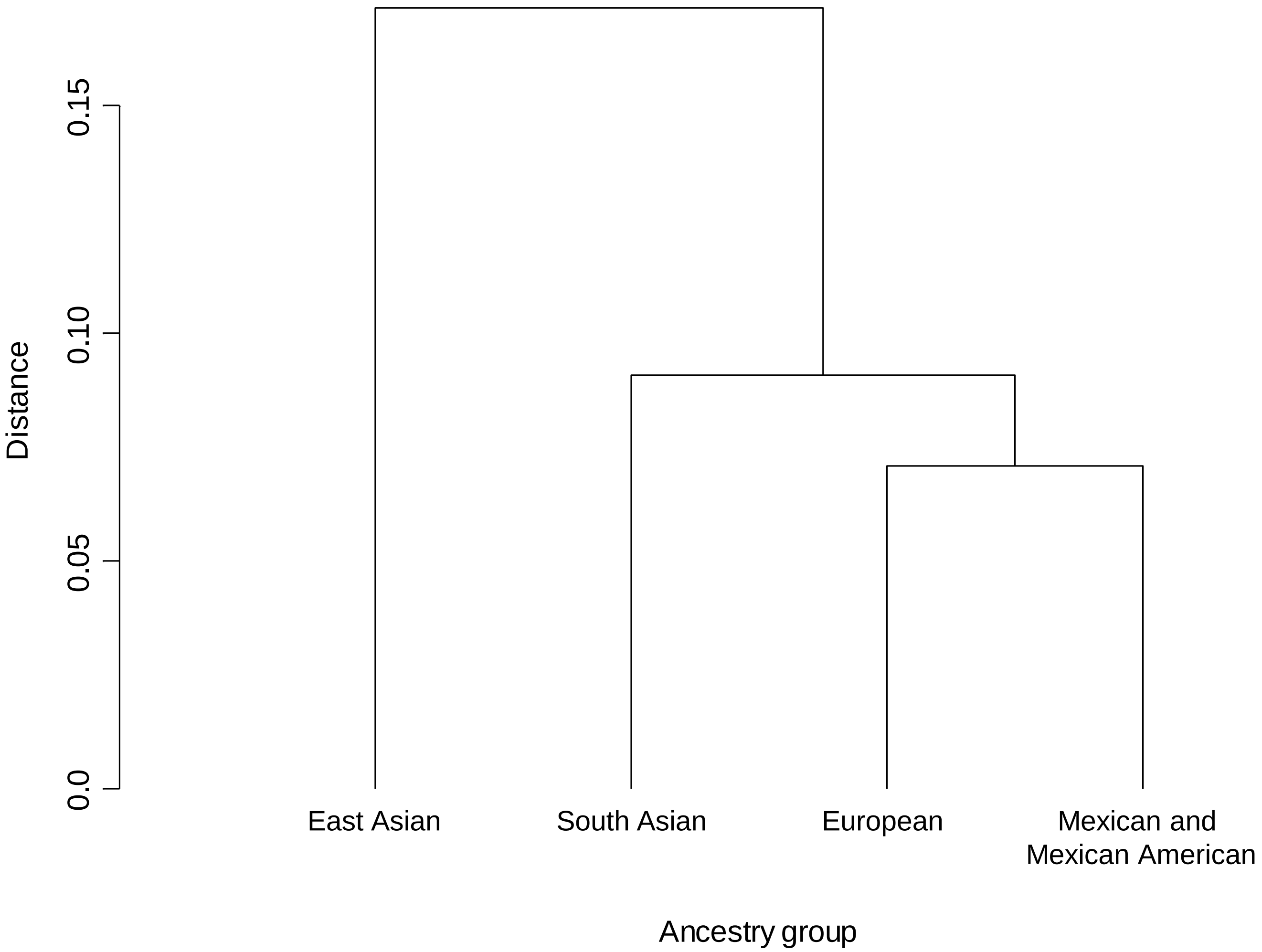
Supplementary Figure 2. ENCODE annotation of *LPP* and *FAF1* loci. Transcription factor binding ChIP sites (TFBS) and Dnase I hypersensitivity sites (DNase HS) are highlighted in black. Chromatin states in 9 ENCODE cell lines (GM12878, HepG2, hESC, HMEC, HSMM, HUVEC, K562, NHEK, and NHLF) are highlighted as follows: strong enhancer (orange), weak enhancer (yellow), active promoter (red), poised promoter (pink), insulator (blue), transcribed (pale green), transcription transition (dark green), repressed (dark grey) and heterochromatin (pale grey).



Supplementary Figure 3. Signal plots constructed on the basis of ancestry-specific meta-analyses at two loci showing greatest improvements in fine-mapping resolution after trans-ethnic meta-analysis: *JAZF1* (top) and *SLC30A8* (bottom). The ancestry-specific meta-analyses were imputed at up to 2.5 million Phase II/III HapMap autosomal SNPs. Each point represents a SNP passing quality control in the ancestry-specific meta-analysis, plotted with their *p*-value (on a -$\log_{10}$ scale) as a function of genomic position (NCBI Build 36). In each plot, the lead SNP from the trans-ethnic meta-analysis across ancestry groups is represented by the purple symbol. The colour coding of all other SNPs indicates LD with the lead SNP (estimated by r^2 from the most closely related reference panel from Phase II HapMap, i.e. CEU for the European, South Asian, and Mexican and Mexican American ancestry groups, and CHB+JPT for the East Asian ancestry group): 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. The shape of the plotting symbol corresponds to the annotation of the SNP: upward triangle for framestop or splice; downward triangle for non-synonymous; square for synonymous or UTR; and circle for intronic or non-coding. Recombination rates are estimated from Phase II HapMap and gene annotations are taken from the University of California Santa Cruz genome browser.



Supplementary Figure 4. Dendogram representing relatedness between ancestry groups included in the trans-ethnic meta-analysis. The distance between each ethnic group is estimated by the genome-wide autosomal mean effect allele frequency difference from the ancestry-specific meta-analysis. The dendogram represents our prior beliefs about the heterogeneity in allelic effects on T2D susceptibility between ancestry groups in the MANTRA analysis.



Supplementary Table 1. Study sample characteristics and genotyping.

(a) Trans-ethnic meta-analysis.

			Sample characteristics					
Study	**Ethnic group (country of origin)**	**Case-control status**	**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 array**
ARIC	European (USA)	Cases	775 (416/359)	56.1 (5.6)	50.9 (10.4)	9.3 (3.6)	30.4 (5.4)	Affymetrix Human SNP Array 6.0
		Controls	7,159 (3,167/3,992)	54.0 (5.7)		5.4 (0.4)	26.4 (4.5)	
deCODE	European (Iceland)	Cases	1,465 (868/597)	68.4 (10.1)	55.1 (12.7)	8.5 (2.7)	30.1 (5.4)	Illumina Human 300K/370K
		Controls	23,194 (7,316/15,878)	59.7 (18.1)		5.3 (0.7)	26.8 (5.0)	
DGDG	European (France)	Cases	679 (413/266)	59.5 (10.1)	45.1 (8.4)	9.2 (3.1)	25.9 (2.8)	Illumina Human 300K
		Controls	697 (281/416)	53.9 (5.6)		5.1 (0.4)	23.2 (1.8)	
DGI	European (Sweden/Finland)	Cases	1,022 (529/493)	65.9 (10.0)	58.0 (10.0)	9.5 (3.1)	28.1 (4.1)	Affymetrix GeneChip 500K
		Controls	1,075 (540/535)	58.0 (10.0)		5.3 (0.5)	27.6 (3.7)	
EUROSPAN	European (various isolates)	Cases	269 (127/142)	62.9 (N/A)	N/A	8.0 (N/A)	29.8 (N/A)	Illumina Human 300K/370K
		Controls	3,710 (1,557/2,153)	49.9 (N/A)		4.8 (N/A)	26.5 (N/A)	
FHS	European (USA)	Cases	674 (386/288)	63.7 (12.4)	N/A	8.6 (2.8)	31.4 (6.5)	Affymetrix GeneChip 500K & MIPS 50K
		Controls	7,664 (3,443/4,221)	52.3 (16.0)		5.3 (0.5)	27.0 (5.1)	
FUSION	European (Finland)	Cases	1,161 (653/508)	62.9 (7.6)	53.7 (9.1)	9.4 (3.1)	30.2 (4.7)	Illumina Human 300K
		Controls	1,174 (574/600)	63.6 (7.4)		5.3 (0.5)	27.1 (3.9)	
HPFS	European (USA)	Cases	1,124 (1,124/0)	55.0 (8.6)	64.0 (8.4)	N/A	27.8 (4.0)	Affymetrix Human SNP Array 6.0
		Controls	1,298 (1,298/0)	55.0 (8.4)		N/A	25.0 (2.9)	
KORAGen	European (Germany)	Cases	433 (255/178)	65.2 (8.3)	58.2 (10.3)	N/A	30.9 (5.0)	Affymetrix GeneChip 500K
		Controls	1,438 (693/745)	61.9 (7.4)		N/A	27.7 (4.3)	
NHS	European (USA)	Cases	1,467 (0/1,467)	43.5 (6.7)	58.7 (10.6)	N/A	27.4 (0.1)	Affymetrix Human SNP Array 6.0
		Controls	1,754 (0/1,754)	43.1 (6.8)		N/A	23.5 (0.1)	
RS1	European (Netherlands)	Cases	1,178 (488/690)	71.7 (8.9)	71.5 (8.9)	N/A	27.4 (4.0)	Illumina Human 550K
		Controls	4,761 (1,928/2,833)	69.0 (9.1)		N/A	26.0 (3.6)	
WTCCC	European (UK)	Cases	1,924 (1,118/806)	58.6 (9.2)	50.3 (9.2)	N/A	30.7 (6.1)	Affymetrix GeneChip 500K
		Controls	2,938 (1,446/1,492)	N/A		N/A	N/A	
CAGE	East Asian (Japan)	Cases	931 (623/308)	66.1 (9.5)	N/A	N/A	24.4 (3.4)	Illumina Human 550K/610K
		Controls	1,404 (844/560)	65.9 (7.4)		N/A	23.1 (3.0)	
CLHNS	East Asian (Philippines)	Cases	159 (0/159)	49.6 (6.1)	N/A	10.7 (3.5)	25.9 (4.3)	Affymetrix GeneChip 500K
		Controls	1,624 (0/1,624)	48.3 (6.1)		5.0 (0.6)	24.4 (4.3)	
KARE	East Asian (Korea)	Cases	1,042 (539/503)	56.4 (8.6)	N/A	7.0 (2.6)	25.5 (3.3)	Affymetrix Human SNP Array 5.0
		Controls	2,943 (1,355/1,588)	51.5 (8.6)		4.5 (0.4)	24.1 (3.0)	
SDCS/SP2(1)	East Asian (Singapore)	Cases	1,082 (402/680)	65.1 (9.7)	55.7 (12.0)	N/A	25.3 (3.9)	Illumina Human 610K
		Controls	1,006 (217/789)	47.7 (11.1)		4.7 (0.5)	22.3 (3.7)	
SDCS/SP(2)	East Asian (Singapore)	Cases	928 (602/326)	63.7 (10.8)	52.2 (14.4)	N/A	25.4 (3.8)	Illumina Human 1M
		Controls	939 (599/340)	46.7 (10.2)		4.7 (0.5)	22.8 (3.4)	
SDGS	East Asian	Cases	1,019 (0/1,019)	51.7 (6.7)	51.7 (6.7)	N/A	26.5 (3.7)	Affymetrix Human SNP Array 6.0

	(China)	Controls	1,710 (1,710/0)	48.7 (8.5)		N/A	23.1 (3.3)	
SiMES	East Asian (Singapore)	Cases	794 (388/406)	62.3 (9.9)	54.4 (11.2)	N/A	27.8 (4.9)	Illumina Human 610K
		Controls	1,240 (595/645)	56.9 (11.4)		N/A	25.1 (4.8)	
TDS	East Asian (China)	Cases	999 (504/495)	59.2 (NA)	50.0 (N/A)	N/A	23.8 (N/A)	Illumina Human 550K
		Controls	1,000 (502/498)	51.2 (NA)		N/A	23.8 (N/A)	
LOLIPOP610	South Asian (UK)	Cases	1,783 (1,478/305)	59.4 (9.2)	N/A	8.6 (3.1)	28.1 (4.6)	Illumina Human 610K
		Controls	4,773 (4,048/725)	53.9 (10.7)		5.2 (0.6)	26.8 (4.2)	
LOLIPOP317	South Asian (UK)	Cases	440 (440/0)	54.1 (10.1)	N/A	8.9 (2.9)	27.6 (4.7)	Illumina Human 300K
		Controls	1,699 (1,699/0)	46.8 (10.1)		5.1 (0.6)	26.6 (4.2)	
PROMIS	South Asian (Pakistan)	Cases	2,361 (1,806/555)	55.0 (9.4)	N/A	13.3 (5.5)	26.0 (4.0)	Illumina Human 650K
		Controls	6,817 (5,658/1,159)	52.9 (10.5)		6.9 (2.9)	25.3 (3.9)	
SINDI	South Asian (Singapore)	Cases	977 (531/446)	60.7 (9.9)	N/A	9.7 (4.4)	27.1 (5.1)	Illumina Human 610K
		Controls	1,169 (566/603)	55.7 (9.7)		5.4 (1.1)	25.3 (4.4)	
Mexico City	Mexican (Mexico)	Cases	967 (303/664)	50.5 (9.2)	43.7 (7.1)	10.2 (4.3)	29.6 (4.8)	Affymetrix Human SNP Array 5.0
		Controls	343 (169/174)	50.7 (5.0)		4.8 (0.4)	27.4 (3.6)	
Starr County	Mexican American (USA)	Cases	837 (333/504)	56.5 (11.8)	46.7 (10.9)	10.0 (4.1)	31.8 (6.4)	Affymetrix Human SNP Array 6.0
		Controls	436 (137/299)	37.6 (9.0)		4.7 (0.5)	29.5 (6.5)	

(b) European ancestry "validation" meta-analysis.

Study	Ethnic group (country of origin)	Case-control status	Sample characteristics					Genotyping array
			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)	
AMC-PAS	European (Netherlands)	Cases	48 (35/13)	44.0 (4.7)	N/A	8.6 (3.2)	29.3 (4.4)	Metabochip
		Controls	442 (333/109)	43.2 (5.3)		5.3 (0.6)	26.6 (4.1)	
BHS	European (Australia)	Cases	51 (38/13)	72.3 (7.8)	N/A	7.8 (4.0)	27.2 (3.9)	Metabochip
		Controls	359 (224/135)	70.0 (9.6)		5.1 (0.9)	26.6 (3.9)	
deCODE Stage 2	European (Iceland)	Cases	722 (433/289)	67.3 (13.6)	N/A	N/A	31.2 (6.3)	Metabochip
		Controls	10,153 (6,604/3,549)	44.3 (26.5)		N/A	N/A	
DILGOM	European (Finland)	Cases	541 (298/243)	60.5 (10.3)	N/A	N/A	30.1 (5.6)	Metabochip
		Controls	3,357 (1,480/1,877)	50.9 (13.5)		N/A	26.5 (4.5)	
DUNDEE	European (UK)	Cases	3,298 (1,940/1,358)	63.5 (9.6)	55.9 (8.9)	N/A	31.9 (6.3)	Metabochip
		Controls	3,708 (1,918/1,790)	59.1 (11.3)		4.9 (0.5)	27.0 (4.5)	
EAS	European (UK)	Cases	110 (64/46)	64.0 (5.6)	N/A	N/A	25.9 (3.3)	Metabochip
		Controls	641 (301/340)	64.5 (5.6)		N/A	25.5 (3.9)	
EGCUT	European (Estonia)	Cases	938 (342/596)	64.1 (10.5)	N/A	N/A	33.4 (5.4)	Metabochip
		Controls	915 (326/589)	51.7 (10.7)		N/A	22.3 (2.5)	
EMIL-ULM	European (Germany)	Cases	755 (510/245)	48.7 (12.0)	45.5 (10.8)	N/A	28.6 (7.1)	Metabochip
		Controls	1,632 (765/867)	45.1 (10.9)		N/A	26.7 (5.0)	
EPIC	European (UK)	Cases	727 (432/295)	61.8 (8.2)	N/A	N/A	29.5 (4.4)	Metabochip
		Controls	927 (393/534)	58.8 (9.4)		N/A	26.1 (3.7)	
FUSION Stage 2	European (Finland)	Cases	1,037 (584/453)	59.7 (8.4)	N/A	7.7 (2.3)	30.8 (5.4)	Metabochip
		Controls	1,157 (691/466)	59.0 (7.6)		5.4 (0.4)	26.9 (3.9)	

D2D2007	European (Finland)	Cases	454 (269/185)	63.4 (7.6)	N/A	7.7 (1.8)	30.6 (5.6)	Metabochip
		Controls	1,229 (455/774)	58.1 (8.2)		5.6 (0.3)	26.2 (4.3)	
Dr’s Extra	European (Finland)	Cases	110 (53/57)	68.4 (5.8)	N/A	6.6 (0.8)	30.9 (5.6)	Metabochip
		Controls	785 (341/444)	66.0 (5.3)		5.4 (0.3)	26.7 (4.0)	
HUNT	European (Norway)	Cases	1,239 (628/611)	64.0 (12.9)	61.9 (11.9)	N/A	29.2 (4.8)	Metabochip
		Controls	1,375 (691/684)	63.5 (13.9)		N/A	26.5 (4.0)	
METSIM	European (Finland)	Cases	1,169 (1,169/0)	60.5 (6.6)	57.0 (8.0)	7.5 (2.0)	30.2 (5.2)	Metabochip
		Controls	651 (651/0)	53.8 (5.0)		5.5 (0.3)	25.9 (3.1)	
GMetS	European (France)	Cases	507 (334/173)	55.9 (9.9)	N/A	N/A	28.5 (3.9)	Metabochip
		Controls	2,553 (1,134/1,419)	47.3 (11.1)		N/A	24.8 (3.8)	
HNR	European (Germany)	Cases	520 (315/205)	62.6 (7.2)	N/A	N/A	30.4 (5.2)	Metabochip
		Controls	3,932 (1,911/2,021)	59.2 (7.8)		N/A	27.5 (4.4)	
IMPROVE	European (Sweden)	Cases	898 (513/385)	64.3 (5.6)	N/A	7.7 (2.2)	29.2 (4.6)	Metabochip
		Controls	2,521 (1,134/1,387)	64.2 (5.3)		5.3 (0.7)	26.5 (3.9)	
KORAGen Stage 2	European (Germany)	Cases	940 (504/436)	61.6 (10.0)	N/A	N/A	30.8 (5.4)	Metabochip
		Controls	4,209 (2,000/2,209)	53.8 (13.2)		N/A	27.2 (4.6)	
PIVUS	European (Sweden)	Cases	113 (70/43)	70.2 (0.2)	N/A	N/A	29.5 (5.1)	Metabochip
		Controls	864 (419/445)	70.2 (0.2)		N/A	26.8 (4.2)	
PMB	European (Sweden/Finland)	Cases	4,976 (2,911/2,065)	58.8 (12.5)	N/A	N/A	28.2 (8.7)	Metabochip
		Controls	3,500 (1,700/1,800)	58.3 (8.4)		N/A	26.4 (4.4)	
SCARFSHEEP	European (Sweden)	Cases	341 (246/95)	59.6 (7.0)	N/A	8.12(5.4)	27.4 (8.4)	Metabochip
		Controls	3,073 (2,211/862)	57.9 (7.3)		4.0 (3.8)	25.4 (6.1)	
STR	European (Sweden)	Cases	320 (141/179)	71.5 (9.3)	N/A	N/A	27.0 (4.1)	Metabochip
		Controls	1,318 (612/706)	74.3 (10.5)		N/A	24.9 (3.8)	
THISEAS	European (Greece)	Cases	327 (229/98)	63.6 (10.6)	N/A	8.0 (2.6)	29.4 (4.8)	Metabochip
		Controls	1,180 (643/537)	58.2 (13.6)		5.3 (0.6)	28.3 (5.0)	
ULSAM	European (Sweden)	Cases	233 (233/0)	71.0 (0.6)	N/A	N/A	27.7 (3.8)	Metabochip
		Controls	942 (942/0)	71.0 (0.6)		N/A	25.9 (3.2)	
WARREN2	European (UK)	Cases	1,117 (647/470)	N/A	45.5 (11.0)	N/A	32.2 (6.6)	Metabochip
		Controls	4,224 (2,394/1,830)	N/A		N/A	N/A	

Supplementary Table 2. Summary of study-specific quality control, imputation and analysis.

(a) Trans-ethnic meta-analysis.

Study	Ethnic group (Country of origin)	Sample quality control		SNP quality control					Imputation		Analysis		
		Call rate	Exclusions	Call rate	HWE	MAF	Imputation	Passed SNPs	Software	Reference panel	Software	Covariates	λ_{GC}
ARIC	European (USA)	≥0.95	Relatedness and duplicates	≥0.90	p>10-6	≥0.01	r2>0.3	2,443,161	MACH	HapMap2 CEU	ProbABEL	Age, sex, and study centre	1.01
deCODE	European (Iceland)	≥0.98	Duplicates	≥0.96	p>10-6	≥0.01	proper-info>0.5	2,338,113	IMPUTE	HapMap2 CEU	SNPTEST	None	1.31
DGDG	European (France)	≥0.95	Duplicates	≥0.95	p>10-4	≥0.01	proper-info>0.5	2,051,387	IMPUTE	HapMap2 CEU	SNPTEST	None	1.10
DGI	European (Sweden/Finland)	≥0.95	Duplicates	≥0.95	p>10-6	≥0.01	proper-info>0.5	2,230,032	IMPUTE	HapMap2 CEU	PLINK and SNPTEST	Age, sex, BMI, and study centre	1.06
EUROSPAN	European (various isolates)	≥0.98	Duplicates	≥0.98	p>10-6	≥0.01	r2>0.5	2,359,525	MACH	HapMap2 CEU	GenABEL and SNPTEST	Age and sex	0.98
FHS	European (USA)	≥0.95	Duplicates	≥0.95	p>10-6	≥0.01	r2>0.3	2,389,929	MACH	HapMap2 CEU	R (GEE correction for relatedness)	Age, sex, and cohort	1.02
FUSION	European (Finland)	≥0.975	Duplicates	≥0.90	p>10-6	≥0.01	r2>0.3	2,413,085	MACH	HapMap2 CEU	MACH2DAT	Age, sex, and birth province	1.04
HPFS	European (USA)	≥0.95	Relatedness and duplicates	≥0.95	p>10-6	≥0.01	N/A	622,575	N/A	N/A	PLINK	Age and BMI	1.03
KORAGen	European (Germany)	≥0.93	Duplicates	≥0.95	p>10-6	≥0.01	proper-info>0.5	2,325,232	IMPUTE	HapMap2 CEU	SNPTEST	Age and sex	1.04
NHS	European (USA)	≥0.98	Relatedness and duplicates	≥0.98	p>10-6	≥0.02	N/A	615,391	N/A	N/A	PLINK	Age and BMI	0.98
RS1	European (Netherlands)	≥0.975	Duplicates	≥0.98	p>10-6	≥0.01	r2>0.5	2,439,672	MACH	HapMap2 CEU	GenABEL and SNPTEST	None	1.01
WTCCC	European (UK)	≥0.97	Duplicates	≥0.95 (≥0.99 for MAF<0.05)	p>10-3	≥0.01	proper-info>0.5	2,308,535	IMPUTE	HapMap2 CEU	PLINK and SNPTEST	None	1.08
CAGE	East Asian (Japan)	≥0.90	Relatedness, duplicates and ethnic outliers	≥0.95	p>10-6	≥0.01	r2>0.3	1,988,685	IMPUTE	HapMap2 CHB+JPT	PLINK	Sex and BMI	1.06
CLHNS	East Asian (Philippines)	≥0.97	Duplicates	≥0.90	p>10-6	≥0.01	r2>0.3	2,049,920	MACH	HapMap2 CHB+JPT+CEU	MACH2DAT	BMI and PCs	1.01
KARE	East Asian (Korea)	≥0.98	Relatedness, duplicates and ethnic outliers	≥0.95	p>10-6	≥0.01	proper-info>0.5	1,419,177	IMPUTE	HapMap2 CHB+JPT	PLINK	Sex, BMI and study centre	1.01
SDCS/SP2(1)	East Asian (Singapore)	≥0.95	Relatedness, duplicates and ethnic outliers	≥0.95	p>10-6	N/A	proper-info>0.5	1,965,414	IMPUTE	HapMap2 CHB+JPT	SNPTEST	Sex and BMI	1.05
SDCS/SP2(2)	East Asian (Singapore)	≥0.95	Relatedness, duplicates and ethnic outliers	≥0.95	p>10-6	N/A	proper-info>0.5	2,248,003	IMPUTE	HapMap2 CHB+JPT	SNPTEST	Sex and BMI	1.06
SDGS	East Asian (China)	≥0.95	Relatedness and duplicates	≥0.95	p>10-5	≥0.05	r2>0.3	2,241,970	MACH	HapMap2 CHB+JPT	MACH2DAT, PLINK	BMI	1.04
SiMES	East Asian (Singapore)	≥0.95	Relatedness, duplicates and ethnic outliers	≥0.95	p>10-6	N/A	proper-info>0.5	1,625,733	IMPUTE	HapMap2 CHB+JPT+CEU+YRI	SNPTEST	Sex, BMI and PCs	1.04
TDS	East Asian (China)	N/A	N/A	≥0.95	p>10-6	≥0.05	r2>0.3	1,890,143	MACH	HapMap2 CHB+JPT	SAS	Sex and BMI	1.04
LOLIPOP610	South Asian (UK)	≥0.95	Relatedness, duplicates, and ethnic outliers	≥0.95	p>10-6	≥0.01	r2>0.3	2,220,688	MACH	HapMap2 CHB+JPT+CEU+YRI	MACH2DAT, PLINK	Study centre, CHD, and PCs	1.02
LOLIPOP317	South Asian	≥0.95	Relatedness, duplicates,	≥0.95	p>10-6	≥0.01	r2>0.3	1,950,903	MACH	HapMap2	MACH2DAT, PLINK	PCs	1.01

	(UK)		and ethnic outliers							CHB+JPT+CEU+YRI			
PROMIS	South Asian (Pakistan)	≥0.95	Relatedness	≥0.97	p>10-6	≥0.01	proper-info>0.4	2,527,357	IMPUTE	HapMap2&3 CEU+GIH	SNPTEST v2	PCs	1.01
SINDI	South Asian (Singapore)	≥0.95	Relatedness, duplicates, and ethnic outliers	≥0.95	p>10-6	≥0.01	proper-info>0.3	2,035,725	IMPUTE	HapMap2 CHB+JPT+CEU+YRI	SNPTEST	PCs	1.03
Mexico City	Mexican (Mexico)	≥0.95	Relatedness and duplicates	≥0.95	p>10-4 (controls)	≥0.05	proper-info>0.5	1,829,070	IMPUTE	HapMap2&3 CHB+ JPT+CEU+YRI+MXL	SNPTEST	Age, sex, and PCs	1.03
Starr County	Mexican American (USA)	≥0.90	Relatedness and duplicates	≥0.90	None	≥0.05	r2 >0.7	1,782,420	MACH	HapMap2 CHB+JPT+CEU+YRI	SNPTEST	Age and sex	1.03

(b) European ancestry "validation" meta-analysis.

Study	**Ethnic group (Country of origin)**	**Sample quality control**		**SNP quality control**					**Imputation**		**Analysis**		
		Call rate	**Exclusions**	**Call rate**	**HWE**	**MAF**	**Imputation**	**Passed SNPs**	**Software**	**Reference panel**	**Software**	**Covariates**	**λ_{QT}**
AMC-PAS	European (Netherlands)	≥0.95	Duplicates and ethnic outliers	≥0.98	p>10-4	≥0.01	N/A	109,525	N/A	N/A	PLINK	Age and sex	1.00
BHS	European (Australia)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	119,893	N/A	N/A	PLINK	Age and sex	0.96
deCODE Stage 2	European (Iceland)	N/A	N/A	N/A	N/A	≥0.01	N/A	125,236	N/A	N/A	SNPTEST	Sex	0.95
DILGOM	European (Finland)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	116,634	N/A	N/A	PLINK	Age, sex, and PCs	0.93
DUNDEE	European (UK)	≥0.95	Duplicates and ethnic outliers	≥0.95 (≥0.99 for MAF<0.05)	p>5.7x10-7	≥0.01	N/A	121,365	N/A	N/A	PLINK	PCs	1.07
EAS	European (UK)	≥0.95		≥0.95	p>10-6	≥0.01	N/A	119,523	N/A	N/A	PLINK	Age and sex	1.00
EGCUT	European (Estonia)	≥0.95	Relatedness and ethnic outliers	≥0.95	p>10-6	≥0.01	N/A	120,720	N/A	N/A	SNPTEST	Age, sex, and PCs	1.00
EMIL-ULM	European (Germany)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	121,684	N/A	N/A	PLINK	Age and sex	1.14
EPIC	European (UK)	≥0.95	Duplicates	≥0.90	p>10-6	≥0.01	N/A	120,527	N/A	N/A	PLINK	Age and sex	0.97
FUSION Stage 2	European (Finland)	≥0.98	Relatedness	≥0.98	p>10-5	≥0.01	N/A	123,853	N/A	N/A	PLINK	Age and sex	0.97
D2D2007	European (Finland)	≥0.98	Relatedness	≥0.98	p>10-5	≥0.01	N/A	123,461	N/A	N/A	PLINK	Age and sex	0.96
Dr's Extra	European (Finland)	≥0.98	Relatedness	≥0.98	p>10-5	≥0.01	N/A	120,746	N/A	N/A	PLINK	Age and sex	0.94
HUNT	European (Norway)	≥0.98	Relatedness	≥0.98	p>10-5	≥0.01	N/A	125,644	N/A	N/A	PLINK	Age, sex and collection site	1.10
METSIM	European (Finland)	≥0.98	Relatedness	≥0.98	p>10-5	≥0.01	N/A	122,600	N/A	N/A	PLINK	Age	1.01
GMetS	European (France)	≥0.95	Duplicates	≥0.95	p>10-4	≥0.01	N/A	123,359	N/A	N/A	PLINK	Age, sex, and BMI	1.11
HNR	European (Germany)	≥0.97	Relatedness and ethnic outliers	≥0.95	p>10-6	≥0.01	N/A	126,675	N/A	N/A	PLINK	Age and sex	1.00
IMPROVE	European (Sweden)	≥0.95	Relatedness and ethnic outliers	≥0.95	p>10-6	≥0.01	N/A	122,320	N/A	N/A	PLINK	Age, sex, and PCs	1.13
KORAGen Stage 2	European	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	120,547	N/A	N/A	PLINK	Age and sex	1.02

	(Germany)												
PIVUS	European (Sweden)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	120,892	N/A	N/A	PLINK	Age and sex	0.97
PMB	European (Sweden/Finland)	≥0.95	Relatedness and ethnic outliers	≥0.95	p>10-6	≥0.01	N/A	119,674	N/A	N/A	PLINK	PCs	1.05
SCARFSHEEP	European (Sweden)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	121,792	N/A	N/A	PLINK	Age, sex, PCs, and MI	1.00
STR	European (Sweden)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	119,375	N/A	N/A	PLINK	Age, sex, PCs and CAD	0.98
THISEAS	European (Greece)	≥0.95	N/A	≥0.95	p>10-6	≥0.01	N/A	120,509	N/A	N/A	PLINK	Age and sex	0.99
ULSAM	European (Sweden)	≥0.95	Duplicates and ethnic outliers	≥0.98	p>10-4	≥0.01	N/A	108,868	N/A	N/A	PLINK	Age	1.00
WARREN2	European (UK)	≥0.95	Relatedness	≥0.95	p>10-6	≥0.01	N/A	119,018	N/A	N/A	PLINK	Age and sex	0.95

Supplementary Table 3. Association summary statistics in each ancestry group (European, East Asian, South Asian, and Mexican and Mexican American) for previously reported lead SNPs at established autosomal T2D susceptibility loci and assessment of heterogeneity in allelic effects after fixed-effects trans-ethnic GWAS meta-analysis of 26,488 cases and 83,964 controls.

				Alleles		European 12,171 cases and 56,862 controls			East Asian 6,952 cases and 11,865 controls			South Asian 5,561 cases and 14,458 controls			Mexican and Mexican American 1,804 cases and 779 controls			Trans-ethnic meta-analysis	
Locus	**Lead SNP**	**Chr**	**Build 36 position (bp)**	**Risk**	**Other**	**RAF**	**OR (95% CI)**	***p*-value**	**RAF**	**OR (95% CI)**	***p*-value**	**RAF**	**OR (95% CI)**	***p*-value**	**RAF**	**OR (95% CI)**	***p*-value**	***p*-value**	**Cochran's *Q* *p*-value**
TCF7L2	rs7903146	10	114,748,339	T	C	0.30	1.40 (1.35-1.46)	1.9E-59	0.05	1.18 (1.03-1.35)	1.6E-02	0.31	1.25 (1.19-1.32)	3.6E-19	0.23	1.16 (0.97-1.38)	1.1E-01	7.8E-75	5.5E-04
PEPD	rs3786897	19	38,584,848	A	G	0.57	1.02 (0.98-1.06)	3.3E-01	0.40	1.17 (1.10-1.24)	3.5E-07	0.72	1.04 (0.99-1.10)	1.5E-01	0.74	0.90 (0.76-1.07)	2.3E-01	3.3E-04	5.5E-04
KLF14	rs13233731	7	130,088,229	G	A	0.49	1.10 (1.06-1.13)	1.7E-07	0.68	0.99 (0.94-1.04)	6.5E-01	0.61	0.99 (0.94-1.04)	6.1E-01	0.61	1.07 (0.93-1.23)	3.4E-01	7.0E-04	6.4E-04
CDKAL1	rs7756992	6	20,787,688	G	A	0.26	1.20 (1.16-1.25)	1.1E-21	0.60	1.14 (1.09-1.20)	4.8E-08	0.27	1.06 (1.01-1.12)	2.0E-02	0.34	1.09 (0.94-1.27)	2.4E-01	1.6E-26	2.6E-03
VPS26A	rs1802295	10	70,601,480	T	C	0.33	1.02 (0.98-1.06)	3.0E-01	0.22	1.01 (0.94-1.09)	8.0E-01	0.27	1.13 (1.07-1.20)	7.7E-06	N/A	N/A	N/A	1.4E-03	4.4E-03
GCC1	rs6467136	7	126,952,194	G	A	0.55	0.99 (0.95-1.03)	5.5E-01	0.68	1.11 (1.05-1.18)	2.4E-04	0.56	1.01 (0.96-1.06)	7.6E-01	0.49	0.96 (0.84-1.10)	5.8E-01	2.0E-01	5.6E-03
TSPAN8	rs7955901	12	69,719,560	C	T	0.47	1.09 (1.05-1.13)	9.0E-06	0.49	0.97 (0.92-1.02)	2.7E-01	0.42	1.03 (0.98-1.08)	2.3E-01	0.54	1.00 (0.87-1.14)	9.9E-01	1.6E-03	6.1E-03
GCKR	rs780094	2	27,594,741	C	T	0.62	1.04 (1.00-1.08)	3.2E-02	0.38	1.06 (1.01-1.11)	2.1E-02	0.75	1.19 (1.11-1.29)	4.2E-06	0.65	0.99 (0.85-1.14)	8.5E-01	1.0E-05	8.7E-03
GRB14	rs3923113	2	165,210,095	A	C	0.61	1.04 (1.00-1.09)	4.0E-02	0.77	1.03 (0.95-1.12)	4.8E-01	0.75	1.15 (1.09-1.21)	8.9E-07	0.76	1.22 (1.03-1.45)	2.3E-02	1.5E-06	1.3E-02
BCAR1	rs7202877	16	73,804,746	T	G	0.90	1.15 (1.07-1.23)	5.0E-05	0.64	1.00 (0.93-1.07)	1.0E+00	0.93	1.06 (0.97-1.16)	1.9E-01	0.93	1.38 (1.02-1.87)	3.5E-02	5.7E-04	1.3E-02
ZFAND3	rs9470794	6	38,214,822	C	T	0.19	0.99 (0.93-1.06)	8.1E-01	0.32	1.11 (1.05-1.18)	2.4E-04	0.12	1.07 (0.99-1.15)	7.3E-02	0.08	0.82 (0.63-1.06)	1.2E-01	3.6E-03	1.4E-02
PSMD6	rs831571	3	64,023,337	C	T	0.81	1.03 (0.99-1.08)	1.8E-01	0.45	1.11 (1.05-1.16)	4.5E-05	0.79	1.03 (0.98-1.09)	2.6E-01	0.91	0.80 (0.63-1.01)	6.3E-02	3.7E-04	1.5E-02
CILP2	rs10401969	19	19,268,718	C	T	0.07	1.13 (1.05-1.21)	9.3E-04	0.42	1.01 (0.90-1.12)	8.9E-01	0.10	1.00 (0.92-1.09)	9.7E-01	0.04	1.59 (1.08-2.35)	1.8E-02	9.7E-03	2.0E-02
RASGRP1	rs7403531	15	36,610,197	T	C	0.22	1.02 (0.98-1.06)	3.8E-01	0.55	1.08 (1.02-1.13)	3.8E-03	0.25	0.97 (0.92-1.03)	3.5E-01	0.39	0.90 (0.77-1.05)	1.8E-01	1.5E-01	2.1E-02
RBMS1	rs7593730	2	160,879,700	C	T	0.79	1.11 (1.06-1.16)	4.3E-06	0.72	1.00 (0.94-1.07)	9.2E-01	0.79	1.01 (0.95-1.07)	7.7E-01	0.86	1.05 (0.86-1.28)	6.2E-01	4.7E-04	2.7E-02
TLE4	rs17791513	9	81,095,410	A	G	0.93	1.21 (1.13-1.31)	4.3E-07	0.90	1.00 (0.89-1.11)	9.4E-01	0.87	1.12 (1.05-1.21)	1.1E-03	0.85	1.21 (0.99-1.47)	6.6E-02	3.2E-08	3.0E-02
ZBED3	rs6878122	5	76,463,067	G	A	0.25	1.13 (1.07-1.18)	3.2E-06	0.09	1.08 (0.94-1.24)	3.0E-01	0.20	1.01 (0.96-1.08)	6.4E-01	N/A	N/A	N/A	6.3E-05	3.1E-02
HHEX/IDE	rs1111875	10	94,452,862	C	T	0.58	1.15 (1.11-1.19)	1.2E-14	0.34	1.15 (1.09-1.22)	2.3E-06	0.44	1.07 (1.02-1.12)	6.9E-03	0.64	1.00 (0.87-1.16)	9.6E-01	3.2E-19	3.4E-02
CDC123	rs11257655	10	12,347,900	T	C	0.23	1.06 (1.01-1.11)	1.7E-02	0.61	1.15 (1.09-1.23)	3.4E-06	0.23	1.12 (1.06-1.18)	5.9E-05	0.30	0.96 (0.81-1.13)	6.2E-01	2.6E-09	4.3E-02
ARAP1 (CENTD2)	rs1552224	11	72,110,746	A	C	0.83	1.13 (1.08-1.19)	1.5E-06	0.89	1.16 (1.05-1.28)	2.5E-03	0.83	1.04 (0.98-1.11)	2.2E-01	N/A	N/A	N/A	1.2E-07	5.5E-02
KCNQ1	rs163184	11	2,803,645	G	T	0.50	1.09 (1.04-1.13)	4.3E-05	0.39	1.16 (1.10-1.23)	1.6E-08	0.53	1.08 (1.03-1.13)	1.2E-03	0.48	1.23 (1.06-1.43)	6.6E-03	1.7E-14	5.8E-02
NOTCH2	rs10923931	1	120,319,482	T	G	0.11	1.10 (1.04-1.17)	5.8E-04	0.05	1.00 (0.86-1.16)	9.9E-01	0.18	1.01 (0.95-1.07)	8.3E-01	0.10	0.89 (0.70-1.13)	3.3E-01	1.7E-02	6.8E-02
JAZF1	rs849135	7	28,162,938	G	A	0.52	1.12 (1.08-1.17)	1.9E-09	0.51	1.01 (0.76-1.33)	9.5E-01	0.73	1.04 (0.98-1.10)	1.6E-01	0.67	1.19 (1.03-1.38)	1.9E-02	1.7E-09	6.9E-02
KCNJ11	rs5215	11	17,365,206	C	T	0.38	1.08 (1.04-1.12)	1.1E-05	0.35	1.14 (1.09-1.20)	1.6E-07	0.37	1.04 (0.99-1.09)	1.1E-01	0.39	1.11 (0.96-1.28)	1.8E-01	3.2E-11	7.2E-02
DGKB	rs17168486	7	14,864,807	T	C	0.19	1.13 (1.07-1.19)	2.1E-06	0.58	1.08 (1.02-1.14)	5.5E-03	0.30	1.04 (0.99-1.10)	1.1E-01	0.45	0.96 (0.82-1.13)	6.5E-01	3.4E-07	7.6E-02
THADA	rs10203174	2	43,543,534	C	T	0.90	1.15 (1.08-1.21)	4.7E-06	0.99	1.57 (0.46-5.34)	4.7E-01	0.85	1.01 (0.92-1.11)	8.3E-01	N/A	N/A	N/A	4.8E-05	8.3E-02
KCNK16	rs1535500	6	39,392,028	T	G	N/A	N/A	N/A	0.59	1.13 (1.08-1.19)	1.8E-06	0.50	1.04 (0.98-1.10)	2.3E-01	0.48	1.06 (0.92-1.22)	4.2E-01	7.5E-06	9.2E-02
ST64GAL1	rs16861329	3	188,149,155	C	T	0.85	1.03 (0.96-1.10)	4.1E-01	0.60	0.92 (0.86-0.99)	1.8E-02	0.77	1.13 (1.07-1.19)	2.2E-05	N/A	N/A	N/A	8.5E-06	1.1E-01
MTNR1B	rs10830963	11	92,348,358	G	C	0.27	1.11 (1.06-1.16)	2.5E-06	0.59	1.00 (0.93-1.08)	9.5E-01	0.37	1.10 (1.03-1.16)	2.3E-03	0.22	1.12 (0.94-1.33)	2.2E-01	2.0E-07	1.2E-01
PTPRD	rs17584499	9	8,869,118	T	C	0.18	1.00 (0.94-1.07)	9.4E-01	0.22	1.09 (1.00-1.19)	4.0E-02	0.26	0.98 (0.93-1.04)	5.5E-01	N/A	N/A	N/A	6.0E-01	1.2E-01
PROX1	rs2075423	1	212,221,342	G	T	0.66	1.08 (1.04-1.12)	1.6E-04	0.73	1.10 (1.02-1.18)	1.3E-02	0.75	1.03 (0.98-1.09)	2.9E-01	0.72	1.23 (1.05-1.46)	1.2E-02	2.2E-06	1.4E-01
HNF4A	rs4812829	20	42,422,681	A	G	0.16	1.07 (1.01-1.12)	1.3E-02	0.33	1.07 (1.01-1.13)	1.6E-02	0.29	1.13 (1.08-1.19)	1.6E-06	0.51	0.98 (0.84-1.14)	7.8E-01	4.6E-08	1.5E-01
GIPR	rs8108269	19	50,850,353	G	T	0.30	1.06 (1.02-1.11)	5.0E-03	0.40	1.12 (1.05-1.19)	3.5E-04	0.32	1.06 (1.01-1.11)	2.8E-02	0.44	0.93 (0.80-1.09)	3.8E-01	4.9E-06	1.5E-01
HMGA2	rs2261181	12	64,498,585	T	C	0.09	1.16 (1.10-1.23)	3.9E-07	0.19	1.09 (1.01-1.18)	2.3E-02	0.18	1.07 (1.00-1.13)	3.6E-02	0.08	0.99 (0.78-1.28)	9.6E-01	3.6E-08	1.8E-01
SPRY2	rs1359790	13	79,615,157	G	A	0.73	1.10 (1.05-1.14)	3.2E-06	0.68	1.05 (0.99-1.11)	1.0E-01	0.83	1.02 (0.96-1.09)	4.7E-01	0.60	1.02 (0.89-1.18)	7.6E-01	5.8E-06	2.2E-01
AP3S2	rs2028299	15	88,175,261	C	A	0.29	1.04 (1.00-1.09)	4.4E-02	0.26	1.08 (1.02-1.14)	1.3E-02	0.32	1.11 (1.05-1.16)	4.5E-05	0.16	1.17 (0.97-1.42)	1.0E-01	5.2E-07	2.4E-01
ADAMTS9	rs6795735	3	64,680,405	C	T	0.59	1.07 (1.03-1.10)	4.4E-04	0.35	1.00 (0.94-1.05)	9.1E-01	0.28	1.06 (1.01-1.12)	2.5E-02	0.25	1.06 (0.91-1.24)	4.6E-01	2.1E-04	2.5E-01
GCK	rs10278336	7	44,211,888	A	G	0.54	1.05 (1.01-1.09)	2.7E-02	0.51	1.01 (0.93-1.08)	9.0E-01	0.55	1.00 (0.95-1.04)	8.6E-01	N/A	N/A	N/A	1.3E-01	2.6E-01
ZFAND6	rs11634397	15	78,219,277	G	A	0.64	1.09 (1.05-1.13)	1.8E-05	0.13	1.00 (0.90-1.11)	9.9E-01	0.53	1.05 (0.99-1.12)	7.6E-02	N/A	N/A	N/A	1.4E-05	2.8E-01

FTO	rs9936385	16	52,376,670	C	T	0.39	1.13 (1.09-1.18)	3.2E-10	0.42	1.09 (1.01-1.17)	3.4E-02	0.32	1.07 (1.02-1.13)	1.0E-02	0.27	1.17 (1.00-1.37)	5.7E-02	1.2E-12	3.0E-01
GLIS3	rs7041847	9	4,277,466	A	G	0.50	1.05 (1.01-1.09)	1.4E-02	0.43	1.10 (1.05-1.15)	9.3E-05	0.56	1.04 (0.99-1.08)	1.5E-01	0.63	1.07 (0.93-1.24)	3.5E-01	5.4E-06	3.1E-01
CCND2	rs11063069	12	4,244,634	G	A	0.21	1.10 (1.04-1.15)	3.2E-04	0.05	0.97 (0.84-1.13)	7.0E-01	0.12	1.02 (0.92-1.14)	6.8E-01	0.11	1.15 (0.92-1.43)	2.1E-01	7.5E-04	3.2E-01
IGF2BP2	rs4402960	3	186,994,381	T	G	0.31	1.13 (1.09-1.17)	1.8E-10	0.42	1.08 (1.02-1.13)	5.9E-03	0.42	1.12 (1.07-1.18)	1.9E-06	0.25	1.22 (1.04-1.43)	1.3E-02	9.5E-18	3.3E-01
TMEM163	rs6723108	2	135,196,450	T	G	0.48	1.01 (0.97-1.05)	7.2E-01	0.50	1.90 (0.65-5.56)	2.4E-01	0.85	1.05 (0.97-1.15)	2.4E-01	N/A	N/A	N/A	4.0E-01	3.3E-01
PPARG	rs1801282	3	12,368,125	C	G	0.88	1.16 (1.10-1.23)	1.7E-08	0.93	1.15 (1.01-1.30)	3.2E-02	0.87	1.09 (1.00-1.18)	4.1E-02	N/A	N/A	N/A	5.7E-10	3.5E-01
HNF1B	rs4430796	17	33,172,153	G	A	0.53	1.13 (1.07-1.09)	6.6E-06	0.42	1.12 (1.05-1.19)	8.3E-04	0.37	1.07 (1.02-1.13)	4.2E-03	N/A	N/A	N/A	8.9E-10	3.6E-01
PRC1	rs12899811	15	89,345,080	G	A	0.30	1.09 (1.04-1.13)	7.1E-05	0.52	1.16 (1.00-1.35)	5.1E-02	0.55	1.05 (1.00-1.10)	3.6E-02	0.66	1.17 (1.01-1.36)	4.3E-02	5.7E-07	3.9E-01
CDKN2A/B	rs10811661	9	22,124,094	T	C	0.82	1.18 (1.13-1.24)	1.2E-12	0.67	1.25 (1.17-1.32)	6.3E-13	0.87	1.20 (1.11-1.31)	1.4E-05	N/A	N/A	N/A	1.1E-27	3.9E-01
HNF1A	rs12427353	12	119,911,284	G	C	0.77	1.12 (1.07-1.18)	2.8E-06	N/A	N/A	N/A	0.95	1.04 (0.87-1.23)	6.9E-01	N/A	N/A	N/A	3.9E-06	3.9E-01
GRK5	rs10886471	10	121,139,393	C	T	0.49	0.99 (0.95-1.03)	6.1E-01	0.64	1.06 (0.99-1.13)	1.0E-01	0.60	1.01 (0.96-1.05)	8.3E-01	0.50	1.03 (0.88-1.20)	7.4E-01	6.1E-01	4.3E-01
ANK1	rs516946	8	41,638,405	C	T	0.77	1.10 (1.06-1.15)	2.1E-06	0.72	1.04 (0.97-1.12)	2.7E-01	0.80	1.08 (1.02-1.14)	1.0E-02	0.81	1.01 (0.85-1.20)	9.4E-01	1.5E-07	4.4E-01
SRR	rs391300	17	2,163,008	C	T	0.62	1.00 (0.96-1.04)	9.5E-01	0.63	1.03 (0.97-1.09)	2.7E-01	0.51	0.99 (0.94-1.03)	6.1E-01	0.66	1.09 (0.92-1.28)	3.2E-01	6.8E-01	5.1E-01
KLHDC5	rs10842994	12	27,856,417	C	T	0.80	1.09 (1.04-1.13)	3.0E-04	0.65	1.03 (0.95-1.12)	5.2E-01	0.88	1.11 (1.03-1.20)	9.1E-03	0.85	1.14 (0.95-1.37)	1.7E-01	7.9E-06	5.3E-01
TP53INP1	rs7845219	8	96,006,678	T	C	0.53	1.08 (1.04-1.12)	3.2E-05	0.37	1.07 (1.01-1.13)	1.4E-02	0.42	1.07 (1.02-1.12)	4.9E-03	0.37	0.97 (0.84-1.12)	6.8E-01	6.4E-08	5.4E-01
C2CD4A	rs7163757	15	60,178,900	C	T	0.56	1.06 (1.02-1.11)	2.2E-03	0.46	1.12 (1.04-1.20)	2.0E-03	0.62	1.05 (1.00-1.11)	4.1E-02	0.52	1.05 (0.91-1.21)	5.1E-01	3.6E-06	5.5E-01
BCL11A	rs243088	2	60,422,249	T	A	0.46	1.09 (1.04-1.13)	2.6E-05	0.57	1.06 (1.00-1.13)	6.4E-02	0.53	1.04 (0.99-1.09)	1.1E-01	0.57	1.03 (0.89-1.20)	7.0E-01	3.2E-06	5.5E-01
DUSP8	rs2334499	11	1,653,425	T	C	0.40	1.07 (1.03-1.11)	1.3E-03	0.63	1.04 (0.98-1.10)	1.7E-01	0.28	1.02 (0.97-1.08)	4.2E-01	0.49	1.00 (0.87-1.15)	9.6E-01	1.0E-03	5.6E-01
SLC30A8	rs3802177	8	118,254,206	G	A	0.70	1.16 (1.11-1.22)	1.3E-10	0.64	1.11 (1.06-1.17)	2.6E-05	0.76	1.13 (1.07-1.19)	2.5E-05	0.75	1.14 (0.95-1.36)	1.5E-01	1.8E-18	6.2E-01
WFS1	rs4458523	4	6,340,887	G	T	0.59	1.09 (1.06-1.13)	5.8E-07	0.95	1.07 (0.96-1.20)	1.9E-01	0.68	1.07 (1.02-1.12)	1.0E-02	0.76	1.19 (1.01-1.39)	3.6E-02	2.1E-09	6.2E-01
ANKRD55	rs459193	5	55,842,508	G	A	0.74	1.05 (1.01-1.10)	2.7E-02	0.66	1.05 (1.00-1.11)	4.3E-02	0.64	1.03 (0.98-1.08)	2.7E-01	0.76	1.14 (0.97-1.34)	1.2E-01	8.9E-04	6.7E-01
TLE1	rs2796441	9	83,498,768	G	A	0.63	1.07 (1.03-1.12)	4.9E-04	0.51	1.10 (1.03-1.17)	6.1E-03	0.52	1.05 (1.00-1.10)	5.6E-02	0.51	1.07 (0.92-1.25)	3.6E-01	1.6E-06	7.7E-01
IRS1	rs2943640	2	226,801,829	C	A	0.63	1.09 (1.05-1.13)	4.8E-06	0.57	1.13 (1.02-1.25)	1.8E-02	0.76	1.09 (1.03-1.16)	6.3E-03	N/A	N/A	N/A	7.2E-09	7.9E-01
UBE2E2	rs7612463	3	23,311,454	C	A	0.87	1.10 (1.04-1.16)	1.6E-03	0.64	1.13 (1.06-1.20)	9.4E-05	0.78	1.09 (1.03-1.15)	3.7E-03	0.94	1.16 (0.86-1.56)	3.3E-01	6.7E-09	8.3E-01
HMG20A	rs7178572	15	75,534,245	G	A	0.70	1.08 (1.04-1.13)	1.9E-04	0.59	1.09 (1.04-1.14)	4.4E-04	0.52	1.10 (1.05-1.15)	4.2E-05	0.66	1.15 (0.99-1.33)	6.7E-02	1.5E-11	8.4E-01
ZMIZ1	rs12571751	10	80,612,637	A	G	0.51	1.09 (1.06-1.13)	7.1E-07	0.47	1.07 (1.00-1.13)	3.7E-02	0.57	1.08 (1.03-1.14)	1.4E-03	0.50	1.09 (0.95-1.25)	2.3E-01	2.4E-10	9.3E-01
ADCY5	rs11717195	3	124,565,088	T	C	0.78	1.09 (1.05-1.14)	2.6E-05	0.50	1.18 (0.67-2.05)	5.7E-01	0.78	1.10 (1.04-1.17)	9.9E-04	0.73	1.15 (0.98-1.36)	8.9E-02	2.2E-08	9.4E-01
MC4R	rs12970134	18	56,035,730	A	G	0.27	1.08 (1.03-1.12)	2.3E-04	0.37	1.07 (1.01-1.14)	3.0E-02	0.37	1.09 (1.04-1.15)	3.6E-04	0.15	1.06 (0.87-1.28)	5.6E-01	2.6E-08	9.5E-01
RND3	rs7560163	2	151,346,182	C	G	N/A	N/A	N/A	0.74	1.05 (0.90-1.22)	5.5E-01	0.97	1.05 (0.84-1.30)	6.9E-01	N/A	N/A	N/A	4.7E-01	9.9E-01
MAEA	rs6815464	4	1,299,901	C	G	N/A	N/A	N/A	0.47	1.10 (1.04-1.16)	4.3E-04	N/A	N/A	N/A	N/A	N/A	N/A	4.4E-04	N/A

Supplementary Table 4. Concordance in the direction of effect of T2D risk alleles identified in meta-analyses of GWAS of European (12,171 cases and 56,862 controls), East Asian (6,952 cases and 11,865 controls), South Asian (5,561 cases and 14,458 controls), and Mexican and Mexican American (1,804 cases and 779 controls) ancestry, after exclusion of the 69 established autosomal susceptibility loci, defined as mapping within 500kb of the previously reported lead SNP.

	Trans-ethnic concordance								
***p*-value threshold**	**Concordant SNPs / Total SNPs**	**%**	**Binomial test *p*-value**	**Concordant SNPs / Total SNPs**	**%**	**Binomial test *p*-value**	**Concordant SNPs / Total SNPs**	**%**	**Binomial test *p*-value**
European meta-analysis	**European into East Asian**			**European into South Asian**			**European into Mexican and Mexican American**		
p≤0.001	180/316	57.0	0.0077	175/316	55.4	0.032	179/316	56.6	0.010
0.001<*p*≤0.01	877/1624	54.0	0.00068	861/1624	53.0	0.0080	886/1624	54.6	0.00013
0.01<*p*≤0.5	2556/5053	50.6	0.21	2604/5053	51.5	0.015	2588/5053	51.2	0.043
0.5<*p*≤1	2535/5039	50.3	0.34	2532/5039	50.2	0.37	2519/5039	50.0	0.51
East Asian meta-analysis	**East Asian into European**			**East Asian into South Asian**			**East Asian into Mexican and Mexican American**		
p≤0.001	233/416	56.0	0.0081	220/416	52.9	0.13	214/416	51.4	0.29
0.001<*p*≤0.01	1117/2120	52.7	0.0071	1090/2120	51.4	0.10	1047/2120	49.4	0.72
0.01<*p*≤0.5	2549/5075	50.2	0.38	2661/5075	52.4	0.00028	2539/5075	50.0	0.49
0.5<*p*≤1	2561/5069	50.5	0.23	2555/5069	50.4	0.29	2563/5069	50.6	0.22
South Asian meta-analysis	**South Asian into European**			**South Asian into East Asian**			**South Asian into Mexican and Mexican American**		
p≤0.001	176/281	62.6	$1.4x10^{-5}$	153/281	54.4	0.076	150/281	53.4	0.14
0.001<*p*≤0.01	837/1552	53.9	0.0011	793/1552	51.1	0.20	788/1552	50.8	0.28
0.01<*p*≤0.5	2625/5045	52.0	0.0020	2558/5045	50.7	0.16	2575/5045	51.0	0.071
0.5<*p*≤1	2521/5037	50.0	0.48	2524/5037	50.1	0.44	2530/5037	50.2	0.38
Mexican and Mexican American meta-analysis	**Mexican and Mexican American into European**			**Mexican and Mexican American into East Asian**			**Mexican and Mexican American into South Asian**		
p≤0.001	155/282	55.0	0.054	143/282	50.7	0.43	151/282	53.5	0.13
0.001<*p*≤0.01	796/1501	53.0	0.010	763/1501	50.8	0.27	745/1501	49.6	0.62
0.01<*p*≤0.5	2542/5026	50.6	0.21	2518/5026	50.1	0.45	2542/5026	50.6	0.21
0.5<*p*≤1	2539/5025	50.5	0.23	2521/5025	50.2	0.41	2531/5025	50.4	0.31

Supplementary Table 5. T2D susceptibility loci attaining strong evidence of association ($p<10^{-5}$), not previously reported at genome-wide significance in any ancestry group, identified through trans-ethnic "discovery" GWAS meta-analysis of 26,488 cases and 83,964 controls of European, East Asian, South Asian, and Mexican and Mexican American ancestry, and follow-up in a "validation" meta-analysis of an additional 21,491 cases and 55,647 controls of European ancestry, genotyped with the Metabochip.

Locus	Lead SNP	Metabochip proxy SNP	HapMap r^2		Chr	Build 36 position (bp)	Alleles		Trans-ethnic "discovery" meta-analysis			European ancestry "validation" meta-analysis			Combined meta-analysis			
			CEU	CHB JPT			Risk	Other	Sample size	OR (95% CI)	*p*-value	Sample size	OR (95% CI)	*p*-value	Sample size	OR (95% CI)	*p*-value	Cochran's *Q* *p*-value
TMEM154	rs6813195				4	153,739,925	C	T	110,214	1.08 (1.05-1.11)	4.2E-09	51,425	1.08 (1.05-1.11)	2.0E-06	161,639	1.08 (1.06-1.10)	**4.1E-14**	9.6E-01
SSR1/RREB1	rs9502570	rs9505118	0.256	0.264	6	7,235,436	A	G	106,952	1.06 (1.04-1.09)	1.9E-06	51,396	1.06 (1.03-1.09)	1.7E-04	158,348	1.06 (1.04-1.08)	**1.4E-09**	7.7E-01
FAF1	rs17106184				1	50,682,573	G	A	110,157	1.11 (1.07-1.16)	1.9E-06	51,428	1.09 (1.04-1.15)	4.8E-04	161,585	1.10 (1.07-1.14)	**4.1E-09**	6.1E-01
POU5F1/TCF19	rs3132524	rs3130501	0.961	1.000	6	31,244,432	G	A	106,231	1.07 (1.04-1.10)	1.5E-06	49,584	1.06 (1.03-1.10)	7.0E-04	155,815	1.07 (1.04-1.09)	**4.2E-09**	7.9E-01
LPP	rs6808574				3	189,223,217	C	T	94,079	1.08 (1.04-1.11)	4.3E-06	46,008	1.06 (1.03-1.09)	2.6E-04	140,087	1.07 (1.04-1.09)	**5.8E-09**	4.8E-01
ARL15	rs702634				5	53,307,177	A	G	103,376	1.08 (1.05-1.11)	3.4E-07	51,421	1.05 (1.02-1.08)	2.1E-03	154,797	1.06 (1.04-1.09)	**6.9E-09**	1.7E-01
MPHOSPH9	rs1727313	rs4275659	0.476	0.039	12	122,013,881	C	T	110,015	1.06 (1.03-1.09)	5.5E-06	51,444	1.06 (1.02-1.09)	4.4E-04	161,459	1.06 (1.04-1.08)	**9.5E-09**	8.5E-01
PLEKHA1	rs10510110	rs2421016	1.000	1.000	10	124,157,502	C	T	107,847	1.05 (1.03-1.08)	1.9E-05	50,197	1.05 (1.02-1.08)	1.6E-03	158,044	1.05 (1.03-1.07)	1.1E-07	7.0E-01
TMEM75	rs1561927				8	129,637,260	C	T	104,569	1.08 (1.05-1.11)	1.9E-06	51,435	1.04 (1.01-1.08)	6.6E-03	156,004	1.06 (1.04-1.09)	1.2E-07	1.5E-01
TMEM18	rs10190052				2	636,674	C	T	104,516	1.09 (1.05-1.13)	7.5E-06	51,447	1.06 (1.02-1.10)	3.4E-03	155,963	1.07 (1.04-1.10)	1.5E-07	3.2E-01
RNF6	rs10507349				13	25,679,528	G	A	110,032	1.07 (1.04-1.09)	5.0E-06	51,447	1.05 (1.01-1.08)	6.7E-03	161,479	1.06 (1.04-1.08)	1.5E-07	4.6E-01
VEGFA	rs9472138				6	43,919,740	T	C	106,235	1.07 (1.04-1.10)	3.0E-06	51,450	1.04 (1.01-1.07)	8.8E-03	157,685	1.06 (1.04-1.08)	2.0E-07	2.0E-01
ETV1	rs7795991				7	13,867,256	G	A	99,500	1.07 (1.04-1.10)	1.7E-06	51,446	1.03 (1.00-1.06)	3.1E-02	150,946	1.05 (1.03-1.07)	7.1E-07	8.4E-02
PCBD2	rs319598				5	134,268,134	C	T	104,492	1.06 (1.04-1.09)	7.7E-07	51,425	1.02 (0.99-1.05)	1.3E-01	155,917	1.05 (1.03-1.07)	2.2E-06	3.6E-02
LYPLAL1	rs2820446				1	217,815,441	C	G	110,143	1.06 (1.04-1.09)	6.9E-06	51,390	1.03 (1.00-1.06)	4.3E-02	161,533	1.05 (1.03-1.07)	2.3E-06	1.6E-01
C6orf173	rs4273712				6	127,006,203	G	A	100,585	1.07 (1.04-1.10)	1.2E-06	51,447	1.02 (0.99-1.06)	1.3E-01	152,032	1.05 (1.03-1.07)	3.0E-06	4.3E-02
C10orf35	rs2812533	rs17578395	0.671	0.373	10	71,085,247	C	A	107,876	1.08 (1.05-1.12)	3.9E-06	26,019	1.03 (0.99-1.08)	1.8E-01	133,895	1.07 (1.04-1.09)	5.0E-06	1.3E-01
IL20RA	rs6937795	rs4407733	1.000	1.000	6	137,340,845	A	G	102,178	1.06 (1.03-1.09)	8.9E-06	49,574	1.03 (1.00-1.06)	7.5E-02	151,752	1.04 (1.02-1.06)	6.6E-06	1.1E-01
CRHR2	rs2284219	rs2284218	1.000	0.888	7	30,680,858	T	C	94,286	1.07 (1.04-1.10)	2.5E-06	26,033	1.02 (0.98-1.06)	3.0E-01	120,319	1.05 (1.03-1.08)	7.7E-06	7.3E-02
PTEN	rs10788575				10	89,758,564	A	G	110,091	1.08 (1.04-1.11)	2.3E-06	51,440	1.02 (0.98-1.07)	2.7E-01	161,531	1.06 (1.03-1.08)	8.7E-06	5.3E-02
CPNE4	rs6792706	rs9840453	1.000	0.955	3	133,260,155	T	G	98,256	1.08 (1.05-1.12)	3.1E-06	51,395	1.03 (0.99-1.06)	1.3E-01	149,651	1.05 (1.03-1.08)	1.2E-05	2.7E-02
THRAP2	rs7133159	rs10774811	0.799	0.602	12	114,349,025	T	C	103,559	1.06 (1.03-1.09)	4.2E-05	51,447	1.03 (1.00-1.06)	7.3E-02	155,006	1.04 (1.02-1.06)	2.4E-05	1.5E-01
MSRA	rs17150816				8	9,828,147	C	A	61,864	1.27 (1.15-1.41)	5.5E-06	51,450	1.06 (0.99-1.13)	8.1E-02	113,314	1.12 (1.06-1.18)	9.3E-05	3.7E-03
PFTK1	rs17163563				7	90,546,497	A	G	78,195	1.19 (1.11-1.28)	2.9E-06	51,439	1.03 (0.98-1.08)	2.8E-01	129,634	1.08 (1.03-1.12)	3.9E-04	1.2E-03
SLIT3	rs11739950				5	168,346,952	A	G	70,709	1.29 (1.16-1.43)	2.5E-06	50,417	1.03 (0.94-1.12)	5.5E-01	121,126	1.12 (1.05-1.20)	6.4E-04	9.7E-04
WNK2	rs10761209	rs10821106	1.000	0.935	9	95,100,580	T	C	104,496	1.06 (1.03-1.09)	1.5E-05	50,409	1.02 (0.99-1.05)	2.4E-01	154,905	1.03 (1.01-1.05)	9.7E-03	2.4E-04
PKP1	rs6427896	N/A																
ATP2B2	rs13071035	N/A																
PLAC9	rs7088994	N/A																
C14orf174	rs11844594	N/A																
LAMA1	rs9948462	N/A																
APOC1	rs4420638	N/A																
C20orf166	rs6062238	N/A																

Supplementary Table 6. Association summary statistics in each ancestry group (European, East Asian, South Asian, and Mexican and Mexican American) for lead SNPs at novel T2D susceptibility loci identified through fixed-effects trans-ethnic GWAS meta-analysis of 26,488 cases and 83,964 controls.

				Alleles		European 12,171 cases and 56,862 controls			East Asian 6,952 cases and 11,865 controls			South Asian 5,561 cases and 14,458 controls			Mexican and Mexican American 1,804 cases and 779 controls			Stage 1 trans-ethnic meta-analysis	
Locus	Lead SNP	Chr	Build 36 position (bp)	Risk	Other	RAF	OR (95% CI)	*p*-value	RAF	OR (95% CI)	*p*-value	RAF	OR (95% CI)	*p*-value	RAF	OR (95% CI)	*p*-value	*p*-value	Cochran's *Q* *p*-value
TMEM154	rs6813195	4	153,739,925	C	T	0.71	1.08 (1.04-1.12)	1.4E-04	0.39	1.10 (1.05-1.15)	1.1E-04	0.62	1.05 (1.00-1.11)	3.4E-02	0.63	1.11 (0.96-1.28)	1.6E-01	4.2E-09	6.8E-01
POU5F1/TCF19	rs3132524	6	31,244,693	C	T	0.73	1.08 (1.04-1.12)	1.1E-04	0.43	1.03 (0.98-1.09)	2.0E-01	0.70	1.08 (1.03-1.14)	2.5E-03	0.76	1.19 (1.01-1.40)	3.7E-02	2.5E-07	3.2E-01
ARL15	rs702634	5	53,307,177	A	G	0.67	1.08 (1.04-1.12)	4.3E-05	0.75	1.10 (1.00-1.20)	4.2E-02	0.77	1.07 (1.01-1.13)	2.4E-02	0.86	1.06 (0.87-1.29)	5.5E-01	3.4E-07	9.7E-01
SSR1/RREB1	rs9502570	6	7,203,616	C	T	0.73	1.08 (1.03-1.12)	1.1E-03	0.35	1.05 (1.00-1.11)	7.0E-02	0.61	1.09 (1.04-1.14)	5.1E-04	0.75	1.03 (0.85-1.21)	7.5E-01	5.7E-07	7.7E-01
MPHOSPH9	rs1727313	12	122,206,806	G	C	0.78	1.07 (1.03-1.12)	9.4E-04	0.53	1.20 (1.03-1.41)	2.1E-02	0.74	1.08 (1.02-1.14)	4.6E-03	0.77	1.10 (0.93-1.30)	2.5E-01	1.2E-06	5.9E-01
FAF1	rs17106184	1	50,682,573	G	A	0.91	1.10 (1.04-1.16)	1.8E-03	0.58	1.14 (1.05-1.22)	2.7E-03	0.94	1.08 (0.98-1.19)	1.3E-01	0.95	1.36 (1.06-1.66)	4.7E-02	1.9E-06	5.2E-01
LPP	rs6808574	3	189,223,217	C	T	0.60	1.08 (1.03-1.12)	2.6E-04	0.98	1.13 (0.85-1.51)	4.1E-01	0.76	1.05 (0.99-1.10)	1.1E-01	0.82	1.49 (1.23-1.80)	3.4E-05	4.3E-06	5.5E-03

Supplementary Table 7. Association summary statistics from the European ancestry validation meta-analysis, stratified according to covariate adjustment: (i) studies that account only for age, sex (unless male- or female-specific), and population structure where necessary (11,327 cases and 31,342 controls); and (ii) all other studies (10,164 cases and 24,305 controls).

Locus	Lead SNP	Chr	Build 36 position (bp)	Alleles[a]		Studies adjusting for age, sex and population structure		Other studies		Cochran's *Q* statistic *p*-value
				Risk	Other	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	
TMEM154	rs6813195	4	153,739,925	C	T	1.08 (1.04-1.12)	1.4E-04	1.08 (1.03-1.12)	1.1E-03	8.6E-01
SSR1/RREB1	rs9505118	6	7,235,436	A	G	1.07 (1.03-1.10)	6.2E-04	1.04 (1.01-1.08)	3.6E-02	4.0E-01
FAF1	rs17106184	1	50,682,573	G	A	1.06 (0.99-1.12)	1.2E-01	1.14 (1.07-1.20)	1.5E-04	7.9E-02
POU5F1/TCF19	rs3130501	6	31,244,432	G	A	1.06 (1.02-1.10)	7.0E-03	1.06 (1.01-1.11)	1.8E-02	9.6E-01
LPP	rs6808574	3	189,223,217	C	T	1.06 (1.02-1.10)	8.6E-03	1.06 (1.02-1.10)	4.2E-03	8.9E-01
ARL15	rs702634	5	53,307,177	A	G	1.03 (0.99-1.07)	1.7E-01	1.08 (1.04-1.12)	5.1E-04	7.5E-02
MPHOSPH9	rs4275659	12	122,013,881	C	T	1.07 (1.03-1.11)	5.7E-04	1.04 (1.00-1.08)	9.8E-02	2.3E-01

.

Supplementary Table 8. T2D association summary statistics for lead SNPs at T1D susceptibility loci identified through fixed-effects trans-ethnic GWAS meta-analysis of 26,488 cases and 83,964 controls.

Locus	T1D lead SNP	Chr	Build 36 position (bp)	Alleles		T2D association	
				T1D risk	Other	OR (95% CI)	p-value
GLIS3	rs10758593	9	4,282,083	A	G	1.07 (1.04-1.10)	5.1E-07
6q22.32	rs9388489	6	126,740,412	G	A	1.06 (1.03-1.08)	9.8E-05
16q23.1	rs7202877	16	73,804,746	G	T	0.93 (0.89-0.97)	5.7E-04
7p12.1	rs4948088	7	50,994,688				1.5E-02
LMO7	rs539514	13	75,224,283	T	A	0.97 (0.95-1.00)	8.8E-02
10q23.31	rs10509540	10	90,013,013	T	C	0.98 (0.95-1.00)	9.3E-02
14q24.1	rs1465788	14	68,333,352	C	T	1.02 (1.00-1.05)	9.4E-02
IL2RA	rs12251307	10	6,163,501	C	T	1.02 (0.99-1.06)	1.3E-01
IL2	rs4505848	4	123,351,942	G	A	1.02 (0.99-1.05)	1.8E-01
PRKCQ	rs11258747	10	6,512,897	T	G	0.98 (0.95-1.01)	2.0E-01
AFF3	rs9653442	2	100,191,799	C	T	1.01 (0.99-1.04)	2.6E-01
IL27	rs4788084	16	28,447,349	C	T	0.98 (0.96-1.01)	2.6E-01
CYP27B1	rs10877012	12	56,448,352				3.0E-01
INS	rs3741208	11	2,126,350	A	G	0.98 (0.95-1.02)	3.1E-01
STAT4	rs7574865	2	191,672,878	T	G	1.01 (0.99-1.04)	3.1E-01
BACH2	rs3757247	6	91,014,184	T	C	0.99 (0.96-1.01)	3.3E-01
ORMDL3	rs2290400	17	35,319,766	C	T	0.99 (0.96-1.02)	3.3E-01
HLA	rs9268645	6	32,516,505	G	C	1.01 (0.99-1.04)	3.3E-01
19q13.32	rs425105	19	51,900,321	T	C	0.98 (0.95-1.02)	3.8E-01
12q13.2	rs1701704	12	54,698,754	G	T	0.99 (0.96-1.02)	3.8E-01
14q32.2	rs4900384	14	97,568,704	G	A	1.01 (0.99-1.04)	4.1E-01
RGS1	rs2816316	1	190,803,436	A	C	1.01 (0.98-1.05)	4.1E-01
PTPN22	rs2476601	1	114,179,091	A	G	1.02 (0.97-1.08)	4.2E-01
RASGRP1	rs17574546	15	36,689,768	C	A	1.01 (0.98-1.05)	4.2E-01
CTLA4	rs3087243	2	204,447,164	G	A	0.99 (0.97-1.02)	4.6E-01
GPR183	rs9585056	13	98,879,767	C	T	0.99 (0.96-1.02)	4.7E-01
DLK1	rs941576	14	100,375,798	A	G	1.01 (0.98-1.04)	4.8E-01
4p15.2	rs10517086	4	25,694,609	A	G	1.01 (0.98-1.05)	4.8E-01
SKAP2	rs7804356	7	26,858,190	T	C	1.01 (0.98-1.04)	5.2E-01
CD226	rs763361	18	65,682,622	T	C	1.01 (0.98-1.03)	5.7E-01
IFIH1	rs1990760	2	162,832,297	T	C	0.99 (0.97-1.02)	5.9E-01
IL10	rs3024505	1	205,006,527	G	A	0.99 (0.95-1.03)	6.1E-01
22q12.2	rs5753037	22	28,911,722	T	C	1.01 (0.98-1.03)	6.4E-01
PTPN2	rs478582	18	12,825,976	T	C	0.99 (0.97-1.02)	6.5E-01
TNFAIP3	rs10499194	6	138,044,330	C	T	0.99 (0.96-1.02)	6.6E-01
15q25.1	rs3825932	15	77,022,501	C	T	0.99 (0.97-1.02)	6.7E-01
SH2B3	rs3184504	12	110,368,991	T	C	1.01 (0.97-1.04)	7.0E-01
EFR3B	rs478222	2	25,155,259	A	T	1.00 (0.98-1.03)	7.1E-01
20p13	rs2281808	20	1,558,551	C	T	0.99 (0.97-1.02)	7.2E-01
12p13.31	rs4763879	12	9,801,431	A	G	1.00 (0.98-1.03)	7.5E-01
6q27	rs924043	6	170,220,950	C	T	1.00 (0.96-1.03)	7.6E-01
TAGAP	rs1738074	6	159,385,965	C	T	1.00 (0.97-1.02)	8.2E-01
17q21.2	rs7221109	17	36,023,812	C	T	1.00 (0.98-1.03)	8.5E-01
UBASH3A	rs9976767	21	42,709,459	G	A	1.00 (0.98-1.03)	8.5E-01
TYK2	rs2304256	19	10,336,652				9.7E-01
IL2RB	rs229541	22	35,921,264	A	G	1.00 (0.98-1.02)	9.7E-01
CCRS	rs11711054	3	46,320,615	G	A	1.00 (0.97-1.03)	9.7E-01
16p13.13	rs2903692	16	11,146,284	G	A	1.00 (0.97-1.03)	9.7E-01

Supplementary Table 9. Association summary statistics for lead SNPs at novel T2D susceptibility loci in a meta-analysis of glycaemic traits in non-diabetic individuals of European descent from the MAGIC Investigators.

(a) Fasting glucose (FG) and fasting glucose adjusted for body-mass index (FGadjBMI) in up to 133,010 individuals.

Locus	Lead SNP	Chr	Build 36 position (bp)	Alleles		FG				FGadjBMI			
				Risk	Other	***N***	***β***	SE	***p*-value**	***N***	***β***	SE	***p*-value**
TMEM154	rs6813195	4	153,739,925	C	T	131,758	-0.0015	0.0023	5.3E-01	123,101	-0.0045	0.0024	6.1E-02
SSR1/RREB1	rs9505118	6	7,235,436	A	G	132,932	0.0091	0.0021	1.0E-05	123,203	0.0084	0.0022	1.2E-04
FAF1	rs17106184	1	50,682,573	G	A	133,005	0.0089	0.0036	1.4E-02	123,259	0.0072	0.0038	6.0E-02
POU5F1/TCF19	rs3130501	6	31,244,432	G	A	131,862	0.0001	0.0024	9.7E-01	123,243	0.0005	0.0025	8.3E-01
LPP	rs6808574	3	189,223,217	C	T	115,536	0.0113	0.0023	8.6E-07	107,010	0.0114	0.0024	2.5E-06
ARL15	rs702634	5	53,307,177	A	G	127,759	0.0041	0.0022	6.4E-02	117,917	0.0049	0.0023	3.7E-02
MPHOSPH9	rs4275659	12	122,013,881	C	T	132,968	-0.0030	0.0022	1.8E-01	123,216	-0.0022	0.0023	3.5E-01

(b) Fasting insulin (FI) and fasting insulin adjusted for body-mass index (FIadjBMI) in up to 108,557 individuals.

Locus	Lead SNP	Chr	Build 36 position (bp)	Alleles		FI				FIadjBMI			
				Risk	Other	***N***	***β***	SE	***p*-value**	***N***	***β***	SE	***p*-value**
TMEM154	rs6813195	4	153,739,925	C	T	107,414	-0.0048	0.0027	7.4E-02	103,342	-0.0036	0.0023	1.1E-01
SSR1/RREB1	rs9505118	6	7,235,436	A	G	108,480	-0.0022	0.0024	3.6E-01	103,434	-0.0007	0.0021	7.4E-01
FAF1	rs17106184	1	50,682,573	G	A	108,555	0.0031	0.0042	4.7E-01	103,492	0.0008	0.0037	8.3E-01
POU5F1/TCF19	rs3130501	6	31,244,432	G	A	107,507	0.0021	0.0027	4.4E-01	103,473	0.0050	0.0024	3.2E-02
LPP	rs6808574	3	189,223,217	C	T	93,485	-0.0023	0.0027	3.9E-01	89,488	0.0000	0.0023	1.0E+00
ARL15	rs702634	5	53,307,177	A	G	103,440	0.0140	0.0026	4.5E-08	98,281	0.0151	0.0022	5.0E-12
MPHOSPH9	rs4275659	12	122,013,881	C	T	108,549	0.0039	0.0026	1.3E-01	103,480	0.0040	0.0022	7.2E-02

(c) Homeostatic model of assessment indices of beta-cell function (HOMA-B) and insulin resistance (HOMA-IR) in up to 37,037 individuals.

Locus	**Lead SNP**	**Chr**	**Build 36 position (bp)**	**Alleles**		**HOMA-B**				**HOMA-IR**			
				Risk	**Other**	***N***	***β***	**SE**	***p*-value**	***N***	***β***	**SE**	***p*-value**
TMEM154	rs6813195	4	153,739,925	C	T	35,361	-0.0024	0.0038	5.4E-01	35,827	-0.0052	0.0047	2.6E-01
SSR1/RREB1	rs9505118	6	7,235,436	A	G	36,439	-0.0052	0.0033	1.1E-01	37,010	-0.0020	0.0040	6.2E-01
FAF1	rs17106184	1	50,682,573	G	A	36,466	-0.0082	0.0060	1.7E-01	37,037	-0.0042	0.0070	5.5E-01
POU5F1/TCF19	rs3130501	6	31,244,432	G	A	35,437	-0.0017	0.0038	6.5E-01	35,903	-0.0012	0.0046	7.9E-01
LPP	rs6808574	3	189,223,217	C	T	35,428	-0.0086	0.0034	1.1E-02	35,894	-0.0021	0.0041	6.1E-01
ARL15	rs702634	5	53,307,177	A	G	36,449	0.0060	0.0035	8.7E-02	37,020	0.0099	0.0043	2.1E-02
MPHOSPH9	rs4275659	12	122,013,881	C	T	36,459	0.0038	0.0036	2.9E-01	37,030	-0.0024	0.0044	5.9E-01

Supplementary Table 10. Association summary statistics for lead SNPs at novel T2D susceptibility loci in a meta-analysis of body-mass index (BMI) and waist-hip ratio adjusted for body-mass index (WHRadjBMI) in up to 123,865 and 77,167 individuals, respectively, of European ancestry from the GIANT Consortium.

			Build 36 position (bp)	Alleles		BMI				WHRadjBMI			
Locus	**Lead SNP**	**Chr**		**Risk**	**Other**	***N***	***β***	**SE**	***p*-value**	***N***	***β***	**SE**	***p*-value**
TMEM154	rs6813195	4	153,739,925	C	T	123,768	-0.0057	0.0054	2.9E-01	77,077	0.0048	0.0052	3.9E-01
SSR1/RREB1	rs9505118	6	7,235,436	A	G	123,744	-0.0017	0.0047	7.2E-01	77,048	-0.0111	0.0046	2.1E-02
FAF1	rs17106184	1	50,682,573	G	A	123,778	-0.0171	0.0080	3.4E-02	77,159	0.0136	0.0078	9.7E-02
POU5F1/TCF19	rs3130501	6	31,244,432	G	A	123,830	-0.0133	0.0053	1.3E-02	77,152	0.0065	0.0052	2.3E-01
LPP	rs6808574	3	189,223,217	C	T	123,829	0.0095	0.0048	4.9E-02	77,162	0.0120	0.0047	1.4E-02
ARL15	rs702634	5	53,307,177	A	G	123,791	-0.0205	0.0051	5.6E-05	77,100	-0.0041	0.0049	4.2E-01
MPHOSPH9	rs4275659	12	122,013,881	C	T	123,839	-0.0129	0.0052	1.3E-02	77,149	0.0012	0.0050	8.1E-01

Supplementary Table 11. Association summary statistics for lead SNPs at novel T2D susceptibility loci in a meta-analysis of lipid traits in up to 100,184 individuals of European ancestry from the Global Lipids Genetics Consortium.

			Build 36 position (bp)	Alleles		Total cholesterol			High-density lipoprotein			Low-density lipoprotein			Triglycerides		
Locus	**Lead SNP**	**Chr**		**Risk**	**Other**	***N***	***Z*-score**	***p*-value**	***N***	***Z*-score**	***p*-value**	***N***	***Z*-score**	***p*-value**	***N***	***Z*-score**	***p*-value**
TMEM154	rs6813195	4	153,739,925	C	T	100,065	-0.114	9.1E-01	99,787	-1.271	2.0E-01	95,341	-0.159	8.7E-01	96,479	0.033	9.7E-01
SSR1/RREB1	rs9505118	6	7,235,436	A	G	100,117	-0.147	8.8E-01	99,832	0.147	8.8E-01	95,389	-0.427	6.7E-01	96,530	0.450	6.5E-01
FAF1	rs17106184	1	50,682,573	G	A	100,183	1.399	1.6E-01	99,899	0.087	9.3E-01	95,454	0.306	7.6E-01	96,597	2.007	4.5E-02
POU5F1/TCF19	rs3130501	6	31,244,432	G	A	97,134	4.160	3.2E-05	96,895	0.857	3.9E-01	92,490	2.592	9.5E-03	93,548	3.140	1.7E-03
LPP	rs6808574	3	189,223,217	C	T	100,184	-0.008	9.9E-01	99,900	-0.788	4.3E-01	95,454	0.273	7.9E-01	96,598	-0.076	9.4E-01
ARL15	rs702634	5	53,307,177	A	G	100,115	1.299	1.9E-01	99,837	-2.287	2.2E-02	95,391	0.762	4.5E-01	96,529	2.563	1.0E-02
MPHOSPH9	rs4275659	12	122,013,881	C	T	100,159	-1.756	7.9E-02	99,877	-1.820	6.9E-02	95,431	-1.167	2.4E-01	96,573	0.995	3.2E-01

Supplementary Table 12. Evidence for *cis*-eQTL expression with lead T2D SNPs at novel T2D susceptibility loci in multiple tissues from public databases and unpublished resources.

Locus	Lead SNP	Chr	Build 36 position (bp)	Transcript	Tissue	*p*-value	Lead *cis*-eQTL SNP					
							SNP	Chr	Build 36 position (bp)	CEU r^2	CHB+JPT r^2	*p*-value
SSR1/RREB1	rs9505118	6	7,235,436	*SSR1*	B cells (CD19+)	2.2E-06	rs1050226	6	7,226,653	0.965	1.000	2.1E-06
POU5F1/TCF19	rs3130501	6	31,244,432	*HCG27*	Blood	8.8E-20	rs9263871	6	31,278,507	0.028	0.545	5.2E-62
				HCG22	LCL	1.9E-16	rs2517552	6	31,115,569	0.426	0.000	2.9E-34
				AL662833.4	Lymph	2.6E-06	rs1265112	6	31,225,998	0.207	0.042	5.3E-29
				HCG27	Monocytes	1.3E-69	Same SNP					
				HLA-DRB5	Monocytes	1.7E-33	rs3129868	6	32,278,507	N/A	N/A	1.0E-320
				HLA-C	Monocytes	7.5E-15	rs4394274	6	31,426,143	N/A	N/A	2.6E-158
				HLA-DRB1	Monocytes	8.3E-15	rs2395166	6	32,496,253	N/A	N/A	4.0E-192
MPHOSPH9	rs4275659	12	122,013,881	*ABCB9*	Liver	7.4E-12	Same SNP					
				SETD8	Lung	2.0E-16	Same SNP					

Supplementary Table 13. Potential functional variants in pilot data from the 1000 Genomes Project that are in strong LD (CEU and CHB+JPT r^2>0.8) with the lead SNPs in the novel susceptibility loci.

Locus	Lead SNP	Chr	Build 36 position (bp)	Functional proxy SNP						
				SNP	Chr	Build 36 position (bp)	CEU r^2	CHB+JPT r^2	Gene	Annotation
SSR1/RREB1	rs9505118	6	7,235,436	rs1050226	6	7,226,653	0.97	0.93	*SSR1*	3'-UTR
				rs8955	6	7,233,296	1.00	1.00	*SSR1*	3'-UTR
				rs11071	6	7,233,543	1.00	0.94	*SSR1*	3'-UTR
				rs3087986	6	7,234,165	1.00	1.00	*SSR1*	3'-UTR
POU5F1/TCF19	rs3130501	6	31,244,432	rs113581344	6	31,237,595	0.96	0.80	*TCF19*	Missense
MPHOSPH9	rs4275659	12	122,013,881	rs61955196	12	122,016,971	0.92	1.00	*ABCB9*	5'-UTR
				rs3759115	12	122,030,232	0.92	0.97	*OGFOD2*	3'-UTR
				rs3741530	12	122,035,600	0.92	0.81	*PITPNM2*	3'-UTR

Supplementary Table 14. Properties of the 99% credible set at ten established T2D susceptibility loci as a function of SNP quality on the basis of association summary statistics from the trans-ethnic meta-analysis of European, East Asian, South Asian and Mexican American ancestry GWAS (26,488 cases and 83,964 controls) for three subsets of variants: (i) all SNPs; (ii) SNPs reported in at least 80% (*N*=88,361) individuals; and (iii) SNPs reported in at least 90% (*N*=99,406) individuals.

		99% credible set: all SNPs			99% credible set: SNPs reported for ≥80% of individuals			99% credible set: SNPs reported for ≥90% of individuals		
Locus	**Chr**	**SNPs**	**Interval (bp)**	**Build 36 location (bp)**	**SNPs**	**Interval (bp)**	**Build 36 location (bp)**	**SNPs**	**Interval (bp)**	**Build 36 location (bp)**
JAZF1	7	4	15,667	28,147,081-28,162,747	4	15,667	28,147,081-28,162,747	4	15,667	28,147,081-28,162,747
SLC30A8	8	2	243	118,253,964-118,254,206	2	243	118,253,964-118,254,206	2	243	118,253,964-118,254,206
CDKAL1	6	2	1,549	20,794,552-20,796,100	2	1,549	20,794,552-20,796,100	2	1,549	20,794,552-20,796,100
HHEX/IDE	10	2	937	94,455,539-94,456,475	2	937	94,455,539-94,456,475	2	937	94,455,539-94,456,475
TCF7L2	10	2	2,309	114,746,031-114,748,339	2	2,309	114,746,031-114,748,339	2	2,309	114,746,031-114,748,339
IGF2BP2	3	12	24,504	186,988,481-187,012,984	12	24,504	186,988,481-187,012,984	12	24,504	186,988,481-187,012,984
FTO	16	10	39,335	52,361,075-52,400,409	10	39,335	52,361,075-52,400,409	10	39,335	52,361,075-52,400,409
CDKN2A/B	9	1	1	22,122,076-22,122,076	1	1	22,122,076-22,122,076	1	1	22,122,076-22,122,076
PPARG	3	21	265,269	12,106,687-12,371,955	21	265,269	12,106,687-12,371,955	17	265,269	12,106,687-12,371,955
MTNR1B	11	15	55,032	92,307,378-92,362,409	13	55,032	92,307,378-92,362,409	7	55,032	92,307,378-92,362,409

Genome-wide trans-ethnic meta-analysis reveals novel insights into the genetic architecture of type 2 diabetes susceptibility

DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) Consortium, Asian Genetic Epidemiology Network Type 2 Diabetes (AGEN-T2D) Consortium, South Asian Type 2 Diabetes (SAT2D) Consortium, Mexican American Type 2 Diabetes (MAT2D) Consortium and Type 2 Diabetes Genetic Exploration by Next-generation sequencing in multi-Ethnic Samples (T2D-GENES) Consortium

SUPPLEMENTARY NOTE

Membership of the DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) Consortium

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Andrew P Morris[1], Benjamin F Voight[2,3], Tanya M Teslovich[4], Teresa Ferreira[1], Ayellet V Segrè[2,5,6], Valgerdur Steinthorsdottir[7], Rona J Strawbridge[8,9], Hassan Khan[10], Harald Grallert[11], Anubha Mahajan[1], Inga Prokopenko[1,12], Hyun Min Kang[4], Christian Dina[13–15], Tonu Esko[16,17], Ross M Fraser[18], Stavroula Kanoni[19], Ashish Kumar[1], Vasiliki Lagou[1], Claudia Langenberg[20], Jian'an Luan[20], Cecilia M Lindgren[1], Martina Müller-Nurasyid[21–23], Sonali Pechlivanis[24], N William Rayner[1,12], Laura J Scott[4], Steven Wiltshire[1], Loic Yengo[25,26], Leena Kinnunen[27], Elizabeth J Rossin[2,5,28,29], Soumya Raychaudhuri[2,30,31], Andrew D Johnson[32], Antigone S Dimas[1,33,34], Ruth J F Loos[20,35–37], Sailaja Vedantam[38,39], Han Chen[40], Jose C Florez[5,6,38,41], Caroline Fox[32,42], Ching-Ti Liu[40], Denis Rybin[43], David J Couper[44], Wen Hong L Kao[45], Man Li[45], Marilyn C Cornelis[46], Peter Kraft[46,47], Qi Sun[46,48], Rob M van Dam[46,49], Heather M Stringham[4], Peter S Chines[50], Krista Fischer[16], Pierre Fontanillas[2], Oddgeir L Holmen[51], Sarah E Hunt[19], Anne U Jackson[4], Augustine Kong[7], Robert Lawrence[52], Julia Meyer[22], John R B Perry[1,53], Carl G P Platou[51,54], Simon Potter[19], Emil Rehnberg[55], Neil Robertson[1,12], Suthesh Sivapalaratnam[56], Alena Stančáková[57], Kathleen Stirrups[19], Gudmar Thorleifsson[7], Emmi Tikkanen[58,59], Andrew R Wood[53], Peter Almgren[60], Mustafa Atalay[61], Rafn Benediktsson[62,63], Lori L Bonnycastle[50], Noël Burtt[2], Jason Carey[2], Guillaume Charpentier[64], Andrew T Crenshaw[2], Alex S F Doney[65,66], Mozhgan Dorkhan[60], Sarah Edkins[19], Valur Emilsson[67], Elodie Eury[25], Tom Forsen[68,69], Karl Gertow[8,9], Bruna Gigante[70], George B Grant[2], Christopher J Groves[12], Candace Guiducci[2], Christian Herder[71], Astradur B Hreidarsson[63], Jennie Hui[72–75], Alan James[72,76,77], Anna Jonsson[60], Wolfgang Rathmann[78], Norman Klopp[11], Jasmina Kravic[60], Kaarel Krjutškov[16], Cordelia Langford[19], Karin Leander[70], Eero Lindholm[60], Stéphane Lobbens[25], Satu Männistö[59], Ghazala Mirza[1], Thomas W Mühleisen[79,80], Bill Musk[72,75,77,81], Melissa Parkin[2], Loukianos Rallidis[82], Jouko Saramies[83], Bengt Sennblad[8,9], Sonia Shah[84], Gunnar Sigurðsson[63,67], Angela Silveira[8,9], Gerald Steinbach[85], Barbara Thorand[86], Joseph Trakalo[1], Fabrizio Veglia[87], Roman Wennauer[85], Wendy Winckler[2], Delilah Zabaneh[84], Harry Campbell[18,88], Cornelia van Duijn[89,90], Andre G Uitterlinden[89–91], Albert Hofman[89], Eric Sijbrands[91], Goncalo R Abecasis[4], Katharine R Owen[12,92], Eleftheria Zeggini[19], Mieke D Trip[56], Nita G Forouhi[20], Ann-Christine Syvänen[93], Johan G Eriksson[59,68,94,95], Leena Peltonen[138], Markus M Nöthen[79,80], Beverley Balkau[96,97], Colin N A Palmer[65,66], Valeriya Lyssenko[60], Tiinamaija Tuomi[95,98], Bo Isomaa[95,99], David J Hunter[46–48], Lu Qi[46,48], Alan R Shuldiner[100–102], Michael Roden[71,103], Ines Barroso[19,104,105], Tom Wilsgaard[106], John Beilby[72–74], Kees Hovingh[56], Jackie F Price[18], James F Wilson[18,88], Rainer Rauramaa[107,108], Timo A Lakka[61,107], Lars Lind[109], George Dedoussis[110], Inger Njølstad[106], Nancy L Pedersen[55], Kay-Tee Khaw[10], Nicholas J Wareham[20], Sirkka M Keinanen-Kiukaanniemi[111,112], Timo E Saaristo[113,114], Eeva Korpi-Hyövälti[115], Juha Saltevo[116], Markku Laakso[57], Johanna Kuusisto[57], Andres Metspalu[16,17], Francis S Collins[50], Karen L Mohlke[117], Richard N Bergman[118], Jaakko Tuomilehto[27,115,119,120], Bernhard O Boehm[121], Christian Gieger[22], Kristian Hveem[51], Stephane Cauchi[25], Philippe Froguel[25,122], Damiano Baldassarre[87,123], Elena Tremoli[87,123], Steve E Humphries[124], Danish Saleheen[10,125], John Danesh[10], Erik Ingelsson[55], Samuli Ripatti[19,58,59], Veikko Salomaa[59], Raimund Erbel[126], Karl-Heinz Jöckel[24], Susanne Moebus[24], Annette Peters[86], Thomas Illig[11,127], Ulf de Faire[70], Anders Hamsten[8,9], Andrew D Morris[65,66], Peter J Donnelly[1,128], Timothy M Frayling[53], Andrew T

Hattersley[129], Eric Boerwinkle[130,131], Olle Melander[60], Sekar Kathiresan[2,5,132], Peter M Nilsson[60], Panos Deloukas[19], Unnur Thorsteinsdottir[7,62], Leif C Groop[60], Kari Stefansson[7,62], Frank Hu[46,48], James S Pankow[133], Josée Dupuis[32,40], James B Meigs[6,134], David Altshuler[2,5,6,135–137], Michael Boehnke[4], and Mark I McCarthy[1,12,92]

[1]Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK. [2]Broad Institute of Harvard and Massachusetts Institute of Technology (MIT), Cambridge, Massachusetts, USA. [3]Department of Pharmacology, University of Pennsylvania–Perelman School of Medicine, Philadelphia, Pennsylvania, USA. [4]Department of Biostatistics, University of Michigan, Ann Arbor, Michigan, USA. [5]Center for Human Genetic Research, Massachusetts General Hospital, Boston, Massachusetts, USA. [6]Department of Medicine, Harvard Medical School, Boston, Massachusetts, USA. [7]deCODE Genetics, Reykjavik, Iceland. [8]Atherosclerosis Research Unit, Department of Medicine Solna, Karolinska Institutet, Stockholm, Sweden. [9]Center for Molecular Medicine, Karolinska University Hospital Solna, Stockholm, Sweden. [10]Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK. [11]Research Unit of Molecular Epidemiology, Helmholtz Zentrum Muenchen, Neuherberg, Germany. [12]Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, UK. [13]Institut National de la Santé et de la Recherche Médicale (INSERM) Unité Mixte de Recherche (UMR) 1087, Nantes, France. [14]Centre National de la Recherche Scientifique (CNRS) UMR 6291, Nantes, France. [15]Department of Biology, Medicine and Health, Nantes University, Nantes, France. [16]Estonian Genome Center, University of Tartu, Tartu, Estonia. [17]Institute of Molecular and Cell Biology, University of Tartu, Tartu, Estonia. [18]Centre for Population Health Sciences, University of Edinburgh, Edinburgh, UK. [19]Wellcome Trust Sanger Institute, Hinxton, Cambridge, UK. [20]Medical Research Council (MRC) Epidemiology Unit, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, UK. [21]Institute of Medical Informatics, Biometry and Epidemiology, Ludwig-Maximilians-Universität, Munich, Germany. [22]Institute of Genetic Epidemiology, Helmholtz Zentrum Muenchen, Neuherberg, Germany. [23]Department of Medicine I, University Hospital Grosshadern, Ludwig-Maximilians-Universität, Munich, Germany. [24]Institute for Medical Informatics, Biometry and Epidemiology, University Hospital of Essen, University Duisburg-Essen, Essen, Germany. [25]CNRS UMR 8199, Institute of Biology and Lille 2 University, Pasteur Institute, Lille, France. [26]Laboratory of Mathematics, CNRS UMR 8524, University Lille 1, Model for Data Analysis and Learning (MODAL) Team, Institut National de Recherche en Informatique et en Automatique (INRIA) Lille Nord-Europe, Lille, France. [27]Diabetes Prevention Unit, National Institute for Health and Welfare, Helsinki, Finland. [28]Health Science and Technology MD Program, Harvard University and Massachusetts Institute of Technology, Boston, Massachusetts, USA. [29]Harvard Biological and Biomedical Sciences Program, Harvard University, Boston, Massachusetts, USA. [30]Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA. [31]Partners Center for Personalized Genomic Medicine, Boston, Massachusetts, USA. [32]National Heart, Lung, and Blood Institute's Framingham Heart Study, Framingham, Massachusetts, USA. [33]Department of Genetic Medicine and Development, University of Geneva Medical School, Geneva, Switzerland. [34]Biomedical Sciences Research Center Al Fleming, Vari, Greece. [35]Charles R Bronfman Institute for Personalized Medicine, Mount Sinai School of Medicine, New York, New York, USA. [36]Child Health and Development Institute, Mount Sinai School of Medicine, New York, New York, USA. [37]Department of Preventive Medicine, Mount Sinai School of Medicine, New York, New York, USA. [38]Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA. [39]Division of Genetics and Endocrinology, Children's Hospital, Boston, Massachusetts, USA. [40]Department of Biostatistics, Boston University School of Public Health, Boston, Massachusetts, USA. [41]Diabetes Research Center, Diabetes Unit, Massachusetts General Hospital, Boston, Massachusetts, USA. [42]Division of Endocrinology and Metabolism, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA. [43]Boston University Data Coordinating Center, Boston, Massachusetts, USA. [44]Collaborative Studies Coordinating Center, Department of Biostatistics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA. [45]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA. [46]Department of Nutrition and Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA. [47]Program in Molecular and Genetic Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA. [48]Channing Laboratory, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts, USA. [49]Saw Swee Hock School of Public Health, National University of Singapore, Singapore. [50]National Human Genome Research Institute, US National Institutes of Health, Bethesda, Maryland, USA. [51]Nord-Trondelag Health Study (HUNT) Research Centre, Department of Public Health and General Practice, Norwegian University of Science and Technology, Levanger, Norway. [52]Centre for Genetic Epidemiology and Biostatistics, The University of Western Australia,

Nedlands, Western Australia, Australia. [53]Genetics of Complex Traits, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Exeter, Exeter, UK. [54]Department of Internal Medicine, Levanger Hospital, Nord-Trøndelag Health Trust, Levanger, Norway. [55]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden. [56]Department of Vascular Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [57]Department of Medicine, University of Eastern Finland and Kuopio University Hospital, Kuopio, Finland. [58]Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland. [59]Department of Chronic Disease Prevention, National Institute for Health and Welfare, Helsinki, Finland. [60]Department of Clinical Science Malmö, Lund University Diabetes Centre, Scania University Hospital, Lund University, Malmö, Sweden. [61]Institute of Biomedicine, Physiology, University of Eastern Finland, Kuopio, Finland. [62]Faculty of Medicine, University of Iceland, Reykjavík, Iceland. [63]Department of Endocrinology and Metabolism, Landspitali University Hospital, Reykjavík, Iceland. [64]Endocrinology-Diabetology Unit, Corbeil-Essonnes Hospital, Corbeil-Essonnes, France. [65]Diabetes Research Centre, Biomedical Research Institute, University of Dundee, Ninewells Hospital, Dundee, UK. [66]Pharmacogenomics Centre, Biomedical Research Institute, University of Dundee, Ninewells Hospital, Dundee, UK. [67]Icelandic Heart Association, Kopavogur, Iceland. [68]Department of General Practice and Primary Health Care, University of Helsinki, Helsinki, Finland. [69]Vaasa Health Care Centre, Vaasa, Finland. [70]Division of Cardiovascular Epidemiology, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden. [71]Institute for Clinical Diabetology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany. [72]Busselton Population Medical Research Institute, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia. [73]PathWest Laboratory Medicine of Western Australia, Queen Elizabeth II Medical Centre, Nedlands, Western Australia, Australia. [74]School of Pathology and Laboratory Medicine, The University of Western Australia, Nedlands, Western Australia, Australia. [75]School of Population Health, The University of Western Australia, Nedlands, Western Australia, Australia. [76]Department of Pulmonary Physiology and Sleep Medicine, West Australian Sleep Disorders Research Institute, Queen Elizabeth II Medical Centre, Nedlands, Western Australia, Australia. [77]School of Medicine and Pharmacology, University of Western Australia, Nedlands, Western Australia, Australia. [78]Institute of Biometrics and Epidemiology, German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf, Düsseldorf, Germany. [79]Institute of Human Genetics, University of Bonn, Bonn, Germany. [80]Department of Genomics, Life & Brain Center, University of Bonn, Bonn, Germany. [81]Respiratory Medicine, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia. [82]Department of Cardiology, University General Hospital Attikon, Athens, Greece. [83]South Karelia Central Hospital, Lappeenranta, Finland. [84]Department of Genetics, Evolution and Environment, University College London (UCL) Genetics Institute, University College London, London, UK. [85]Department of Clinical Chemistry and Central Laboratory, University of Ulm, Ulm, Germany. [86]Institute of Epidemiology II, Helmholtz Zentrum Muenchen, Neuherberg, Germany. [87]Centro Cardiologico Monzino, IRCCS, Milan, Italy. [88]MRC Institute of Genetics and Molecular Medicine at the University of Edinburgh, Western General Hospital, Edinburgh, UK. [89]Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands. [90]Netherland Genomics Initiative, Netherlands Consortium for Healthy Ageing and Centre for Medical Systems Biology, Rotterdam, The Netherlands. [91]Department of Internal Medicine, Erasmus University Medical Center, Rotterdam, The Netherlands. [92]Oxford National Institute for Health Research Biomedical Research Centre, Churchill Hospital, Oxford, UK. [93]Molecular Medicine, Department of Medical Sciences, Uppsala University, Uppsala, Sweden. [94]Unit of General Practice, Helsinki University General Hospital, Helsinki, Finland. [95]Folkhälsan Research Center, Helsinki, Finland. [96]INSERM CESP U1018, Villejuif, France. [97]University Paris Sud 11, UMRS 1018, Villejuif, France. [98]Department of Medicine, Helsinki University Hospital, University of Helsinki, Helsinki, Finland. [99]Department of Social Services and Health Care, Jakobstad, Finland. [100]Division of Endocrinology, Diabetes and Nutrition, University of Maryland School of Medicine, Baltimore, Maryland, USA. [101]Geriatric Research Education and Clinical Center, Baltimore Veterans Administration Medical Center, Baltimore, Maryland, USA. [102]Program in Personalized and Genomic Medicine, University of Maryland School of Medicine, Baltimore, Maryland, USA. [103]Department of Medicine/Metabolic Diseases, Heinrich Heine University Düsseldorf, Düsseldorf, Germany. [104]University of Cambridge Metabolic Research Laboratories, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, UK. [105]National Institute for Health Research (NIHR) Cambridge Biomedical Research Centre, Institute of Metabolic Science, Addenbrooke's Hospital, Cambridge, UK. [106]Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, Tromsø, Norway. [107]Kuopio Research Institute of Exercise Medicine, Kuopio, Finland. [108]Department of Clinical Physiology and Nuclear Medicine, Kuopio University Hospital, Kuopio, Finland. [109]Department of Medical Sciences, Uppsala University, Akademiska Sjukhuset, Uppsala, Sweden. [110]Department of Dietetics-Nutrition, Harokopio University, Athens, Greece. [111]Faculty of Medicine, Institute of Health Sciences, University of Oulu, Oulu, Finland. [112]Unit of General

Practice, Oulu University Hospital, Oulu, Finland. [113]Finnish Diabetes Association, Tampere, Finland. [114]Pirkanmaa Hospital District, Tampere, Finland. [115]Department of Internal Medicine, South Ostrobothnia Central Hospital, Seinäjoki, Finland. [116]Department of Medicine, Central Finland Central Hospital, Jyväskylä, Finland. [117]Department of Genetics, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA. [118]Diabetes and Obesity Research Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA. [119]Red RECAVA Grupo RD06/0014/0015, Hospital Universitario La Paz, Madrid, Spain. [120]Centre for Vascular Prevention, Danube-University Krems, Krems, Austria. [121]Division of Endocrinology and Diabetes, Department of Internal Medicine, University Medical Centre Ulm, Ulm, Germany. [122]Genomic Medicine, Imperial College London, Hammersmith Hospital, London, UK. [123]Department of Pharmacological Sciences, University of Milan, Milan, Italy. [124]Institute of Cardiovascular Science, University College London, London, UK. [125]Center for Non Communicable Diseases Pakistan, Karachi, Pakistan. [126]Clinic of Cardiology, West German Heart Centre, University Hospital of Essen, University Duisburg-Essen, Essen, Germany. [127]Hannover Unified Biobank, Hannover Medical School, Hannover, Germany. [128]Department of Statistics, University of Oxford, Oxford, UK. [129]Diabetes Genetics, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Exeter, Exeter, UK. [130]Human Genetics Center, University of Texas Health Science Center at Houston, Houston, Texas, USA. [131]Human Genome Sequencing Center at Baylor College of Medicine, Houston, Texas, USA. [132]Cardiovascular Research Center, Massachusetts General Hospital, Boston, Massachusetts, USA. [133]Division of Epidemiology and Community Health, University of Minnesota, Minneapolis, Minnesota, USA. [134]General Medicine Division, Massachusetts General Hospital, Boston, Massachusetts, USA. [135]Department of Genetics, Harvard Medical School, Boston, Massachusetts, USA. [136]Department of Molecular Biology, Harvard Medical School, Boston, Massachusetts, USA. [137]Diabetes Unit, Massachusetts General Hospital, Boston, Massachusetts, USA. [138]Deceased.

Membership of the Asian Genetic Epidemiology Network Type 2 Diabetes (AGEN-T2D) Consortium

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Yoon Shin Cho[1], Chien-Hsiun Chen[2,3], Cheng Hu[4], Jirong Long[5], Rick Twee Hee Ong[6], Xueling Sim[7], Fumihiko Takeuchi[8], Ying Wu[9], Min Jin Go[1], Toshimasa Yamauchi[10], Yi-Cheng Chang[11], Soo Heon Kwak[12], Ronald C W Ma[13], Ken Yamamoto[14], Linda S Adair[15], Tin Aung[16,17], Qiuyin Cai[5], Li-Ching Chang[2], Yuan-Tsong Chen[2], Yutang Gao[18], Frank B Hu[19], Hyung-Lae Kim[1,20], Sangsoo Kim[21], Young Jin Kim[1], Jeannette Jen-Mai Lee[22], Nanette R Lee[23], Yun Li[9,24], Jian Jun Liu[25], Wei Lu[26], Jiro Nakamura[27], Eitaro Nakashima[27,28], Daniel Peng-Keat Ng[22], Wan Ting Tay[16], Fuu-Jen Tsai[3], Tien Yin Wong[16,17,29], Mitsuhiro Yokota[30], Wei Zheng[5], Rong Zhang[4], Congrong Wang[4], Wing Yee So[13], Keizo Ohnaka[31], Hiroshi Ikegami[32], Kazuo Hara[10], Young Min Cho[12], Nam H Cho[33], Tien-Jyun Chang[11], Yuqian Bao[4], Åsa K Hedman[34], Andrew P Morris[34], Mark I McCarthy[34,35], Ryoichi Takayanagi[36], Kyong Soo Park[12,37], Weiping Jia[4], Lee-Ming Chuang[11,38], Juliana C N Chan[13], Shiro Maeda[39], Takashi Kadowaki[10], Jong-Young Lee[1], Jer-Yuarn Wu[2,3], Yik Ying Teo[6,7,22,25,40], E Shyong Tai[22,41,42], Xiao Ou Shu[5], Karen L Mohlke[9], Norihiro Kato[8], Bok-Ghee Han[1], and Mark Seielstad[25,43,44]

[1]Center for Genome Science, National Institute of Health, Osong Health Technology Administration Complex, Chungcheongbuk-do, Cheongwon-gun, Gangoe-myeon, Yeonje-ri, Korea. [2]Institute of Biomedical Sciences, Academia Sinica, Nankang, Taipei, Taiwan. [3]School of Chinese Medicine, China Medical University, Taichung, Taiwan. [4]Shanghai Diabetes Institute, Shanghai Key Laboratory of Diabetes Mellitus, Department of Endocrinology and Metabolism, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China. [5]Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt-Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee, USA. [6]Graduate School for Integrative Science and Engineering, National University of Singapore, Singapore, Singapore. [7]Centre for Molecular Epidemiology, National University of Singapore, Singapore, Singapore. [8]Research Institute, National Center for Global Health and Medicine, Shinjuku-ku, Tokyo, Japan. [9]Department of Genetics, University of North Carolina, Chapel Hill, North Carolina, USA. [10]Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan. [11]Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan. [12]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea. [13]Department of Medicine and Therapeutics, Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong, China. [14]Division of Genome Analysis, Research Center for Genetic Information, Medical Institute of Bioregulation, Kyushu University, Higashi-ku, Fukuoka, Japan. [15]Department of Nutrition, University of North Carolina, Chapel Hill, North Carolina, USA. [16]Singapore Eye Research Institute, Singapore National Eye Centre, Singapore, Singapore. [17]Department of Ophthalmology, National University of Singapore, Singapore, Singapore. [18]Department of Epidemiology, Shanghai Cancer Institute, Shanghai, China. [19]Department of Nutrition and Epidemiology, Harvard School of Public Health, Boston, Massachusetts, USA. [20]Department of Biochemistry, School of Medicine, Ewha Womans University, Seoul, Korea. [21]School of Systems Biomedical Science, Soongsil University, Dongjak-gu, Seoul, Korea. [22]Department of Epidemiology and Public Health, National University of Singapore, Singapore, Singapore. [23]Office of Population Studies Foundation Inc., University of San Carlos, Cebu City, Philippines. [24]Department of Biostatistics, University of North Carolina, Chapel Hill, North Carolina, USA. [25]Genome Institute of Singapore, Agency for Science, Technology and Research, Singapore, Singapore. [26]Shanghai Institute of Preventive Medicine, Shanghai, China. [27]Division of Endocrinology and Diabetes, Department of Internal Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan. [28]Department of Diabetes and Endocrinology, Chubu Rosai Hospital, Nagoya, Japan. [29]Centre for Eye Research Australia, University of Melbourne, East Melbourne, Victoria, Australia. [30]Department of Genome Science, Aichi-Gakuin University, School of Dentistry, Nagoya, Japan. [31]Department of Geriatric Medicine, Graduate School of Medical Sciences, Kyushu University, Higashi-ku, Fukuoka, Japan. [32]Department of Endocrinology, Metabolism and Diabetes, Kinki University School of Medicine, Osaka-sayama, Osaka, Japan. [33]Department of Preventive Medicine, Ajou University School of Medicine, Suwon, Korea. [34]Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK. [35]Oxford Centre for Diabetes,

Endocrinology and Metabolism, University of Oxford, Churchill Hospital, Oxford, UK. [36]Department of Internal Medicine and Bioregulatory Science, Graduate School of Medical Sciences, Kyushu University, Higashi-ku, Fukuoka, Japan. [37]World Class University program, Department of Molecular Medicine and Biopharmaceutical Sciences, Graduate School of Convergence Science and Technology and College of Medicine, Seoul National University, Seoul, Korea. [38]Graduate Institute of Clinical Medicine, National Taiwan University School of Medicine, Taipei, Taiwan. [39]Laboratory for Endocrinology and Metabolism, RIKEN Center for Genomic Medicine, Yokohama, Japan. [40]Department of Statistics and Applied Probability, National University of Singapore, Singapore, Singapore. [41]Department of Medicine, National University of Singapore, Singapore, Singapore. [42]Duke-National University of Singapore Graduate Medical School, Singapore, Singapore. [43]Institute for Human Genetics, University of California, San Francisco, California, USA. [44]Blood Systems Research Institute, San Francisco, California, USA.

Membership of the South Asian Type 2 Diabetes (SAT2D) Consortium

As at publication of the South Asian ancestry meta-analysis, August 2011

Jaspal S Kooner[1–3], Danish Saleheen[4,5], Xueling Sim[6], Joban Sehmi[1,2], Weihua Zhang[7], Philippe Frossard[4], Latonya F Been[8], Kee-Seng Chia[6,9], Antigone S Dimas[10,11], Neelam Hassanali[12], Tazeen Jafar[13,14], Jeremy B M Jowett[15], Xinzhong Li[1], Venkatesan Radha[16], Simon D Rees[17,18], Fumihiko Takeuchi[19], Robin Young[5], Tin Aung[20,21], Abdul Basit[22], Manickam Chidambaram[16], Debashish Das[2], Elin Grundberg[23], Åsa K Hedman[11], Zafar I Hydrie[22], Muhammed Islam[13], Chiea-Chuen Khor[6,21,24], Sudhir Kowlessur[25], Malene M Kristensen[15], Samuel Liju[16], Wei-Yen Lim[6], David R Matthews[12], Jianjun Liu[24], Andrew P Morris[11], Alexandra C Nica[10], Janani M Pinidiyapathirage[26], Inga Prokopenko[11], Asif Rasheed[4], Maria Samuel[4], Nabi Shah[4], A Samad Shera[27], Kerrin S Small[23,28], Chen Suo[6], Ananda R Wickremasinghe[26], Tien Yin Wong[20,21,29], Mingyu Yang[30], Fan Zhang[30], Goncalo R Abecasis[31], Anthony H Barnett[17,18], Mark Caulfield[32], Panos Deloukas[33], Timothy M Frayling[34], Philippe Froguel[35], Norihiro Kato[19], Prasad Katulanda[12,36], M Ann Kelly[17,18], Junbin Liang[30], Viswanathan Mohan[16,37], Dharambir K Sanghera[8], James Scott[1], Mark Seielstad[38], Paul Z Zimmet[15], Paul Elliott[7,39], Yik Ying Teo[6,9,24,40,41], Mark I McCarthy[11,12,42], John Danesh[5], E Shyong Tai[9,43,44], and John C Chambers[2,3,7]

[1]National Heart and Lung Institute (NHLI), Imperial College London, Hammersmith Hospital, London, UK. [2]Ealing Hospital National Health Service (NHS) Trust, Middlesex, UK. [3]Imperial College Healthcare NHS Trust, London, UK. [4]Center for Non-Communicable Diseases Pakistan, Karachi, Pakistan. [5]Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK. [6]Centre for Molecular Epidemiology, National University of Singapore, Singapore. [7]Epidemiology and Biostatistics, Imperial College London, London, UK. [8]Department of Pediatrics, Section of Genetics, College of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA. [9]Department of Epidemiology and Public Health, National University of Singapore, Singapore. [10]Department of Genetic Medicine and Development, University of Geneva Medical School, Geneva, Switzerland. [11]Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, UK. [12]Oxford Centre for Diabetes, Endocrinology & Metabolism, University of Oxford, Churchill Hospital, Oxford, UK. [13]Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan. [14]Department of Medicine, Aga Khan University, Karachi, Pakistan. [15]Baker IDI Heart and Diabetes Institute, Melbourne, Victoria, Australia. [16]Department of Molecular Genetics, Madras Diabetes Research Foundation–Indian Council of Medical Research (ICMR) Advanced Centre for Genomics of Diabetes, Chennai, India. [17]College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK. [18]BioMedical Research Centre, Heart of England NHS Foundation Trust, Birmingham, UK. [19]Department of Gene Diagnostics and Therapeutics, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan. [20]Department of Ophthalmology, National University of Singapore, Singapore. [21]Singapore Eye Research Institute, Singapore National Eye Centre, Singapore. [22]Baqai Institute of Diabetology and Endocrinology, Karachi, Pakistan. [23]Department of Twin Research and Genetic Epidemiology, King’s College London, London, UK. [24]Genome Institute of Singapore, Agency for Science, Technology and Research, Singapore. [25]Ministry of Health, Port Louis, Mauritius. [26]Department of Public Health, Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka. [27]Diabetic Association Pakistan, Karachi, Pakistan. [28]Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, UK. [29]Center for Eye Research Australia, University of Melbourne, Melbourne, Victoria, Australia. [30]Beijing Genomics Institute, Shenzhen, China. [31]Center for Statistical Genetics, Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan, USA. [32]Clinical Pharmacology and Barts and the London Genome Centre, William Harvey Research Institute, Barts and the London School of Medicine, Queen Mary University of London, London, UK. [33]Human Genetics, Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, UK. [34]Genetics of Complex Traits, Institute of Biomedical and Clinical Science, Peninsula Medical School, University of Exeter, Exeter, UK. [35]Genomics of Common Diseases, School of Public Health, Imperial College London, Hammersmith Hospital, London, UK. [36]Diabetes Research Unit, Department of Clinical Medicine, University of Colombo, Colombo, Sri Lanka. [37]Dr Mohan’s Diabetes Specialties Centre, Chennai, India. [38]Institute of Human Genetics, University of California, San Francisco,

California, USA. [39]Medical Research Council (MRC)-Health Protection Agency (HPA) Centre for Environment and Health, Imperial College London, London, UK. [40]Department of Statistics and Applied Probability, National University of Singapore, Singapore. [41]National University of Singapore Graduate School for Integrative Science and Engineering, National University of Singapore, Singapore. [42]Oxford National Institute for Health Research (NIHR) Biomedical Research Centre, Churchill Hospital, Oxford, UK. [43]Department of Medicine, National University of Singapore, Singapore. [44]Duke-National University of Singapore Graduate Medical School, Singapore.

Membership of the Mexican American Type 2 Diabetes (MAT2D) Consortium

As at publication of the Mexican and Mexican American ancestry meta-analysis, May 2011

Jennifer E Below[1], Graeme I Bell[2,3], Jorge Escobedo[4], S Krithika[5], Jesus Kumate[6], Adan Valladares-Salgado[7], Nancy J Cox[2,3], Miguel Cruz[7], Craig L Hanis[8], and Esteban J Parra[5]

[1]Department of Genome Sciences, University of Washington, Seattle, WA 98195, USA. [2]Department of Medicine, University of Chicago, Chicago, IL, 60637, USA. [3]Department of Human Genetics, University of Chicago, Chicago, IL, 60637, USA. [4]Unidad de Investigacion en Epidemiologia Clinica, Hospital General Regional I, Dr. Carlos MacGregor, IMSS, Mexico City, Mexico. [5]Department of Anthropology, University of Toronto at Mississauga, 3359 Mississauga Road North, Mississauga, ON L5L 1C6, Canada. [6]Fundacion IMSS, Av. Paseo de la Reforma 476, Mz. Poniente, Col. Juarez, Deleg. Cuauhtemoc, C.P. 06600, Mexico City, Mexico. [7]Unidad de Investigacion Medica en Bioquimica, Hospital de Especialidades, Centro Medico Nacional Siglo XXI, IMSS, Av. Cuauhtemoc 330, Col. Doctores, C.P. 06720, Mexico City, Mexico. [8]Human Genetics Center, University of Texas Health Science Center at Houston, P.O. Box 20186, Houston, TX 77225, USA.

Membership of the Type 2 Diabetes Genetic Exploration by Next-generation sequencing in multi-Ethnic Samples (T2D-GENES) Consortium

As at June 2013

Gonçalo Abecasis[1], Marcio Almeida[2], David Altshuler[3,4,5,6,7,8,9], Jennifer L Asimit[10], Gil Atzmon[11], Mathew Barber[12], Nicola L Beer[13], Graeme I Bell[12,14], Jennifer Below[15], Tom Blackwell[1], John Blangero[2], Michael Boehnke[1], Donald W Bowden[16,17,18,19], Noël Burtt[3], John Chambers[20,21,22], Han Chen[23], Peng Chen[24], Peter S Chines[25], Yoon Shin Cho[26], Sungkyoung Choi[27], Claire Churchhouse[3], Pablo Cingolani[28], Belinda K Cornes[29], Nancy Cox[12,14], Aaron G Day-Williams[10], Ravindranath Duggirala[2], Josée Dupuis[23], Thomas Dyer[2], Shuang Feng[1], Juan Fernandez-Tajes[30], Teresa Ferreira[30], Tasha E Fingerlin[31], Jason Flannick[3,5], Jose Florez[3,5,6], Pierre Fontanillas[3], Timothy M Frayling[32], Christian Fuchsberger[1], Eric R Gamazon[14], Kyle Gaulton[30], Saurabh Ghosh[33], Anna Gloyn[13], Robert L Grossman[14,34], Jason Grundstad[34], Craig Hanis[15], Allison Heath[34], Heather Highland[15], Momoko Horikoshi[30], Ik-Soo Huh[27], Jeroen R Huyghe[1], Kamran Ikram[29,35,36,37], Kathleen A Jablonski[38], Goo Jun[1], Norihiro Kato[39], Jayoun Kim[27], Young Jin Kim[40], C Ryan King[41], Jaspal Kooner[21,22,42], Min-Seok Kwon[27], Hae Kyung Im[41], Markku Laakso[43], Kevin Koi-Yau Lam[24], Jaehoon Lee[27], Jong Young Lee[44], Selyeong Lee[27], Sungyoung Lee[27], Donna M Lehman[45], Heng Li[3], Cecilia M Lindgren[30], Xuanyao Liu[24,46], Oren E Livne[12], Adam E Locke[1], Anubha Mahajan[30], Julian B Maller[30,47], Alisa K Manning[3], Taylor J Maxwell[15], Alexander Mazoure[48], Mark I McCarthy[13,30,49], James B Meigs[6,50], Byungju Min[27], Karen L Mohlke[51], Andrew P Morris[30], Solomon Musani[52], Yoshihiko Nagai[48], Maggie C Y Ng[16,17], Dan Nicolae[12,14,53], Sohee Oh[27], Nicholette Palmer[16,17,18], Taesung Park[27], Toni I Pollin[54], Inga Prokopenko[30,55], David Reich[3,4], Manuel A Rivas[30], Laura J Scott[1], Mark Seielstad[56], Xueling Sim[1], RobertSladek[48,57], Philip Smith[58], Ioanna Tachmazidou[10], E Shyong Tai[24,35,59], Yik Ying Teo[60,61,62,63,64], Tanya M Teslovich[1], Jason Torres[12,14], Vasily Trubetskoy[12,14], Sara M Willems[65], Amy L Williams[3,4], James G Wilson[66], Steven Wiltshire[30,69], Sungho Won[67], Andrew R Wood[32], Wang Xu[59], Joon Yoon[27], Matthew Zawistowski[1], Eleftheria Zeggini[10], Weihua Zhang[20], and Sebastian Zöllner[1,68]

[1]Department of Biostatistics, Center for Statistical Genetics, University of Michigan, Ann Arbor, Michigan 48109, USA. [2]Department of Genetics, Texas Biomedical Research Institute, San Antonio, Texas 78227, USA. [3]Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, Massachusetts 02142, USA. [4]Department of Genetics, Harvard Medical School, Boston, Massachusetts 02115, USA. [5]Center for Human Genetic Research and Diabetes Research Center (Diabetes Unit), Massachusetts General Hospital, Boston 02114,Massachusetts, USA. [6]Department of Medicine, Harvard Medical School, Boston, Massachusetts 02115, USA. [7]Center for Human Genetic Research, Massachusetts General Hospital, Boston, Massachusetts 02114, USA. [8]Department of Molecular Biology, Harvard Medical School, Boston, Massachusetts 02114, USA. [9]Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA. [10]Wellcome Trust Sanger Institute, Hinxton, Cambridge, CB10 1HH, UK. [11]Department of Medicine, Department of Genetics, Albert Einstein College of Medicine, Bronx, New York10461, USA. [12]Department of Human Genetics, University of Chicago, Chicago, Illinois 60637, USA. [13]Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, OX3 7LJ, UK. [14]Department of Medicine, University of Chicago, Chicago, Illinois 60637, USA. [15]Human Genetics Center, University of Texas Health Science Center at Houston, Houston, Texas 77030, USA. [16]Center for Genomics and Personalized Medicine Research, Wake Forest School of Medicine, Winston-Salem, North Carolina 27157,USA. [17]Center for Diabetes Research, Wake Forest School of Medicine, Winston-Salem, North Carolina 27157, USA. [18]Department of Biochemistry, Wake Forest School of Medicine, Winston-Salem, North Carolina 27157, USA. [19]Internal Medicine-Endocrinology, Wake Forest School of Medicine, Winston-Salem, North Carolina 27157, USA. [20]Department of Epidemiology and Biostatistics, Imperial College London, London SW7 2AZ, UK. [21]Imperial College Healthcare NHS Trust, London W2 1NY, UK. [22]Ealing Hospital National Health Service (NHS) Trust, Middlesex UB1 3HW, UK. [23]Department of Biostatistics,

Boston University School of Public Health, Boston, Massachusetts 02115, USA. [24]Saw Swee Hock School of Public Health, National University of Singapore, Singapore 117597, Singapore. [25]National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20892, USA. [26]Department of Biomedical Science, Hallym University, Chuncheon, Gangwon-do, 200-702 South Korea. [27]Seoul National University, Seoul 110-799, South Korea. [28]McGill Centre for Bioinformatics, McGill University, Montréal, Quebec, H3G 0B1, Canada. [29]Singapore Eye Research Institute, Singapore National Eye Centre, Singapore 168751, Singapore. [30]Wellcome Trust Centre for Human Genetics, University of Oxford, Oxford, OX3 7BN, UK. [31]Department of Epidemiology, Colorado School of Public Health, Aurora, Colorado 80045, USA. [32]Genetics of Complex Traits, University of Exeter Medical School, Exeter, EX4 4SB, UK. [33]Human Genetics Unit, Indian Statistical Institute, 203 B.T. Road, Kolkata 700018, India [34]Institute for Genomics and Systems Biology,University of Chicago, Chicago, Illinois 60637, USA. [35]Duke National University of Singapore Graduate Medical School, Singapore 169857, Singapore. [36]Department of Ophthalmology, National University of Singapore and National University Health System, Singapore 119228, Singapore. [37]Department of Ophthalmology, Erasmus Medical Center, Rotterdam 3000 CA, the Netherlands. [38]The Biostatistics Center, GeorgeWashington University, Rockville, Maryland 20852, USA. [39]Department of Gene Diagnostics and Therapeutics, Research Institute, National Center for Global Health and Medicine, Tokyo162-8655, Japan. [40]Department of Neurology, Konkuk University School of Medicine, Seoul143-701, South Korea. [41]Department of Health Studies, University of Chicago, Chicago, Illinois60637, USA. [42]National Heart and Lung Institute (NHLI), Imperial College London, Hammersmith Hospital, London W12 0HS, UK. [43]Department of Medicine, University of Eastern Finland, Kuopio Campus and Kuopio University Hospital, FI-70211 Kuopio, Finland. [44]Center for Genome Science, Korea National Institute of Health, Osong Health Technology Administration Complex, Chungcheongbuk-do, 363-951, South Korea. [45]Division of Clinical Epidemiology, Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas 78229, USA. [46]Graduate School for Integrative Science and Engineering, National University of Singapore, Singapore 117456, Singapore. [47]Department of Statistics, University of Oxford, Oxford, OX1 3TG, UK. [48]McGill University, Montréal, Québec H3A 0G4, Canada. [49]Oxford NIHR Biomedical Research Centre, Churchill Hospital, Headington, OX3 7LE, UK. [50]General Medicine Division, Massachusetts General Hospital, Boston, Massachusetts 02114, USA. [51]Department of Genetics, University of North Carolina-Chapel Hill, Chapel Hill, North Carolina 27599, USA. [52]Department of Medicine, University of Mississippi Medical Center, Jackson, Mississippi 39126, USA. [53]Department of Statistics, University of Chicago, Chicago, Illinois 60637, USA. [54]Department of Medicine, Program for Personalized and Genomic Medicine, University of Maryland School of Medicine, Baltimore, Maryland21201, USA. [55]Genomics of Common Disease, Imperial College London, Hammersmith Hospital, London, W12 0NN, UK. [56]University of California San Francisco, San Francisco, California 94143, USA. [57]Department of Medicine, Royal Victoria Hospital, Montréal, Québec H3A 1A1, Canada. [58]National Institute of Diabetes and Digestive and Kidney Disease, National Institutes of Health, Bethesda, MD 20817, USA. [59]Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore117597, Singapore. [60]Department of Epidemiology and Public Health, National University of Singapore, Singapore 117597, Singapore. [61]Centre for Molecular Epidemiology, National University of Singapore, Singapore 117456, Singapore. [62]Genome Institute of Singapore, Agency for Science, Technology and Research, Singapore 138672, Singapore. [63]Graduate School for Integrative Science and Engineering, National University of Singapore, Singapore 117456, Singapore. [64]Department of Statistics and Applied Probability, National University of Singapore, Singapore 117546, Singapore. [65]Department of Genetic Epidemiology, Erasmus Medical Center, Rotterdam 3000 CA, the Netherlands. [66]Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, Mississippi 39216, USA. [67]Chung-Ang University, Seoul156-756, South Korea. [68]Department of Psychiatry, University of Michigan, Ann Arbor, Michigan 48109, USA. [69]Deceased.

Resources interrogated for expression analyses

We interrogated public databases and unpublished resources for *cis*-eQTL expression with lead Ps in the novel susceptibility loci in multiple tissues: fresh lymphocytes[1], fresh leukocytes[2], leukocyte samples in individuals with Celiac disease[3], lymphoblastoid cell lines (LCL) derived from asthmatic children[4], HapMap LCL from 3 populations[5], a separate study on HapMap CEU LCL[6], CD19+ B cells[7], peripheral blood monocytes[7-9], dendritic cells before and after Mycobacterium tuberculosis infection[10], omental and subcutaneous adipose[11,12], stomach[12] and whole blood samples[11,13,14], endometrial carcinomas[15], brain cortex[7,16,17], 3 large studies of brain regions including prefrontal cortex, visual cortex and cerebellum, (Emilsson, personal communication), liver[12,18,19], osteoblasts[20], lung[21], skin[22] and additional fibroblast, T cell and LCL samples[23,24].

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