

Supporting Online Material for

A Genome-Wide Association Study of Type 2 Diabetes in Finns Detects Multiple Susceptibility Variants

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This PDF file includes:

Author Contributions Materials and Methods Figures S1 to S3 Tables S1 to S7 References

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Methods

Sample description

Stage 1: In the results reported here, we analyzed 1,161 T2D cases and 1,174 NGT controls from the Finland-United States Investigation of NIDDM Genetics (FUSION) (1, 2) and Finrisk 2002 (3) studies as our stage 1 sample (Tables S1, S2A). T2D was defined according to 1999 World Health Organization (WHO) criteria (4) of fasting plasma glucose concentration ≥ 7.0 mmol/l or 2-h plasma glucose concentration ≥ 11.1 mmol/l, by report of diabetes medication use, or based on medical record review. FUSION cases with known or probable type 1 diabetes among their first degree relatives were excluded. Normal glucose tolerance (NGT) was defined as having fasting glucose < 6.1 mmol/l and 2-h glucose < 7.8 mmol/l (4). The 789 FUSION cases each reported at least one T2D sibling; the 372 Finrisk 2002 T2D cases came from a Finnish population-based risk factor survey. Controls included 219 subjects from Vantaa, Finland who were NGT at ages 65 and 70 years, 304 NGT spouses of FUSION subjects, and 651 Finrisk 2002 NGT subjects. The stage 1 controls were approximately frequency-matched to the stage 1 cases by five-year age category, sex, and birth province. We refer to these FUSION and Finrisk 2002 cases and controls in the text as the FUSION stage 1 sample. For quantitative trait and quality control analyses, we genotyped 122 FUSION offspring, yielding 119 mother-fatheroffspring trios, 1 mother-father-two-offspring quartet, and one parent-offspring pair. For quality control, we successfully genotyped 79 duplicate samples and five CEU HapMap parent-child trios.

Stage 2: 1,215 Finnish T2D cases and 1,258 Finnish NGT controls were selected for stage 2 from the Dehko 2D (D2D) (5), Health 2000 (6), Finrisk 1987 (7), Finrisk 2002 (3), Savitaipale

Diabetes (*8*), and Action LADA (*9*) studies (Tables S1, S2B) and classified according to WHO 1999 criteria (*4*). The D2D, Health 2000, Finrisk 1987, and Savitaipale Diabetes studies are population-based surveys; Action LADA is a study of latent autoimmune diabetes in adults (LADA) in recently-diagnosed diabetes patients. We chose T2D cases from Action LADA who were GAD antibody negative and therefore unlikely to have LADA. For all studies except Action LADA, NGT controls were approximately frequency-matched within each study to the T2D cases by five-year age category, sex, and birth province. Action LADA cases were approximately frequency-matched in the same way with additional controls from the other studies. Our stage 2 sample consists of 327 cases and 399 controls from D2D, 127 cases and 224 controls from Health 2000, 266 cases and 397 controls from Finrisk 1987, 52 controls from Finrisk 2002, 122 cases and 186 controls from Savitaipale, and 373 cases from Action LADA (Table S2B). For quality control in stage 2, we successfully genotyped 56 duplicate samples.

Informed consent: Informed consent was obtained from each study participant, and the study protocol was approved by the ethics committee or institutional review board in each of the participating centers.

Genotyping

GWA genotyping: Stage 1 and quality control samples were genotyped on Illumina InfiniumTM II HumanHap300 BeadChips v.1.0 in the Johns Hopkins University Genetic Resources Core Facility (GRCF) SNP Center at the Center for Inherited Disease Research (CIDR) using the Illumina Infinium II assay protocol (*10*). An in-house LIMS was used for sample and reagent

tracking and lab workflow control (11). ~1 µg of genomic DNA (15 µL at 70 ng/µl) was used as input for the Infinium II assay.

Intensity data for each sample were normalized using BeadStudio v.2.3.25 and, for quality control within CIDR, genotypes were determined using the Illumina-provided standard definition cluster-file for the HumanHap300 v.1.0 product. These cluster boundaries were determined by Illumina using 111 unique HapMap samples: 47 CEU, 36 YRI, and 28 CHB/JPT. BeadStudio sample sheets were generated from our in-house LIMS. Sample and batch level quality control was done by monitoring sample call rates, sex, heterozygote frequencies, and lab workflow related variables using data generated from BeadStudio and our LIMS. 35 genotyped samples fell below our sample call rate threshold of < 97.5% and were repeated; 28 of the repeated samples gave call rates > 97.5%. The remaining 7 samples were excluded from analyses.

To obtain genotypes for analysis, we re-clustered the genotype data using cluster boundaries determined with our own data. We removed samples for 15 people identified as likely first or second degree relatives of other sampled individuals based on their genotype data (*12*). We checked for consistency in genotyping within each of 79 duplicate sample pairs, with Mendelian inheritance among the 122 parent-offspring sets, and with Hardy-Weinberg Equilibrium (HWE) using the unrelated individuals (*13*). After initial analyses, we manually reviewed in BeadStudio the clustering of the genotype data for our most strongly associated SNPs.

SNPs were dropped from all analyses if the HWE p-value was $< 10^{-6}$, the total number of Mendelian inconsistencies and duplicate pair discrepancies was > 3, or the SNP call rate was < 3

90%; and flagged for further attention if the HWE p-value was $< 10^{-4}$, the total number of Mendelian inconsistencies and duplicate pair discrepancies was > 1, or the SNP call rate < 95%. All genotypes were oriented to the forward strand. There is little risk of strand ambiguities as there are no C/G or A/T polymorphisms included in the Illumina 300K HumanHap panel.

For the 315,635 SNPs that passed our quality control criteria, the genotype consistency rate among 79 duplicate sample pairs was 99.996%, the Mendelian consistency rate in 122 parent-child sets was 99.967%, and the concordance rate for 15 samples genotyped both in our study and by the HapMap consortium was 99.82%. 80.8% of SNPs had call frequency of 100%, and 99.68% of SNPs had call frequencies > 95%.

Confirmation and replication genotyping: We carried out focused, lower-throughput genotyping with the Sequenom Homogeneous MassEXTEND or iPLEX Gold SBE assays at the National Human Genome Research Institute (NHGRI). For 26 GWA SNPs re-genotyped in the stage 1 samples on a different genotyping platform (Sequenom), we observed a genotype consistency rate of 99.92%; these included the SNPs with the strongest evidence of T2D association. We also genotyped SNPs in the FUSION stage 2 samples or in the combined FUSION stage 1+2 samples to follow up interesting results based on (a) FUSION genotyped and imputed SNPs; (b) the FUSION-DGI-WTCCC GWA results comparison; and (c) prior T2D association results in our own or other studies. 80 of the 82 attempted SNPs had genotype call frequency > 94% and HWE p-value > .001. The genotype consistency rate among duplicate samples was 99.9% and the average call frequency was 97.1%.

7

Statistical analysis

T2D association: We tested for T2D-SNP association using logistic regression under the additive genetic model that is multiplicative on the OR scale with adjustment for five-year age category, sex, and birthplace. This test is the logistic regression equivalent to the Cochran-Armitage test for trend (*14*) and is hence robust to departures from Hardy-Weinberg equilibrium. We repeated some analyses including BMI, waist, systolic blood pressure, or diastolic blood pressure as an additional covariate to assess the impact of these variables on evidence for SNP-T2D association. For X-chromosome markers, we treated hemizygous males as homozygotes, consistent with X inactivation for most of the chromosome. We presented and followed up on results based on this additive model for ease of comparison between groups. We also analyzed SNPs using recessive and dominant models; no SNP reached genome-wide significance in FUSION stage 1 data, although additional T2D-prediposing variants may be among the SNPs identified by these models.

To evaluate empirically the distribution of p-values observed in our GWA stage 1 study, we permuted case/control status and re-ran the entire GWA analysis 100 times. We counted the number of p-values $< 10^{-5}$ or $< 10^{-4}$ within each permuted dataset and found our study to fall within the permuted distribution.

Statistical significance: Following the recommendation of the International HapMap Consortium based on analysis of the ENCODE data, we declared a T2D-SNP association "genome-wide significant" if the nominal p-value for the SNP was $< 5 \ge 10^{-8}$ (15). In so doing,

we dealt with the multiple comparisons problem suggested by carrying out the equivalent of ~ 1 million tests.

Sample size calculation: For each SNP in Table 1, we calculated the sample size necessary to detect T2D-SNP association at significance level .05 and power 80% under an additive model. We converted the FUSION-DGI-WTCCC/UKT2D all-data OR to a risk ratio assuming T2D prevalence 10%, and used this risk ratio and FUSION stage 1+2 control risk allele frequency as the population allele frequency in the sample size calculation (*16*).

Imputation: We applied a computationally efficient hidden Markov model based algorithm (*17*, *18*) to impute genotypes in FUSION samples for 2.25 million autosomal SNPs genotyped by the International HapMap Consortium (*15*), but not present on the Illumina HumanHap300 BeadChip. The method combines our FUSION Illumina GWA genotype data with phased chromosomes for the HapMap CEU samples and then infers the unknown FUSION genotypes probabilistically by searching for similar stretches of flanking haplotype in the HapMap CEU reference sample. In this process, we used the genotype data from the 290,690 FUSION Illumina GWA autosomal SNPs which passed our quality control criteria and had minor allele frequency > 5%. For each individual at each imputed SNP, we calculated an average allele dosage score based on 90 iterations of the imputation algorithm. We assessed the quality of the results for each SNP by calculating (a) the proportion of iterations that agreed with the most likely genotype (imputation consistency) and (b) the ratio of the observed variance of dosage scores across samples to the expected variance given the imputed allele frequency of the SNP

(estimated r^2). 2.15 million of the HapMap autosomal SNPs had minor allele frequency > 1% in the CEU sample; of these, 2.09 million met our quality control criterion of an estimated r^2 > .30.

We evaluated the accuracy of our imputation procedure by comparing imputed genotypes to actual genotypes for 510 SNPs not present on the Illumina GWA panel but that we had previously genotyped in 1,190 individuals in our stage 1 samples (19). The average concordance rate between imputed and actual alleles (genotypes) was 98.5% (97.1%), suggesting that the HapMap CEU sample provides an appropriate basis for SNP genotype imputation in Finns, consistent with our previous findings that allele frequencies, haplotype frequencies, and linkage disequilibrium (LD) measures are remarkably similar between the CEU samples and a set of the Finnish individuals that overlaps with those included in this study (19). We also genotyped 23 SNPs imputed in our stage 1 data; 16 of these SNPs had stage 1 imputation-based p-values $< 10^{\circ}$ ⁵. For most of these SNPs, the p-values for the actual genotypes were very similar to those for the imputed genotypes, although often slightly less significant (Table S6); large differences occurred most often for estimated r^2 values nearer the quality control threshold. Differences reflect variability in the imputation-based p-value estimates and our choice to follow up strong imputation-based association results, an example of the "winner's curse." This variability in pvalue estimates for imputed SNPs did not lead to an increased overall false positive rate for the study since we have chosen to genotype each such SNP in stage 1 as well as stage 2.

To test for disease-SNP association for imputed SNPs allowing for the effects of covariates, we used logistic regression models in which the SNP effect was represented by its mean imputed

allele dosage score, an approach that takes into account the degree of uncertainty of genotype imputation (*18*).

Combined analysis: We used a fixed effects model to estimate the combined ORs, 95% confidence intervals (CIs), and p-values for the GWA genotype or imputed data for FUSION and the GWA genotype data from DGI and WTCCC studies (*20*). We used the same approach to combine all available data from the FUSION, DGI, and WTCCC/UKT2D studies. All results are based on genotypes predicted from the forward strand of the genome sequence. When we describe results across studies for non-identical SNPs, we report LD estimates based on FUSION genotype data when available and on imputed data when not.

SNP selection for stage 2 genotyping: We selected SNPs for genotyping in the FUSION stage 2 samples based on the results of the FUSION GWA and the comparison of the FUSION, DGI, and WTCCC GWA results. To enrich for SNPs with interesting biological functions from the FUSION GWA, we weighted the association p-value according to our interest in the SNP based on genome annotation, using an algorithm similar to the one described by Roeder et al. (21), with weights as described in Table S7. Our algorithm advantaged genotyped SNPs that tagged any HapMap SNP annotated as non-synonymous, frameshift, or critical splice site variants, or located in or around interesting T2D candidate genes using an LD threshold of $r^2 \ge .8$ in the CEU HapMap sample. It did so by dividing the p-value by the product of the maximal relevant weighting factor and the relevant bonus factors. For imputed SNPs, we assigned the weight based only on the imputed SNP itself. From SNPs with weighted p-values $\le 10^{-4}$, we formed sets of SNPs within 100 kb of each other and ranked these sets based on the smallest weighted p-

11

value. From each of these sets, we selected a strongly associated SNP for stage 2 genotyping, giving some preference to genotyped over imputed SNPs to reduce stage 1 genotyping requirements and to focus on SNPs for which we had more accurate genotype information. If an imputed SNP was chosen, we genotyped stage 1 and 2 samples.

Risk prediction: We predicted T2D risk in the FUSION sample based on the ten identified T2D susceptibility variants listed in Table 1. T2D cases and NGT controls with complete genotype data were included in the analysis. To obtain a sample with ~10% T2D prevalence, the 2,176 NGT controls were included nine times each and the 2,102 T2D cases once each in a logistic regression analysis. Figure 2 displays the proportion of T2D individuals for twenty equal intervals of predicted T2D risk. 95% CIs for the proportion of T2D cases were constructed using the original, not the expanded, sample.

Linkage and association: To assess the possible predictive value of T2D linkage for T2D association, we counted the number of our ten T2D-associated loci (Table 1) for which the T2D linkage LOD score was > 0.2 in our FUSION affected sibling pair families (2). We then divided the genome into 5 cM bins and noted that 22% of such bins had T2D LOD score > 0.2 in our T2D linkage scan. The observed count of six of the ten loci with T2D LOD > 0.2 is \sim 3-times greater than expected by chance, and has exact binomial p-value of .01, consistent with the hypothesis that very modest linkage evidence is somewhat predictive of the presence of a locus detectable by association methods.

Gene expression analysis

RNAs from human tissues were purchased from Clontech and represented pooled samples from several individuals. Purified human pancreatic islets were obtained from Islet Cell Resource Centers (IRB Exemption number 3072) and the National Disease Research Interchange (IRB Exemption number 3269) with approval by the National Institutes of Health Office of Human Subjects Research. Anonymous human blood donor samples from the NIH Clinical Center Division of Transfusion Medicine were provided as buffy coat isolations from whole blood centrifugation. Human adipocytes were purchased from Cambrex as differentiated cultures, and cell cultures -- 293T (human embryonic kidney), HeLa (human cervical carcinoma), and HepG2 (human hepatocellular carcinoma) -- were purchased from ATCC (the American Type Culture Collection). Lymphoblastoid cell lines from CEPH individuals were purchased from the Coriell Cell Repositories. RNA from cell cultures, islets, blood, and adipocytes was prepared with Trizol Reagent (Invitrogen) followed by RNeasy Kit (Qiagen). RNA from four individual samples was used to prepare pooled cDNA for islets, adipocytes, blood, and lymphoblasts. cDNA was prepared from 1 ug of total RNA, using SuperScript III reverse transcriptase and random hexamers (Invitrogen). cDNA equivalent to 25-50 ng of total RNA was used for each quantitative PCR. All PCRs were performed in 10 ul volume in replicates of 3 or 4 using the 7900 Real-Time PCR System (ABI) in 384 well plates; average values were used for calculations. The PCR with 2xSYBR Green PCR mix (Qiagen) and specific primers was designed over exon boundaries to amplify only from cDNA:

CDKAL1_f: GAAGAATCTTTTGATTCCAAGTTTT CDKAL1_r: GCAGCACCATTCTGGAACTC CDKN2A_f: ATCTATGCGGGGCATGGTTACT

CDKN2A_r: CAACGCACCGAATAGTTACG CDKN2B_f: CGGGGGACTAGTGGAGAAGGT CDKN2B r: ACCAGCGTGTCCAGGAAG

PCRs were carried out for 15 min at 95 C, followed by 40 cycles of 15 sec at 95 C, 15 sec at 59 C, and 45 sec at 72 C. Post-PCR melting curve analysis was used after each run. Gel-purified PCR fragments were also sequenced to ensure the specificity of amplification and splicing. An expression assay for human beta-2 microglobulin (*B2M*) Hs00187842_m1 was purchased from ABI and used according to the instructions. Ct values (cycle at threshold) were determined from real-time PCR. The expression of target genes was normalized to expression of B2M according to the equation dCt = Ct _{B2M} - Ct _{target}, compared to expression in pancreas by equation ddCt = dCt _{tissue} - dCt _{pancreas}, then converted to fold difference as fold difference = 2 ^{ddCt} (ABI, User Bulletin #2 on relative quantification). We were unable to assess confidently the tissue distribution of *IGF2BP2* mRNA because of very high similarity (> 95%) to three processed pseudogenes on chromosomes 1, 8, and 12.

Supplementary Figure Legends

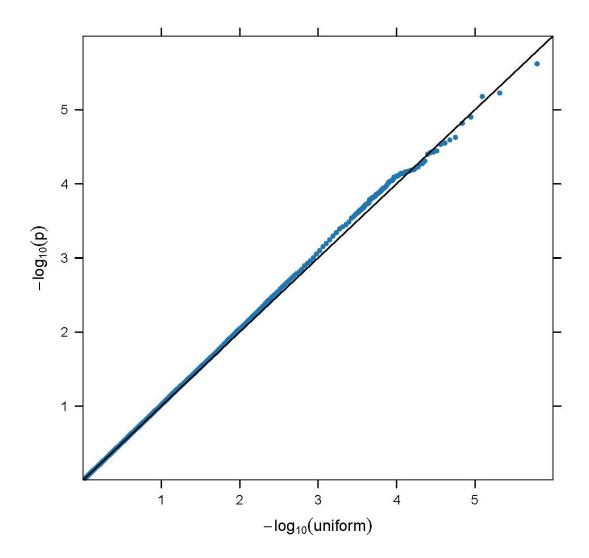
Figure S1. Quantile-quantile plot for T2D association -log₁₀ p-values for FUSION stage 1 samples and p-values expected under the null distribution for FUSION GWA SNPs.

Figure S2. Plot of T2D association and LD in FUSION stage 1 sample for region surrounding *SLC30A8*. The top panel contains RefSeq genes. The second panel shows the T2D association $-\log_{10}$ p-values in FUSION stage 1 samples for SNPs genotyped in the GWA panel (•) or imputed (o). The third panel shows T2D association $-\log_{10}$ p-values for each SNP in a logistic regression model correcting for the reference SNP rs13266634 (•, red dot). A decrease in the $-\log_{10}$ p-value from the second to the third panel indicates that the association signal of the tested SNPs can be explained, at least in part, by the reference SNP. The reference SNP is a non-synonymous coding SNP, and was chosen because of its potential of being the actual functional variant responsible for the association signal; choice of another strongly associated SNP nearby would have resulted in a similar picture. The fourth panel shows recombination rate in cM per Mb for the HapMap CEU sample (*15*). The fifth and sixth panels show linkage disequilibrium r² and D' based on FUSION stage 1 genotyped and imputed data.

Figure S3. Expression of *CDKAL1* (first panel), *CDKN2A* (second panel), and *CDKN2B* (third panel) in human tissues and cells. The level of expression of each gene was determined by quantitative RT-PCR, and normalized to the beta-2-microglobulin (*B2M*) housekeeping gene. The data are presented as fold difference relative to expression in pancreas, which is set at 1.0.

293T cells are human embryonic kidney, HeLa are human cervical carcinoma, and HepG2 are human hepatocellular carcinoma.

Figure S1





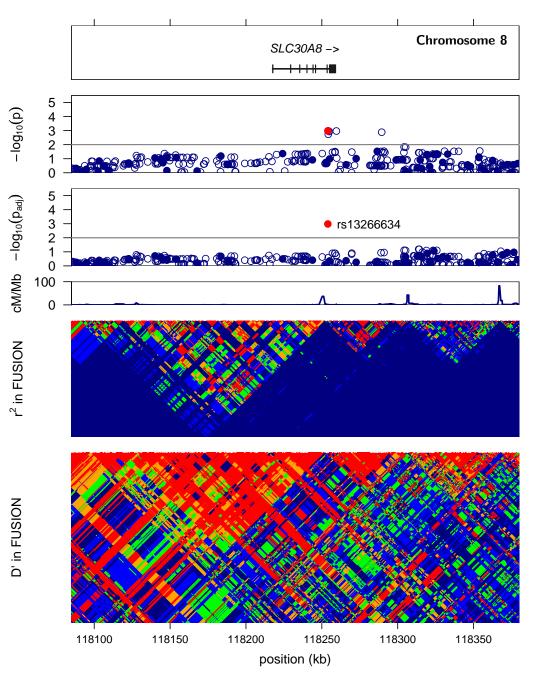


Figure S3

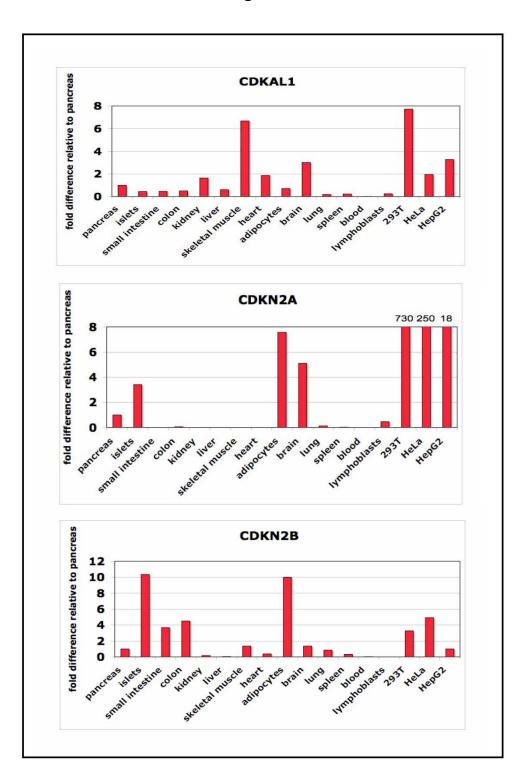


Table S1. Characteristics of stage 1 and stage 2 case and control samples

		Sta	ge 1			Sta	ge 2		
	Cas	ses	Con	trols	Ca	ses	Controls		
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
N	1161		1174		1215		1258		
Male	653		574		724		768		
Female	508		600		491		490		
Age of Diagnosis (years)	53.0	12.0			56.0	12.0			
Study Age (years)	63.4	11.2	64.0	11.7	60.0	11.5	59.0	10.6	
BMI (kg/m ²)	29.8	6.1	26.8	5.0	30.1	6.7	26.4	4.9	
Fasting Plasma Glucose (mmol/l)	8.4	3.9	5.4	0.7	7.2 ^a	2.1 ^a	5.4 ^b	0.6 ^b	

 a^{n} = 204 and b^{n} = 583 values converted from whole blood to plasma glucose equivalent using prediction equation from the European Diabetes Epidemiology Group (22), of which b^{n} = 262 fasted < 8 hours

Table S2A. Detailed characteristics of stage 1 case and control samples

			FUS	ION			Finrisk 2002				
	Ca	ses	Controls		Controls from Finrisk 2002		Cases		Controls		
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
Ν	789		523 ^a		276		372		375		
Male	429		194		163		224		217		
Female	360		329		113		148		158		
Age of Diagnosis (years)	51.0	11.0					59.0	12.0			
Study Age (years)	64.2	10.1	69.6	7.7	62.0	9.0	61.0	12.0	61.0	12.0	
BMI (kg/m ²)	29.3	6.2	27.3	5.5	26.5	4.5	30.7	6.0	26.6	4.4	
Fasting Plasma Glucose (mmol/l)	9.6	4.7	5.1	0.6	5.6	0.5	7.3	1.3	5.6	0.5	

^aComprised of 219 FUSION controls from Vantaa who were NGT at ages 65 and 70 years, and 304 NGT spouses of FUSION T2D subjects

Table S2B. Detailed characteristics of stage 2 case and control samples

		D	2D			Health	n 2000			Action	LADA			Finri	sk 1987		Sa	ivitaipale D	Diabetes Study	
	Case	s	Contr	ols	Case	S	Contro	ols	Case	s	Contro	ols	Case	s	Cont	rols	Case	es	Contr	rols
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
N	327		314		127		124		373		402 ^a		266		300		122		118	
Male	184		176		67		66		235		259		171		202		67		65	
Female	143		138		60		58		138		143		95		98		55		53	
Age of Diagnosis (years)	60.0	13.0			55.0	13.0			55.0	10.0			55.0	13.0			55.1	11.7		
Study Age (years)	64.0	11.4	64.3	12.0	61.0	15.0	59.0	12.0	60.2	10.8	58.0	9.0	58.0	11.0	57.0	12.0	57.9	13.4	57.0	13.0
BMI (kg/m ²)	29.9	7.1	26.4	4.9	30.3	5.4	26.5	5.6	30.3	6.9	26.3	4.7	30.5	6.1	26.7	4.8	28.3	7.1	25.4	4.5
Fasting Plasma Glucose (mmol/l)	7.2	2.0	5.4	0.5	7.3	2.0	5.4	0.5	7.3	2.4	5.5 ^b	0.6 ^b	6.9°	3.0°	5.1 ^{cd}	0.6 ^{cd}	7.2°	0.9°	5.6°	0.4 ^c

^a85 D2D, 100 Health 2000, 52 Finrisk 2002, 97 Finrisk 1987, and 68 Savitaipale Diabetes Study controls ^bn=165 values converted from whole blood to plasma glucose equivalent using prediction equation from the European Diabetes Epidemiology Group (22), of which n=52 fasted < 8 hours ^call values converted from whole blood to plasma glucose equivalent using prediction equation from the European Diabetes Epidemiology Group (22)

 $^{d}n=210$ fasted < 8 hours

Table S3. FUSION stage 1 T2D association: genotyped (bold) and imputed (non-bold) SNPs with p-value < .0001. Sets of SNPs, where each SNP is within 100kb of the preceding SNP, are delimited by lines.

				FUSION risk allele/	Control	Case				Genotyped p-value	
			Position	non-risk	risk	risk				for imputed	Genotype
SNP	Genes	Chr	(bp)	allele	frequency	frequency	OR	95% CI	p-value	SNP	in Stage 2
rs527912	CDA	1	20,679,589	G/A	.670	.723	1.304	1.141-1.49	9.4 x 10 ⁻⁵		
rs3820321	PINK1	1	20,708,133	G/A	.602	.663	1.291	1.142-1.459	4.0 x 10 ⁻⁵		
rs607254	DDOST, KIF17, PINK1	1	20,726,186	G/A	.601	.663	1.294	1.145-1.463	3.4 x 10 ⁻⁵		
rs589709	DDOST, KIF17, PINK1	1	20,729,293	G/A	.601	.663	1.297	1.147-1.465	2.9 x 10 ⁻⁵		
rs640742	DDOST, KIF17, PINK1	1	20,729,860	A/C	.601	.663	1.297	1.147-1.465	2.9 x 10 ⁻⁵		Yes
rs623817	DDOST, KIF17, PINK1	1	20,731,384	G/A	.601	.663	1.297	1.147-1.467	3.1 x 10 ⁻⁵		
rs674114	DDOST, KIF17	1	20,734,978	G/A	.615	.668	1.321	1.151-1.516	6.8 x 10 ⁻⁵		
rs630484	DDOST, KIF17	1	20,737,912	G/T	.616	.670	1.332	1.159-1.530	4.8 x 10 ⁻⁵		
rs12118760	DDOST, KIF17	1	20,745,110	T/C	.736	.767	1.708	1.331-2.191	2.2 x 10 ⁻⁵		
rs1932397		1	`29,732,290	T/C	.168	.215	1.351	1.164-1.569	7.1 x 10 ⁻⁵		
rs6603926		1	29,735,248	A/G	.168	.215	1.352	1.164-1.57	7.0 x 10 ⁻⁵		
rs9662524		1	29,739,496	G/C	.168	.215	1.351	1.164-1.569	7.3 x 10 ⁻⁵		
rs915409		1	29,740,363	T/C	.168	.215	1.351	1.164-1.569	7.3 x 10 ⁻⁵		
rs9286938		1	29,746,194	T/C	.168	.214	1.345	1.159-1.562	9.1 x 10 ⁻⁵		
rs9659523		1	29,746,693	A/C	.169	.215	1.344	1.157-1.56	1.0 x 10 ⁻⁴		
rs271306		1	29,751,757	G/C	.168	.214	1.344	1.157-1.561	1.0 x 10 ⁻⁴		
rs17356414		1	59,031,529	C/T	.548	.607	1.311	1.158-1.485	1.7 x 10 ⁻⁵	8.0 x 10 ⁻⁴	Yes
rs6676059		1	59,041,777	G/A	.548	.606	1.312	1.159-1.485	1.7 x 10 ⁻⁵		
rs12133457		1	59,042,784	G/A	.548	.606	1.312	1.159-1.485	1.7 x 10 ⁻⁵		
rs17025978	KCNA10	1	110,781,653	G/A	.914	.947	1.705	1.347-2.158	6.6 x 10 ⁻⁶		Yes
rs17025982	KCNA10	1	110,782,336	T/C	.910	.943	1.699	1.342-2.151	7.8 x 10 ⁻⁶		
rs2790372		1	110,799,166	C/A	.937	.962	1.750	1.320-2.319	7.5 x 10 ⁻⁵		
rs2799765		1	110,800,193	T/C	.937	.962	1.748	1.317-2.319	8.5 x 10 ⁻⁵		
rs1626078		1	110,801,281	C/T	.937	.962	1.748	1.316-2.322	8.9 x 10 ⁻⁵		
rs1622675		1	110,801,684	A/T	.937	.962	1.758	1.321-2.338	8.3 x 10 ⁻⁵		
rs1627572		1	110,801,712	G/A	.938	.962	1.756	1.319-2.338	8.9 x 10 ⁻⁵		
rs2501354	SLAMF8, VSIG8	1	156,628,715	G/A	.355	.415	1.274	1.129437	8.1 x 10 ⁻⁵		
rs2501350	SLAMF8, VSIG8	1	156,630,077	G/C	.379	.437	1.288	1.136459	7.0×10^{-5}		
rs357973		2	3,292,094	G/A	.942	.961	1.975	1.394-2.798	9.3 x 10 ⁻⁵		
rs357971		2	3,292,963	G/C	.942	.961	1.977	1.395-2.802	9.1 x 10 ⁻⁵		
rs2338545	PLB1	2	28,711,426	G/A	.202	.252	1.332	1.157534	6.3 x 10 ⁻⁵		
rs2249434	SCLY	2	238,757,753	C/G	.076	.110	1.497	1.221835	9.1 x 10 ⁻⁵		
rs1391136	5021	3	21,136,392	C/T	.838	.874	1.425	1.195-1.700	7.5 x 10 ⁻⁵		
rs11926889		3	30,253,294	G/A	.880	.911	1.537	1.243-1.900	6.1×10^{-5}		
rs1434006		3	30,268,508	C/T	.904	.934	1.586	1.268-1.984	$4.4 \ge 10^{-5}$		
rs13075234		3	30,269,434	C/T C/T	.904	.946	1.707	1.311-2.223	5.8×10^{-5}		
rs10440137		3	30,270,978	G/T	.922	.940	1.581	1.266-1.974	$4.4 \ge 10^{-5}$		
rs9870410		3	30,270,978 30,283,763	C/T	.904 .904	.934 .935	1.581 1.579	1.267-1.974 1.267-1.967	3.8 x 10 ⁻⁵		
rs13092602		3	30,283,703	G/A	.904	.939	1.660	1.324-2.081	3.8×10^{-6} 8.2 x 10 ⁻⁶		
rs1495586		3	30,302,792	G/A G/A	.900	.939	1.666	1.327-2.091	8.2 x 10 8.2 x 10 ⁻⁶		
rs17081352		3	30,307,851	G/A C/A	.907	.940	1.698	1.342-2.148	8.2 x 10 7.6 x 10 ⁻⁶	5.5 x 10 ⁻⁶	Yes
rs9843153		3	30,307,831	C/A G/T	.910	.942 .944	1.698	1.342-2.148	7.6 x 10 8.4 x 10 ⁻⁶	J.J X 10	1 05
rs11714343		3	<u>30,308,232</u> 34,437,873	T/C	.915	.944	1.722	1.210-1.791	9.6 x 10 ⁻⁵		

				FUSION						Genotyped	
				risk allele/	Control	Case				p-value	
	_		Position	non-risk	risk	risk				for imputed	Genotyped
SNP	Genes	Chr	(bp)	allele	frequency	frequency	OR	95% CI	p-value	SNP	in Stage 2?
rs739984	PTPRG	3	61,975,357	G/A	.729	.777	1.320	1.150-1.515	7.2 x 10 ⁻⁵		
rs12490128	TMEM108	3	134,391,491	A/C	.118	.162	1.465	1.234-1.739	1.1×10^{-5}		
rs13072106	TMEM108	3	134,425,451	T/C	.118	.155	1.414	1.188-1.682	8.7 x 10 ⁻⁵		Yes
rs10512891	TMEM108	3	134,431,557	A/T	.118	.156	1.415	1.189-1.684	8.3 x 10 ⁻⁵		
rs7650741	TMEM108	3	134,432,277	T/C	.118	.156	1.416	1.189-1.684	8.2 x 10 ⁻⁵		
rs7612595	TMEM108	3	134,439,991	T/C	.118	.156	1.418	1.192-1.688	7.5 x 10 ⁻⁵		
rs16840161	TMEM108	3	134,478,424	A/G	.117	.158	1.444	1.213-1.718	3.1 x 10 ⁻⁵		
rs17297332	TMEM108	3	134,480,782	G/C	.121	.162	1.447	1.216-1.723	2.9 x 10 ⁻⁵		
rs7625110	TMEM108	3	134,494,477	T/G	.117	.158	1.446	1.215-1.722	2.9 x 10 ⁻⁵		
rs10512896	TMEM108	3	134,499,457	G/C	.117	.158	1.450	1.218-1.726	2.7 x 10 ⁻⁵		
rs1708373	TMEM108	3	134,502,025	G/A	.117	.158	1.451	1.219-1.728	2.5 x 10 ⁻⁵		
rs1197316	TMEM108	3	134,522,283	G/A	.117	.158	1.455	1.222-1.734	2.3 x 10 ⁻⁵		
rs1920021	TMEM108	3	134,554,123	T/C	.118	.158	1.450	1.216-1.729	3.1 x 10 ⁻⁵		
rs823968		3	136,542,755	C/T	.382	.436	1.274	1.131-1.436	6.7 x 10 ⁻⁵		
rs4687296	MAP3K13	3	186,595,002	T/C	.225	.276	1.325	1.158-1.516	3.9 x 10 ⁻⁵		
rs4687299	MAP3K13	3	186,595,361	A/G	.225	.276	1.325	1.158-1.515	4.0 x 10 ⁻⁵		Yes
rs886374	SORCS2	4	7,856,440	T/C	.211	.270	1.385	1.209-1.587	2.4 x 10 ⁻⁶		Yes
rs6815292	ATP8A1	4	42,251,192	A/G	.244	.291	1.308	1.144-1.496	7.9 x 10 ⁻⁵		
rs7665824	ATP8A1	4	42,252,481	T/G	.244	.291	1.309	1.145-1.496	7.8 x 10 ⁻⁵		
rs11726581	ATP8A1	4	42,257,935	C/T	.244	.291	1.309	1.145-1.497	7.7 x 10 ⁻⁵		
rs11722556	ATP8A1	4	42,258,828	T/C	.244	.291	1.309	1.145-1.497	7.5 x 10 ⁻⁵		
rs17630357	ATP8A1	4	42,266,042	A/T	.774	.821	1.346	1.160-1.562	8.2 x 10 ⁻⁵		
rs4317238	ATP8A1	4	42,267,105	A/G	.774	.821	1.346	1.160-1.562	8.1 x 10 ⁻⁵		
rs16854359	ATP8A1	4	42,269,100	C/G	.241	.290	1.313	1.149-1.501	5.7 x 10 ⁻⁵		
rs9994372	ATP8A1	4	42,269,138	T/C	.251	.301	1.335	1.166-1.527	2.5 x 10 ⁻⁵		
rs10034439	ATP8A1	4	42,287,090	C/T	.776	.826	1.374	1.182-1.598	3.1 x 10 ⁻⁵		
rs13139219	ATP8A1	4	42,294,231	C/A	.779	.827	1.346	1.160-1.561	7.8 x 10 ⁻⁵		Yes
rs6812080	ATP8A1	4	42,319,554	G/A	.779	.828	1.349	1.163-1.565	7.0×10^{-5}		
rs13116032	ATP8A1	4	42,320,518	G/T	.779	.828	1.349	1.163-1.565	7.0 x 10 ⁻⁵		
rs5022521	ELOVL6	4	111,486,191	T/C	.858	.884	1.785	1.349-2.361	4.1 x 10 ⁻⁵		
rs1030231	220,20	5	66,353,021	G/A	.198	.245	1.330	1.152-1.536	9.3 x 10 ⁻⁵		
rs10476844		5	142,096,902	T/C	.014	.023	4.666	2.212-9.841	3.5 x 10 ⁻⁵		
rs961730	ARHGAP26	5	142,114,126	C/T	.014	.023	4.696	2.254-9.784	2.4×10^{-5}		
rs1347133	ARHGAP26	5	142,114,120	C/T	.014	.024	4.745	2.275-9.899	2.4×10^{-5} 2.1 x 10 ⁻⁵		
rs968076	ARHGAP26	5	142,116,491	G/A	.014	.024	4.787	2.293-9.993	2.0×10^{-5}		
rs7714907	ARHGAP26	5	142,125,570	G/A G/A	.014	.024	5.319	2.473-11.441	1.2×10^{-5}		
rs7732207	ARHGAP26	5	142,125,613	A/G	.014	.023	5.317	2.472-11.439	1.2×10^{-5} 1.2×10^{-5}		
rs764387	ARHGAP26	5	142,125,869	T/C	.014	.023	5.326	2.472-11.474	1.2×10^{-5} 1.2×10^{-5}		
rs7737018	ARHGAP26	5	142,126,283	C/G	.014	.023	5.317	2.462-11.483	1.2×10^{-5} 1.3 x 10 ⁻⁵		
rs6898675	ARHGAP26	5	142,120,285	T/C	.014	.023	5.320	2.456-11.526	1.3×10^{-5} 1.4 x 10 ⁻⁵		
rs6894433	ARHGAP26	5	142,131,845	C/T	.014	.023	5.315	2.452-11.523	1.4×10^{-5} 1.4 x 10 ⁻⁵		
rs707177	ARHGAP26	5	142,232,076	A/G	.372	.023	1.308	1.146-1.493	6.4×10^{-5}		
rs447923	ARHGAP26	5	142,232,070	T/C	.325	.373	1.308	1.148-1.519	9.2×10^{-5}		
rs26707	ARHGAP26	5	142,232,441	G/C	.323	.303	1.321	1.148-1.519	9.2×10^{-5} 3.0×10^{-5}		
1320/07	AMIGAF20	5	142,233,037	U/C	.230	.505	1.525	1.100-1.313	J.0 X 10		

			Position	FUSION risk allele/ non-risk	Control risk	Case risk				Genotyped p-value for imputed	Genotyped
SNP	Genes	Chr	(bp)	allele	frequency	frequency	OR	95% CI	p-value	SNP	in Stage 2?
rs26706	ARHGAP26	5	142,237,044	C/G	.253	.306	1.324	1.159-1.513	3.2×10^{-5}		
rs27779	ARHGAP26	5	142,239,267	A/C	.250	.304	1.326	1.162-1.513	2.5×10^{-5}		Yes
rs27546	ARHGAP26	5	142,245,929	T/A	.250	.302	1.321	1.157-1.508	3.5 x 10 ⁻⁵		
rs11970389	TUBB2B, LOC389362	6	3,195,655	T/C	.041	.063	1.845	1.351-2.518	9.2 x 10 ⁻⁵		
rs4713992		6	36,720,183	A/G	.730	.764	1.525	1.240-1.875	5.7 x 10 ⁻⁵		
rs7750445	ZFAND3	6	37,872,955	G/C	.114	.158	1.483	1.244-1.769	9.4 x 10 ⁻⁶	4.1 x 10 ⁻⁵	Yes
rs17235125		6	79,437,555	A/G	.871	.906	1.459	1.207-1.762	8.0 x 10 ⁻⁵		
rs17235167		6	79,437,614	C/G	.871	.906	1.459	1.208-1.763	7.8 x 10 ⁻⁵		
rs17235209		6	79,437,636	C/T	.871	.906	1.461	1.209-1.765	7.6 x 10 ⁻⁵		
rs17826801		6	79,437,741	A/G	.871	.906	1.460	1.208-1.764	7.8 x 10 ⁻⁵		
rs2021966	ENPP1	6	132,192,132	A/G	.585	.634	1.320	1.150-1.516	7.2 x 10 ⁻⁵	2.6 x 10 ⁻⁴	Yes
rs2813539	SYNE1	6	152,613,828	G/A	.382	.435	1.312	1.150-1.496	4.8 x 10 ⁻⁵		
rs1408460	SYNE1	6	152,614,232	C/G	.460	.518	1.267	1.126-1.426	8.3 x 10 ⁻⁵		
rs719764	SYNE1	6	152,614,487	C/G	.483	.538	1.293	1.141-1.466	5.4 x 10 ⁻⁵		
rs2673776	SYNE1	6	152,614,926	G/T	.458	.516	1.265	1.125-1.422	8.0 x 10 ⁻⁵		
rs2635441	SYNE1	6	152,615,257	A/G	.460	.517	1.264	1.123-1.422	9.4 x 10 ⁻⁵		
rs13212052		6	166,264,601	T/C	.979	.992	2.979	1.668-5.323	8.2 x 10 ⁻⁵		
rs2791300		7	18,102,317	C/G	.704	.752	1.319	1.149-1.514	7.7 x 10 ⁻⁵		
rs4721708		7	18,143,542	C/T	.702	.760	1.373	1.199-1.572	3.8 x 10 ⁻⁶		
rs615545		7	18,165,111	C/T	.694	.751	1.361	1.190-1.556	5.9 x 10 ⁻⁶		Yes
rs2470984	SLC13A1	7	122,368,680	A/C	.297	.348	1.279	1.130-1.448	9.0 x 10 ⁻⁵		Yes
rs6466855	SLC13A1	7	122,371,141	A/G	.294	.346	1.289	1.137-1.462	7.0 x 10 ⁻⁵		
rs6964272	SLC13A1	7	122,373,978	T/C	.265	.317	1.333	1.168-1.52	1.7 x 10 ⁻⁵		
rs13444183	SLC13A1	7	122,377,232	G/T	.265	.317	1.333	1.168-1.521	1.8 x 10 ⁻⁵		
rs6963735	SLC13A1	7	122,394,634	C/T	.256	.306	1.350	1.176-1.549	1.8 x 10 ⁻⁵		
rs10280430	SLC13A1	7	122,399,306	C/T	.255	.305	1.350	1.176-1.549	1.9 x 10 ⁻⁵		
rs1880178	SLC13A1	7	122,403,062	T/C	.255	.305	1.350	1.176-1.55	1.9 x 10 ⁻⁵		
rs10954654		7	138,816,342	C/T	.725	.776	1.337	1.166-1.533	2.8 x 10 ⁻⁵		Yes
rs10277603		7	138,816,687	C/T	.592	.645	1.354	1.179-1.554	1.5×10^{-5}		
rs10261979		7	138,816,832	G/C	.601	.653	1.367	1.187-1.574	1.3 x 10 ⁻⁵		
rs10262338		7	138,816,913	A/G	.592	.645	1.355	1.180-1.555	1.5 x 10 ⁻⁵		
rs9692401		7	138,817,247	C/T	.584	.637	1.364	1.187-1.567	1.1 x 10 ⁻⁵		
rs9691662		7	138,817,453	A/G	.592	.645	1.353	1.179-1.554	1.6 x 10 ⁻⁵		
rs9690418		7	138,817,495	G/A	.592	.645	1.353	1.179-1.553	1.6 x 10 ⁻⁵		
rs12707449		7	138,817,983	A/T	.592	.645	1.353	1.179-1.553	1.6 x 10 ⁻⁵		
rs10271287		7	138,819,517	T/C	.592	.645	1.353	1.179-1.554	1.6 x 10 ⁻⁵		
rs38732	MRPS33	7	140,158,346	T/A	.069	.096	1.680	1.296-2.178	6.9 x 10 ⁻⁵		
rs9274	MRPS33	7	140,159,215	A/G	.048	.076	1.639	1.279-2.101	7.5×10^{-5}		
rs544081	~	7	140,209,733	G/A	.048	.076	1.643	1.282-2.106	6.7 x 10 ⁻⁵		
rs488795		7	140,211,070	T/G	.048	.076	1.643	1.282-2.105	6.8×10^{-5}		
rs512509		, 7	140,211,331	T/C	.048	.076	1.643	1.282-2.105	6.7×10^{-5}		
rs548245		7	140,212,951	T/C	.047	.075	1.635	1.274-2.099	8.9 x 10 ⁻⁵		
rs471817		7	140,214,431	A/C	.048	.076	1.643	1.282-2.105	6.8×10^{-5}		
		, 7	140,221,134	A/G	.048	.076	1.642	1.282-2.105	6.8 x 10 ⁻⁵		

			Position	FUSION risk allele/ non-risk	Control risk	Case risk				Genotyped p-value for imputed	Genotyped
SNP	Genes	Chr	(bp)	allele	frequency	frequency	OR	95% CI	p-value	SNP	in Stage 2?
rs528957	LOC642421	7	140,222,643	T/C	.048	.076	1.634	1.276-2.094	7.8 x 10 ⁻⁵		
rs557962	200012121	7	140,232,924	T/C	.047	.076	1.650	1.287-2.115	5.9 x 10 ⁻⁵		Yes
rs7842241	C8orf68	8	1,056,317	G/A	.634	.688	1.285	1.134-1.456	8.1 x 10 ⁻⁵		
rs979728	DLC1	8	13,435,309	T/C	.371	.405	1.464	1.209-1.772	8.6 x 10 ⁻⁵		
rs1852027	CNBD1	8	88,076,230	G/A	.552	.611	1.269	1.127-1.428	7.6 x 10 ⁻⁵		
rs17707746	PTDSS1	8	97,384,821	C/A	.041	.065	1.750	1.317-2.326	8.7 x 10 ⁻⁵		
rs883655	PTDSS1	8	97,386,357	C/T	.041	.065	1.751	1.317-2.328	8.9 x 10 ⁻⁵		
rs13439240	PTDSS1	8	97,387,836	T/C	.041	.065	1.752	1.317-2.330	8.9 x 10 ⁻⁵		
rs7830293	GPR20	8	142,442,691	C/T	.066	.099	1.597	1.276-1.999	3.6 x 10 ⁻⁵		
rs6578167	GPR20	8	142,450,474	C/A	.065	.098	1.578	1.264-1.970	4.7 x 10 ⁻⁵		
rs7839244	GPR20	8	142,457,437	A/G	.066	.098	1.553	1.248-1.932	6.8 x 10 ⁻⁵		Yes
rs4961268	GPR20	8	142,464,393	G/A	.064	.097	1.586	1.271-1.980	3.7 x 10 ⁻⁵		
rs4961755	BNC2	9	16,759,812	C/G	.121	.158	1.467	1.213-1.774	7.0 x 10 ⁻⁵		
rs12683158	NFIL3	9	91,266,820	C/T	.927	.954	1.736	1.333-2.261	3.2 x 10 ⁻⁵		
rs13297268	NFIL3	9	91,267,696	G/A	.927	.954	1.745	1.338-2.277	3.0 x 10 ⁻⁵	9.0 x 10 ⁻⁵	Yes
rs13289738	NFIL3	9	91,271,701	G/T	.926	.951	1.793	1.354-2.372	3.3 x 10 ⁻⁵		
rs7856348	CYLC2	9	102,835,550	C/A	.541	.591	1.308	1.144-1.495	7.9 x 10 ⁻⁵		
rs1330146		9	107,631,794	G/A	.545	.603	1.289	1.142-1.455	3.7 x 10 ⁻⁵		
rs10816576		9	107,633,222	G/A	.545	.603	1.289	1.142-1.455	3.7 x 10 ⁻⁵		
rs10121193		9	107,660,601	A/G	.382	.426	1.348	1.161-1.565	8.4 x 10 ⁻⁵		
rs4543877		10	65,172,027	C/G	.439	.497	1.330	1.173-1.507	7.7 x 10 ⁻⁶		
rs3864799		10	65,172,388	G/C	.439	.497	1.330	1.173-1.508	7.5 x 10 ⁻⁶		
rs3912165		10	65,187,697	A/G	.427	.485	1.349	1.186-1.534	4.5 x 10 ⁻⁶		
rs10740140		10	65,189,760	A/G	.428	.485	1.290	1.145-1.452	2.5 x 10 ⁻⁵		
rs4746396		10	65,194,129	C/G	.436	.494	1.274	1.136-1.429	3.1 x 10 ⁻⁵		
rs16918864		10	65,228,767	G/C	.430	.487	1.275	1.136-1.431	3.4 x 10 ⁻⁵		
rs3104056		10	71,180,045	G/A	.974	.986	3.162	1.736-5.758	6.3 x 10 ⁻⁵		
rs17747324	TCF7L2	10	114,742,493	C/T	.141	.181	1.445	1.214-1.719	3.0 x 10 ⁻⁵		
rs7903146	TCF7L2	10	114,748,339	T/C	.179	.229	1.388	1.197-1.610	1.2 x 10 ⁻⁵		Yes
rs12243326	TCF7L2	10	114,778,805	C/T	.163	.213	1.429	1.224-1.667	5.0 x 10 ⁻⁶		
rs12255372	TCF7L2	10	114,798,892	T/G	.156	.203	1.400	1.201-1.632	1.5 x 10 ⁻⁵		Yes
rs12288214		11	41,772,225	G/A	.915	.946	1.681	1.316-2.147	2.5 x 10 ⁻⁵		
rs12284861		11	41,787,876	A/G	.915	.946	1.685	1.320-2.150	2.1 x 10 ⁻⁵		
rs11036577		11	41,792,460	C/T	.914	.946	1.684	1.320-2.148	2.1 x 10 ⁻⁵		
rs12797436		11	41,798,917	A/C	.913	.944	1.624	1.279-2.062	5.4 x 10 ⁻⁵		
rs12274732		11	41,805,501	C/T	.914	.946	1.682	1.319-2.145	2.1 x 10 ⁻⁵		
rs12275923		11	41,818,526	A/C	.914	.946	1.685	1.321-2.150	2.0 x 10 ⁻⁵		
rs12294552		11	41,821,081	G/C	.913	.944	1.629	1.282-2.069	5.2 x 10 ⁻⁵		
rs11036600		11	41,823,651	A/G	.914	.946	1.685	1.321-2.150	2.0×10^{-5}		
rs11600495		11	41,828,609	C/A	.914	.944	1.622	1.273-2.065	7.3 x 10 ⁻⁵		
rs10160442		11	41,833,678	T/C	.914	.946	1.683	1.318-2.148	2.2 x 10 ⁻⁵		
rs3763827		11	41,834,454	G/C	.913	.943	1.625	1.278-2.066	5.9×10^{-5}		
rs6485288		11	41,837,914	A/G	.906	.939	1.616	1.285-2.032	3.2×10^{-5}		
rs12280294		11	41,838,323	G/T	.914	.945	1.683	1.318-2.150	2.3 x 10 ⁻⁵		

				FUSION risk allele/	Control	Case				Genotyped p-value	
			Position	non-risk	risk	risk				for imputed	Genotyped
SNP	Genes	Chr	(bp)	allele	frequency	frequency	OR	95% CI	p-value	SNP	in Stage 2?
rs12281155		11	41,843,640	C/G	.914	.945	1.684	1.318-2.151	2.3 x 10 ⁻⁵		
rs12786634		11	41,845,196	C/T	.914	.945	1.683	1.318-2.150	2.3 x 10 ⁻⁵		
rs12277557		11	41,849,152	A/T	.912	.943	1.686	1.320-2.155	2.2 x 10 ⁻⁵		
rs12793795		11	41,854,702	G/A	.906	.936	1.588	1.258-2.005	8.4 x 10 ⁻⁵		
rs12271525		11	41,858,437	G/A	.891	.925	1.512	1.228-1.860	8.1 x 10 ⁻⁵		
rs7928200		11	41,859,109	A/G	.891	.925	1.512	1.229-1.861	8.0 x 10 ⁻⁵		
rs12273344		11	41,859,353	G/T	.890	.925	1.516	1.233-1.863	6.5 x 10 ⁻⁵		
rs12788548		11	41,862,957	C/T	.891	.925	1.513	1.229-1.862	7.9 x 10 ⁻⁵		
rs12288738		11	41,868,875	T/C	.890	.924	1.511	1.229-1.858	7.5 x 10 ⁻⁵		
rs1588439		11	41,871,182	G/A	.890	.924	1.511	1.229-1.858	7.5 x 10 ⁻⁵		
rs16936067		11	41,871,820	G/T	.906	.936	1.580	1.252-1.993	9.5 x 10 ⁻⁵		
rs9300039		11	41,871,942	C/A	.890	.925	1.520	1.236-1.869	6.0 x 10 ⁻⁵		Yes
rs11036622		11	41,872,742	C/T	.890	.924	1.516	1.232-1.864	6.9 x 10 ⁻⁵		
rs11036624		11	41,878,246	T/C	.891	.925	1.525	1.236-1.881	6.8 x 10 ⁻⁵		
rs12797038		11	41,880,453	C/T	.907	.937	1.598	1.260-2.026	9.0 x 10 ⁻⁵		
rs12804210		11	41,880,999	T/C	.891	.925	1.549	1.251-1.919	5.1 x 10 ⁻⁵		
rs11036627		11	41,881,290	C/A	.904	.937	1.662	1.314-2.103	1.8 x 10 ⁻⁵	1.9 x 10 ⁻⁵	Yes
rs11036628		11	41,881,352	G/A	.904	.937	1.662	1.313-2.103	1.8 x 10 ⁻⁵		
rs7114241		11	41,882,103	T/C	.891	.925	1.552	1.251-1.924	5.2 x 10 ⁻⁵		
rs7128743		11	41,882,275	C/A	.891	.925	1.552	1.252-1.925	5.2 x 10 ⁻⁵		
rs12288361		11	41,883,303	C/T	.891	.925	1.553	1.252-1.927	5.1 x 10 ⁻⁵		
rs12802634		11	41,886,138	T/C	.891	.925	1.554	1.252-1.928	5.2 x 10 ⁻⁵		
rs12802862		11	41,886,267	T/C	.891	.925	1.554	1.252-1.928	5.2 x 10 ⁻⁵		
rs11608189		11	41,887,387	G/T	.907	.937	1.609	1.267-2.045	7.9 x 10 ⁻⁵		
rs11602004		11	41,900,843	G/T	.907	.938	1.616	1.271-2.053	7.0 x 10 ⁻⁵		
rs11602127		11	41,901,557	G/A	.907	.938	1.628	1.280-2.070	5.6 x 10 ⁻⁵		
rs10501281		11	41,922,935	C/T	.915	.947	1.617	1.276-2.048	5.3 x 10 ⁻⁵		
rs11823992		11	41,926,856	A/T	.918	.949	1.651	1.294-2.105	4.0 x 10 ⁻⁵		
rs7101809		11	41,933,715	T/C	.918	.949	1.653	1.295-2.109	4.1 x 10 ⁻⁵		
rs12287052		11	41,935,144	A/G	.918	.949	1.651	1.289-2.114	5.6 x 10 ⁻⁵		
rs11036642		11	41,940,997	T/A	.921	.951	1.699	1.318-2.191	3.3 x 10 ⁻⁵		
rs17553408		11	41,951,928	T/G	.918	.949	1.650	1.288-2.115	5.8 x 10 ⁻⁵		
rs12293408		11	41,956,332	C/T	.921	.951	1.695	1.315-2.186	3.5 x 10 ⁻⁵		
rs16936200		11	41,963,315	A/C	.906	.939	1.635	1.294-2.067	3.0 x 10 ⁻⁵		
rs11036649		11	41,965,524	A/G	.906	.939	1.634	1.293-2.066	3.1×10^{-5}		
rs12576408		11	41,971,203	G/T	.906	.939	1.633	1.292-2.064	3.2 x 10 ⁻⁵		
rs11036652		11	41,971,269	T/C	.907	.939	1.629	1.288-2.058	3.5 x 10 ⁻⁵		
rs7107246		11	41,972,428	C/A	.883	.915	1.630	1.287-2.064	4.0×10^{-5}		
rs11604966		11	41,972,736	T/C	.907	.940	1.623	1.285-2.051	3.8×10^{-5}		
rs10837766		11	41,984,377	T/C	.840	.882	1.472	1.232-1.759	$1.8 \ge 10^{-5}$	8.6 x 10 ⁻⁵	Yes
rs17554005		11	41,989,148	A/C	.916	.947	1.686	1.312-2.166	3.4×10^{-5}	0.0 .1 10	1.05
rs17554054		11	41,990,218	T/C	.916	.947	1.682	1.310-2.161	3.6×10^{-5}		
rs17554081		11	41,990,280	A/G	.916	.946	1.677	1.306-2.154	3.9×10^{-5}		
rs2862456		11	41,990,280	C/T	.916	.946	1.668	1.300-2.134	4.5×10^{-5}		
152002750		11	41,990,709	A/G	.916	.946	1.666	1.299-2.137	4.5×10^{-5} 4.6×10^{-5}		

SNP	Genes	Chr	Position	FUSION risk allele/ non-risk	Control risk	Case risk	OR	95% CI	n value	Genotyped p-value for imputed SNP	Genotyped
rs17462994	Genes	11	(bp) 41,991,889	allele T/C	frequency .916	frequency .946	1.666	1.299-2.137	p-value 4.6 x 10 ⁻⁵	SINP	in Stage 2?
				G/A	.916		2.303	1.515-3.500	4.6×10^{-5} 5.2 x 10 ⁻⁵		
rs12792932 rs12806859		11 11	127,226,772	G/A T/G		.984 .984	2.303	1.515-5.500	5.2×10^{-5} 5.2×10^{-5}		
		11	127,234,379 127,328,409	G/A	.967 .963		2.299 2.197	1.314-3.492	3.2×10^{-5} 8.3 x 10 ⁻⁵		
rs12799032 rs12792749		11				.980 .980		1.465-3.275	8.5×10^{-5}		
		11	127,336,192	G/A T/G	.963		2.191 2.191	1.465-3.275	8.6 x 10 ⁻⁵ 8.7 x 10 ⁻⁵		
rs12797631			127,341,608		.963	.980			8.7×10^{-5} 8.8×10^{-5}		
rs12796900		11	127,341,924	C/A	.963	.980	2.191	1.465-3.276	8.8×10^{-5}		
rs12793901		11	127,345,185	G/A	.963	.980	2.198	1.468-3.290	8.6 x 10 ⁻⁵	4.0 10-5	37
rs11616188	LTBR, SCNN1A	12	6,373,003	A/G	.474	.522	1.400	1.201-1.633	1.6×10^{-5}	4.8 x 10 ⁻⁵	Yes
rs7313533		12	6,386,116	A/G	.702	.742	1.394	1.179-1.649	9.8 x 10 ⁻⁵		
rs12581386	COROIC	12	107,585,465	C/A	.962	.977	2.546	1.571-4.126	7.6 x 10 ⁻⁵		
rs3825253	CORO1C	12	107,611,747	A/G	.973	.989	2.575	1.604-4.134	3.6 x 10 ⁻⁵		Yes
rs7957463	FLJ20674, WSB2	12	116,981,026	T/C	.577	.633	1.274	1.134-1.432	4.2 x 10 ⁻⁵		
rs7958110	FLJ20674, WSB2	12	116,981,479	T/C	.577	.633	1.273	1.133-1.430	4.4 x 10 ⁻⁵		
rs4767658	FLJ20674, WSB2	12	116,982,161	T/C	.577	.633	1.274	1.134-1.430	4.1 x 10 ⁻⁵		Yes
rs7488309	FLJ20674, WSB2	12	116,982,890	G/A	.577	.633	1.273	1.133-1.430	4.3 x 10 ⁻⁵		
rs2711747	CCDC60	12	118,360,953	T/G	.014	.025	3.401	1.842-6.280	4.9 x 10 ⁻⁵		
rs1918416		12	118,463,133	C/T	.808	.853	1.383	1.181-1.618	4.9 x 10 ⁻⁵		
rs804628		12	118,468,458	G/C	.816	.856	1.432	1.204-1.702	4.4 x 10 ⁻⁵		
rs2669161		12	120,663,139	C/G	.846	.884	1.457	1.210-1.755	6.3 x 10 ⁻⁵		
rs2707069		12	120,666,804	C/T	.846	.884	1.462	1.212-1.764	6.4 x 10 ⁻⁵		
rs1287527		13	80,731,274	T/C	.085	.120	1.493	1.226-1.819	6.1 x 10 ⁻⁵		
rs1287526		13	80,734,028	G/A	.088	.123	1.480	1.219-1.796	6.4 x 10 ⁻⁵		
rs982864		13	80,735,627	C/T	.075	.109	1.512	1.229-1.859	7.7 x 10 ⁻⁵		
rs2801597		13	80,736,045	G/A	.075	.109	1.512	1.229-1.859	7.8 x 10 ⁻⁵		
rs1287533		13	80,740,650	A/T	.083	.117	1.490	1.220-1.820	8.2 x 10 ⁻⁵		
rs9545851		13	81,234,888	T/C	.525	.583	1.279	1.135-1.441	5.1 x 10 ⁻⁵		
rs9545852		13	81,237,495	C/T	.525	.583	1.278	1.134-1.440	5.2 x 10 ⁻⁵		
rs9531246		13	81,239,573	C/A	.525	.583	1.278	1.134-1.439	5.3 x 10 ⁻⁵		
rs9545853		13	81,242,579	T/C	.526	.583	1.277	1.134-1.438	5.4 x 10 ⁻⁵		
rs11149214		13	81,283,609	C/A	.526	.583	1.276	1.133-1.438	5.5 x 10 ⁻⁵		
rs9545870		13	81,286,274	A/G	.526	.583	1.276	1.133-1.438	5.5 x 10 ⁻⁵		
rs3891591		13	81,291,969	C/T	.517	.573	1.276	1.131-1.440	6.9 x 10 ⁻⁵		
rs9545903		13	81,344,914	T/C	.459	.514	1.270	1.128-1.430	7.2×10^{-5}		
rs10135197		14	38,123,411	T/C	.598	.654	1.288	1.138-1.458	6.1 x 10 ⁻⁵		
rs8014198		14	38,132,529	G/A	.616	.670	1.291	1.137-1.464	7.0×10^{-5}		
rs9788490		14	38,132,689	C/G	.603	.659	1.287	1.138-1.455	5.5×10^{-5}		
rs11849174		14	38,147,149	G/A	.603	.660	1.287	1.138-1.455	5.4 x 10 ⁻⁵		
rs10145493		14	38,151,139	G/A G/A	.603	.659	1.287	1.138-1.455	5.6×10^{-5}		
rs12435438		14	38,154,195	T/C	.553	.612	1.318	1.161-1.495	1.7×10^{-5}		
rs1349241		14	38,155,189	T/C T/C	.553	.612	1.318	1.161-1.495	1.7×10^{-5} 1.8 x 10 ⁻⁵		
rs10141957		14	38,157,020	G/A	.535	.610	1.318	1.167-1.500	1.0×10^{-5} 1.1 x 10 ⁻⁵		
rs2122331		14	38,157,020	G/A G/C	.549	.575	1.323	1.133-1.435	5.2×10^{-5}		
rs8010489		14	38,163,618	G/A	.523	.575	1.273	1.135-1.435	3.2×10^{-5} 4.5 x 10 ⁻⁵		
180010489		14	38,103,018	U/A	.323	.384	1.281	1.13/-1.444	4.3 X 10		

		~1	Position	FUSION risk allele/ non-risk	Control risk	Case risk				Genotyped p-value for imputed	Genotyped
SNP	Genes	Chr	(bp)	allele	frequency	frequency	OR	95% CI	p-value	SNP	in Stage 2?
rs1449720		14	38,165,318	A/G	.512	.573	1.269	1.128-1.428	6.8 x 10 ⁻⁵		
rs12164874		14	38,172,603	C/T	.515	.577	1.278	1.136-1.439	4.5×10^{-5}		
rs10138342		14	38,186,108	A/C	.526	.587	1.284	1.139-1.448	$4.0 \ge 10^{-5}$		
rs7153699		14	38,188,807	C/T	.518	.579	1.279	1.136-1.440	4.4×10^{-5}		
rs6571865		14	38,191,421	T/C	.518	.580	1.281	1.137-1.442	4.1×10^{-5}		
rs7141696		14	38,192,126	T/C	.518	.580	1.281	1.138-1.443	4.0×10^{-5}		
rs8006474		14	38,196,248	G/C	.527	.589	1.290	1.144-1.454	3.1×10^{-5}		
rs2122333		14	38,233,119	C/T	.542	.610	1.321	1.171-1.491	5.3×10^{-6}	4 4 4 6 5	
rs1449725		14	38,246,572	C/T	.543	.610	1.322	1.172-1.492	4.9×10^{-6}	1.1 x 10 ⁻⁵	Yes
rs2899883		14	38,255,604	G/T	.539	.604	1.320	1.169-1.491	7.0 x 10 ⁻⁶		
rs2319392	GPHN	14	66,136,844	T/A	.014	.023	4.396	2.050-9.426	5.0 x 10 ⁻⁵		
rs3825569	LOC388015	14	100,420,051	C/T	.583	.640	1.292	1.143-1.46	3.7 x 10 ⁻⁵		
rs12910827		15	56,417,311	T/G	.024	.047	2.592	1.738-3.866	1.3 x 10 ⁻⁶	6.3 x 10 ⁻⁶	Yes
rs11634708	LOC56964, PEX11A, PLIN	15	88,037,214	C/T	.433	.485	1.315	1.153-1.500	4.1 x 10 ⁻⁵		
rs10521095		16	13,528,936	A/G	.206	.256	1.351	1.174-1.554	2.3 x 10 ⁻⁵		Yes
rs6498423		16	13,531,381	A/G	.206	.256	1.351	1.174-1.555	2.4×10^{-5}		
rs12162088		16	13,547,393	G/A	.130	.169	1.407	1.185-1.671	8.8 x 10 ⁻⁵		
rs16962270		16	13,547,426	T/A	.130	.169	1.409	1.186-1.673	8.7 x 10 ⁻⁵		
rs2033254	CETP	16	55,567,486	T/C	.646	.693	1.367	1.177-1.587	$4.0 \ge 10^{-5}$		
rs12708980	CETP	16	55,569,880	T/G	.633	.677	1.385	1.184-1.621	$4.4 \ge 10^{-5}$	C.	
rs1800774	CETP	16	55,573,046	C/T	.640	.686	1.399	1.195-1.639	2.8 x 10 ⁻⁵	7.3 x 10 ⁻⁶	Yes
rs11646114	FOXC2, MTHFSD	16	85,141,275	T/A	.868	.894	1.658	1.285-2.140	8.9 x 10 ⁻⁵	0.002	Yes
rs9911259	PRKCA	17	62,085,377	C/A	.435	.493	1.274	1.134-1.432	4.4 x 10 ⁻⁵		
rs16959880	PRKCA	17	62,085,528	A/G	.435	.493	1.274	1.134-1.432	4.3 x 10 ⁻⁵		
rs8077110	PRKCA	17	62,087,049	A/G	.435	.493	1.274	1.134-1.432	4.3 x 10 ⁻⁵		
rs1024740	PRKCA	17	62,088,152	C/G	.435	.493	1.275	1.134-1.432	4.3 x 10 ⁻⁵		
rs7207345	PRKCA	17	62,093,747	T/C	.707	.755	1.307	1.144-1.492	7.5 x 10 ⁻⁵		
rs17384005		18	1,565,020	A/G	.810	.839	1.864	1.409-2.467	1.1 x 10 ⁻⁵	.10	Yes
rs1785710		18	21,612,825	G/C	.648	.702	1.295	1.142-1.468	5.1 x 10 ⁻⁵		
rs7229654		18	35,549,984	A/G	.959	.978	2.024	1.412-2.902	8.0 x 10 ⁻⁵		
rs1596583		18	35,550,893	G/A	.959	.979	2.033	1.418-2.916	7.3 x 10 ⁻⁵		
rs9675995		18	35,574,907	G/A	.959	.978	2.020	1.410-2.895	8.3 x 10 ⁻⁵		
rs10853467		18	35,582,328	A/G	.959	.978	2.021	1.410-2.896	8.2 x 10 ⁻⁵		
rs616444	SETBP1	18	40,739,522	A/C	.882	.917	1.465	1.208-1.778	9.0 x 10 ⁻⁵		
rs175200		22	18,543,063	A/G	.494	.555	1.282	1.138-1.445	4.1 x 10 ⁻⁵	5.5 x 10 ⁻⁵	Yes
rs438798		22	18,544,053	G/A	.494	.555	1.282	1.138-1.444	4.2 x 10 ⁻⁵		
rs520698	LOC150207	22	19,349,434	G/A	.702	.757	1.377	1.199-1.582	5.4 x 10 ⁻⁶		
rs565979		22	19,353,500	C/T	.679	.730	1.295	1.139-1.472	7.0 x 10 ⁻⁵		Yes
rs479275		22	19,353,777	T/A	.656	.708	1.283	1.131-1.455	9.5 x 10 ⁻⁵		
rs491228	DKFZp434N035	22	19,357,925	G/A	.679	.730	1.294	1.138-1.471	7.5 x 10 ⁻⁵		
rs591446	DKFZp434N035	22	19,359,204	A/G	.656	.708	1.283	1.131-1.454	9.7 x 10 ⁻⁵		
rs2267339	CACNG2	22	35,290,742	G/T	.610	.666	1.333	1.169-1.521	1.6 x 10 ⁻⁵	4.5 x 10 ⁻⁶	Yes

Table S4. Confirmed T2D susceptibility loci	expanded FUSION results
Rick	

			Risk allele R/							Risk a	allele									
			Non-risk	-	ontrols			Cases (r	/	frequ	ency		Additive			Dominant			Recessive	
SNP	Gene	Stage	allele N	RR	RN	NN	RR	RN	NN	control	case	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
rs1801282	PPARG	1	C/G	778	336	45	834	298	19	.816	.854	1 303	1.111-1.529	.0011	2 399	1.387-4.151	.0011	1 270	1.059-1.523	.0097
131001202	TTINO	2	C/G	840	337	38	838	293	37	.830	.843		0.924-1.256	0.34		0.612-1.555	.92		0.929-1.327	.25
		1+2	C/G	1618	673	83	1672	591	56	.823	.848		1.071-1.333	.0014		1.056-2.114	.022		1.058-1.362	.0046
rs4402960	IGF2BP2	1	T/G	102	471	585	148	495	498	.291	.347	1.276	1.126-1.446	1.2 x 10 ⁻⁴	1.316	1.115-1.555	.0012	1.520	1.160-1.992	.0022
		2	T/G	142	498	595	122	553	515	.317	.335	1.073	0.951-1.211	.25	1.197	1.018-1.408	.029	0.872	0.672-1.131	.30
		1+2	T/G	244	969	1180	270	1048	1013	.304	.341	1.175	1.078-1.281	2.4 x 10 ⁻⁴	1.263	1.125-1.418	7.3 x 10 ⁻⁵	1.155	0.960-1.390	.13
rs7754840	CDKAL1	1	C/G	154	522	439	190	531	400	.372	.406		1.022-1.304	.021		0.979-1.387	.084		1.019-1.628	.034
		2	C/G	141	574	509	153	565	466	.350	.368		0.959-1.223	.20		0.926-1.290	.29		0.890-1.463	.30
		1+2	C/G	295	1096	948	343	1096	866	.360	.387	1.120	1.028-1.220	.0095	1.129	1.002-1.271	.046	1.220	1.030-1.444	.021
rs13266634	SLC30A8	1	C/T	421	577	176	506	500	155	.604	.651	1.222	1.084-1.379	.0010	1.157	0.913-1.466	.23	1.380	1.166-1.634	1.8 x 10 ⁻⁴
		2	C/T	470	561	192	505	516	160	.614	.646		1.016-1.286	.026		0.952-1.511	.12		1.008-1.406	.040
		1+2	C/T	891	1138	368	1011	1016	315	.609	.649	1.184	1.089-1.287	6.8 x 10 ⁻⁵	1.175	0.997-1.385	.053	1.289	1.146-1.449	2.3x 10 ⁻⁵
rs10811661	CDKN2A/B	1	T/C	809	308	13	850	256	18	.852	.870	1.168	0.980-1.392	.082	0.763	0.369-1.576	.46	1.223	1.011-1.480	.038
		2	T/C	893	309	33	911	256	23	.848	.873	1.223	1.039-1.441	.015	1.345	0.779-2.322	.28	1.254	1.042-1.510	.017
		1+2	T/C	1702	617	46	1761	512	41	.850	.872	1.204	1.069-1.356	.0022	1.112	0.724-1.708	.63	1.245	1.091-1.421	.001
rs1111875	HHEX	1	C/T	333	568	273	372	549	240	.526	.557	1.128	1.006-1.266	.039		0.954-1.420	.13	1.187	0.992-1.420	.061
		2	C/T	332	596	285	333	581	250	.519	.536		0.943-1.187	.34		0.926-1.369	.23		0.866-1.246	.68
		1+2	C/T	665	1164	558	705	1130	490	.522	.546	1.097	1.012-1.189	.025	1.148	0.999-1.318	.051	1.120	0.986-1.271	.081
rs7903146	TCF7L2	1	T/C	32	356	786	55	422	684	.179	.229		1.197-1.610		1.422	1.198-1.688			1.161-2.850	.0079
		2	T/C	33	383	810	68	393	711	.183	.226		1.122-1.495		1.266	1.069-1.498	.0061		1.382-3.262	4.1×10^{-4}
		1+2	T/C	65	739	1596	123	815	1395	.181	.227	1.343	1.213-1.488	1.4 x 10 ⁻⁸	1.344	1.192-1.514	1.2 x 10 ⁻⁶	1.993	1.464-2.712	7.1 x 10 ⁻⁶
rs5219	KCNJ11	1	T/C	221	562	346	271	538	296	.445	.489	1.204	1.069-1.357	.0022	1.214	1.007-1.463	.042	1.366	1.114-1.675	.0027
		2	T/C	284	622	328	271	624	295	.482	.490	1.035	0.922-1.162	.56	1.112	0.925-1.338	.26	0.979	0.807-1.186	.83
		1+2	T/C	505	1184	674	542	1162	591	.464	.489	1.109	1.021-1.204	.014	1.152	1.011-1.312	.034	1.142	0.994-1.312	.060
rs9300039		1	C/A	929	232	13	992	161	7	.890	.925	1.520	1.236-1.869	6.0 x 10 ⁻⁵	1.797	0.702-4.600	.21	1.563	1.254-1.948	6.2 x 10 ⁻⁵
		2	C/A	988	227	17	1007	170	5	.894	.924				3.445	1.247-9.520	.0094		1.150-1.771	.0012
		1+2	C/A	1917	459	30	1999	331	12	.892	.924	1.478	1.280-1.705	6.8 x 10 ⁻⁸	2.470	1.252-4.874	.0062	1.490	1.279-1.737	2.7 x 10 ⁻⁷
rs8050136	FTO	1	A/C	192	562	420	213	538	410	.403	.415		0.920-1.162	.58		0.841-1.186	.99		0.904-1.397	.29
		2	A/C	150	585	492	185	566	427	.361	.397		1.046-1.329	.0070		0.998-1.394	.053		1.077-1.725	.0098
		1+2	A/C	342	1147	912	398	1104	837	.381	.406	1.107	1.019-1.203	.017	1.091	0.969-1.229	.15	1.240	1.058-1.453	.0078

Table S5. FUSION stage 1, stage 2, and stage 1 + 2 T2D association results for 80 SNPs. SNPs were selected for stage 1 or stage 2 genotyping based on results in the FUSION GWA, combined evidence from FUSION, DGI, and WTCCC GWAs, or previous reports.

				Risk	Control	<u>ge 1</u> Case	<u>Stag</u> Control	Case	Stage Control	Case										
				allele/	risk	risk	risk	risk	risk	risk										
		Position		non-risk	allele	allele	allele	allele	allele	allele		Stage 1			Stage 2			Stage 1 +	2	Reason for
	Chr	(bp)	Genes	allele	freq	freq	freq	freq	freq	freq	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	follow-up
s640742	1	20,729,860	CDA, DDOST, KIF17, PINK1	A/C	.601	.663	.616	.613	.609	.638	1.297			0.992		.89		1.037-1.225	.0047	FUSION GW
s17356414	1	59,031,529	-	C/T	.694	.736	.719	.708	.707	.722		1.096-1.422			0.841-1.081	.46		0.991-1.186	.077	FUSION Imp
s17025978	1	110,781,653	KCNA10	G/A	.914	.947	.934	.930	.924	.939		1.347-2.158			0.752-1.178	.60		1.082-1.491	.0033	FUSION GV
s10494217	1	119,181,230	TBX15	G/T	.708	.735	.740	.725	.724	.730		1.004-1.298	.044		0.816-1.058	.27		0.937-1.124	.58	Combined G
s7599781	2	43,590,377	PLEKHH2, THADA	T/C	.942	.958	.954	.950	.948	.954		1.119-1.953	.0056		0.683-1.172	.42		0.947-1.390	.16	Combined G
s6704803	2	158,175,059	ACVR1C, PSCDBP	C/T	.928	.946	.938	.942	.933 .823	.944 .848		1.033-1.675	.025 .0011		0.851-1.380	.52		1.011-1.419	.036 .0014	Combined G
s1801282 s17081352	3 3	12,368,125 30,307,851	PPARG, LOC643925	C/G	.816	.854 .940	.830 .928	.843 .927	.823	.848		1.111-1.529 1.339-2.109			0.924-1.256 0.780-1.224	.34 .84		1.071-1.333 1.090-1.494	.0014	Combined G
s17081332 s13072106	3	134,425,451	- BFSP2, TMEM108	C/A T/C	.905 .118	.155	.143	.142	.130	.149		1.188-1.682			0.780-1.224	.84		1.038-1.311	.0023	FUSION Imp FUSION GV
s4687299	3	186,595,361	MAP3K13	A/G	.225	.276	.268	.260	.247	.268		1.158-1.515			0.841-1.092	.53		1.017-1.225	.020	FUSION G
s17289925	3	186,917,362	C3orf65, IGF2BP2, LOC646600	C/T	.018	.022	.020	.020	.019	.021		0.775-1.801	.44		0.719-1.613	.72		0.836-1.492	.46	Follow-up
s4402960	3	186,994,389	IGF2BP2	T/G	.291	.347	.317	.335	.304	.341	1 276	1.126-1.446	1.2×10^{-4}	1 073	0.951-1.211	.25	1 175	1.078-1.281	2.4 x 10 ⁻⁴	Combined G
s734312	4	6,421,426	WFS1	A/G	.478	.506	.482	.485	.480	.496		0.980-1.236	.11		0.899-1.134	.87		0.973-1.145	.19	Combined G
s886374	4	7,856,440	SORCS2	T/C	.211	.270	.233	.221	.222	.245		1.209-1.587			0.824-1.081	.40		1.036-1.253	.007	FUSION G
s13139219	4	42,294,231	ATP8A1	C/A	.779	.827	.796	.805	.788	.816		1.160-1.561	-		0.911-1.214	.50		1.070-1.314	.0011	FUSION G
s6834248	4	95,447,456	LOC644429, PGDS, SMARCAD1	T/C	.772	.786	.779	.765	.775	.776		0.963-1.275	.15		0.800-1.056	.23		0.907-1.104	.99	Combined G
2720460	4	104,412,290	BDH2, CENPE, DHRS6, LOC133308	A/G	.571	.607	.574	.579	.573	.593	1.154	1.025-1.299	.018	1.012	0.899-1.140	.84	1.084	0.998-1.179	.057	Combined G
\$27779	5	142,239,267	ARHGAP26	A/C	.250	.304	.259	.269	.255	.286	1.326	1.162-1.513	2.5 x 10 ⁻⁵	1.044	0.917-1.190	.52	1.171	1.068-1.283	7.5 x 10 ⁻⁴	FUSION G
3733876	5	176,315,601	RAP80	G/A	.765	.805	.791	.798	.778	.801	1.277	1.109-1.471	6.6 x 10 ⁻⁴	1.051	0.909-1.215	.50	1.156	1.046-1.278	.0046	FUSION G
\$4712523	6	20,765,543	CDKAL1	G/A	.372	.407	.349	.366	.360	.387	1.164	1.032-1.312	.013	1.084	0.959-1.224	.20		1.032-1.222	.0073	Follow-u
\$10946398	6	20,769,013	CDKAL1	C/A	.368	.404	.347	.364	.357	.384	1.163	1.029-1.315	.016	1.081	0.956-1.222	.22	1.122	1.029-1.223	.0087	Combined Im
s7754840	6	20,769,229	CDKAL1	C/G	.372	.406	.350	.368	.360	.387	1.155	1.022-1.304	.021		0.959-1.223	.20	1.120	1.028-1.220	.0095	Follow-u
s2206734	6	20,802,863	CDKAL1	T/C	.174	.200	.168	.174	.171	.187		1.016-1.375	.030		0.911-1.234	.45		1.003-1.241	.043	Combined G
s4496780	6	21,187,627	CDKAL1	G/T	.104	.093	.092	.106	.098	.100		0.730-1.086	.25		0.994-1.471	.057		0.911-1.200	.53	Follow-u
s9271366	6	32,694,832	HLADQA1, HLADRA, HLADRB1	A/G	.858	.862	.857	.867	.858	.864		0.878-1.241	.63		0.936-1.303	.24		0.948-1.202	.28	Combined G
s11751469	6	33,912,525	-	C/T	.563	.609	.574	.585	.568	.597		1.073-1.362	.0018		0.933-1.182	.41		1.032-1.219	.007	Combined G
s7750445	6	37,872,955	ZFAND3	G/C	.136	.180	.163	.135	.150	.157	1.407				0.694-0.956	.012	1.053		.37	FUSION Imp
s9472138	6	43,919,740	-	T/C	.310	.314	.305	.321	.308	.318		0.911-1.166	.63		0.946-1.212	.28		0.963-1.145	.27	New Asso
s7450789	6	111,923,668	LOC643749, REV3L, TRAF3IP2	T/G	.903	.919	.908	.912	.906	.916		1.001-1.506			0.877-1.304	.51		0.990-1.314	.068	Combined G
s2021966	6	132,192,132	ENPP1	A/G	.576	.630	.606	.621	.592	.626		1.107-1.403			0.939-1.190	.36		1.056-1.247	.0012	FUSION Imp
\$615545	7	18,165,111	-	C/T	.694	.751	.708	.733	.701	.742		1.190-1.556			0.998-1.289	.053		1.127-1.355		FUSION G
\$10281305	7	54,664,618	-	G/T	.735	.772	.738	.757	.737	.765		1.069-1.401	.0033		0.961-1.261	.16		1.048-1.268	0.0033	Combined G
s17158686	7 7	83,439,407	SEMA3A SLC13A1	T/G A/C	.951 .297	.957 .348	.959 .316	.958 .298	.955 .307	.958 .323		0.874-1.528 1.130-1.448	.31 9.0 x 10 ⁻⁵		0.751-1.351 0.822-1.054	.96		0.881-1.316 0.993-1.181	.47 .073	Combined G FUSION G
s2470984 s10954654	7	122,368,680 138,816,342	SLCISAI	C/T	.725	.348	.735	.298	.730	.323		1.150-1.448	-		0.822-1.034	.26 .21	1.085		1.6 x 10 ⁻⁴	FUSION G
\$557962	7	140,232,924	- LOC642421, MRPS33	T/C	.047	.076	.059	.058	.053	.067		1.287-2.115			0.932-1.243	.89		1.075-1.514	.0052	FUSION G
s13266634	8	118,253,964	SLC30A8	C/T	.604	.651	.614	.646	.609	.649	1.222	1.084-1.379	.001	1.143	1.016-1.286	.026	1.184	1.089-1.287	6.8 x 10 ⁻⁵	FUSION G
s7839244	8	142,457,437	GPR20	A/G	.066	.098	.082	.080	.074	.089		1.248-1.932			0.784-1.192	.75		1.044-1.407	.012	FUSION G
s1063192	9	21,993,367	CDKN2A, CDKN2B	A/G	.556	.582	.587	.584	.572	.583		0.975-1.228	.13		0.879-1.114	.85		0.963-1.134	.29	Follow-u
564398	9	22,019,547	CDKN2A, CDKN2B	T/C	.566	.596	.596	.590	.582	.593		0.994-1.258	.064		0.863-1.091	.61	1.045		.30	Follow-u
s2383208	9	22,122,076	-	A/G	.842	.862	.836	.864	.839	.863		1.002-1.400	.047		1.057-1.456	.0082	1.219			Combined G
s10811661	9	22,124,094	-	T/C	.852	.870	.848	.873	.850	.872		0.980-1.392	.082		1.039-1.441	.015		1.069-1.356	.0022	Follow-u
s13297268	9	91,267,696	NFIL3	G/A	.924	.952	.945	.949	.935	.950	1.650	1.280-2.128			0.848-1.413	.49		1.132-1.618		FUSION Imp
s2185935		114,581,796	-	C/T	.667	.675	.661	.662	.664	.669		0.904-1.160			0.895-1.136	.89		0.935-1.110	.68	Combined G
s1416904	9	131,363,871	KIAA0515, POMT1, UCK1	T/C	.931	.952	.925	.935	.928	.943		1.150-1.902			0.892-1.397	.34		1.074-1.498	.0049	Combined G
s1270874	10	29,879,870	SVIL	C/A	.753	.799	.780	.777	.767	.788		1.123-1.498			0.849-1.120	.72		1.012-1.234	.028	FUSION Imp
s9422546	10	43,391,505	ZNF239, ZNF485	G/T	.628	.631	.640	.651	.634	.641		0.894-1.138			0.945-1.203	.30		0.951-1.127	.42	Combined G
s13088	10	49,985,899	C10orf72	G/A	.369	.398	.363	.384	.366	.391		1.003-1.277	.044		0.953-1.207	.24		1.013-1.198	.024	Combined G
s1359624	10	91,385,408	FLJ37201, MPHOSPH1, PANK1	C/T	.247	.290	.268	.265	.258	.277	1.222	1.072-1.394	.0027	0.973	0.853-1.110	.68	1.108	1.010-1.215	.030	FUSION G

Table S5. FUSION stage 1, stage2, and stage 1 + 2 T2D association results for 80 SNPs (continued)

					Stag	ge 1	Stag	e 2	Stage	1 + 2										
				Risk	Control		Control	Case	Control	Case										
				allele/	risk	risk	risk	risk	risk	risk										
		Position		non-risk	allele	allele	allele	allele	allele	allele		Stage 1			Stage 2			Stage 1 + 2		Reason for
	Chr	(bp)	Genes	allele	freq	freq	freq	freq	freq	freq		95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	follow-up
	10	94,452,862	HHEX	C/T	.526	.557	.519	.536	.522	.546	1.128	1.006-1.266	.039	1.058	0.943-1.187	.35	1.097	1.012-1.189	.025	New Assoc
rs7923837	10	94,471,897	-	G/A	.603	.631	.591	.613	.597	.622	1.122	0.997-1.263	.057	1.090	0.970-1.226	.15	1.107	1.019-1.203	.016	Combined GWA/
450(5(5	10	114 746 021	<i>TCT71</i> 2	T (1	214	250	217	240	216	240	1.057	1 000 1 450	0017	1 107	1 0 27 1 2 (0	012	1 221	1 107 1 246	6 4 10-5	New Assoc
rs4506565	10	114,746,031	TCF7L2	T/A	.214	.250	.217	.248	.216	.249	1.257	1.089-1.450	.0017	1.18/	1.037-1.360	.013	1.221	1.107-1.346	6.4 x 10 ⁻⁵	FUSION Imputed/
rs7903146	10	114,748,339	TCF7L2	T/C	.179	.229	.183	.226	.181	.227	1 200	1.197-1.610	1.3 x 10 ⁻⁵	1 205	1.122-1.495	2.0×10^{-4}	1 2 4 2	1.213-1.488	1.4×10^{-8}	Prev Assoc FUSION GWA/
18/903140	10	114,740,555	ICF/L2	1/C	.1/9	.229	.105	.220	.101	.221	1.300	1.19/-1.010	1.5 x 10	1.295	1.122-1.495	3.9 X 10	1.545	1.213-1.400	1.4 X 10	Prev Assoc
rs12255372	10	114,798,892	TCF7L2	T/G	.156	.203	.165	.199	.161	.201	1 400	1.201-1.632	1.5×10^{-5}	1 244	1.070-1.447	.0044	1 3 1 8	1.184-1.467	3.6×10^{-7}	FUSION GWA/
1312233372	10	114,790,092	101/12	1/0	.150	.205	.105	.177	.101	.201	1.400	1.201-1.052	1.5 X 10	1.244	1.070-1.447	.0044	1.510	1.104-1.407	5.0 X 10	Prev Assoc
rs5219	11	17,366,148	ABCC8, KCNJ11	T/C	.445	.489	.482	.490	.464	.489	1 204	1.069-1.357	.0022	1 035	0.922-1.162	.56	1.109	1.021-1.204	.014	Combined Imputed/
10021)	••	17,500,110	112000, 1101011	1,0							1.201	1.009 1.007		1.050	0.922 11102	.00	1.102	1.021 1.201	.011	Prev Assoc
rs9300039	11	41,871,942	-	C/A	.890	.925	.894	.924	.892	.924	1.520	1.236-1.869	6.0 x 10 ⁻⁵	1.442	1.179-1.764	3.2 x 10 ⁻⁴	1.478	1.280-1.705	6.8 x 10 ⁻⁸	FUSION GWA
rs11036627	11	41,881,290	-	C/A	.912	.946	.924	.946	.918	.946	1.665	1.313-2.110	1.9 x 10 ⁻⁵	1.466	1.159-1.856	.0013	1.563	1.324-1.846	9.2 x 10 ⁻⁸	FUSION Imputed
rs10837766	11	41,984,377	-	T/C	.827	.869	.846	.870	.836	.870	1.397	1.181-1.652	8.6 x 10 ⁻⁵	1.252	1.058-1.482	.0088	1.313	1.166-1.477	5.8 x 10 ⁻⁶	FUSION Imputed
rs7480010	11	42,203,294	LOC387761	G/A	.174	.174	.162	.171	.168	.172	1.004	0.863-1.169	.96	1.078	0.925-1.257	.333	1.034	0.929-1.151	.54	New Assoc
rs4379834	11	44,115,014	ALX4, EXT2, PHACS	G/A	.316	.316	.295	.306	.305	.311	0.980	0.865-1.111	.76		0.936-1.207	.35	1.027	0.940-1.123	.55	New Assoc
	12	6,373,003	LTBR, SCNN1A	A/G	.426	.484	.445	.455	.436	.470		1.131-1.426			0.927-1.167	.50	1.148		8.3 x 10 ⁻⁴	FUSION Imputed
rs3751262	12	12,509,957	DUSP16,	G/A	.914	.932	.917	.904	.916	.918	1.298	1.038-1.623	.022	0.853	0.698-1.043	.12	1.039	0.896-1.205	.61	Combined GWA
			LOH12CR1																	
	12	53,385,263	-	A/T	.699	.721	.682	.702	.690	.711		0.966-1.251	.15		0.989-1.266	.075	1.109		.022	Combined Imputed
	12	69,697,828	-	T/G	.425	.442	.426	.438	.425	.440		0.949-1.205	.27		0.951-1.193	.27	1.063		.14	Combined Imputed
rs3825253	12	107,611,747	CORO1C, DAO,	A/G	.973	.989	.987	.986	.908	.988	2.575	1.604-4.134	3.6 x 10 ⁻⁵	0.991	0.602-1.631	.97	1.678	1.204-2.337	.0019	FUSION GWA
2200455	10	100.006.006	SSH1	0.1	015	020	0.2.1	020	010	020	1.1.00	0.999-1.361	051	0.007	0.057.1.1(1	07	1.075	0.065 1.107	10	
	12 12	108,086,236	ACACB FLJ20674, WSB2	G/A T/C	.815 .577	.839 .633	.821 .609	.820 .613	.818 .593	.829 .623		1.134-1.430	.051		0.857-1.161	.97 .68	1.075	0.965-1.197 1.045-1.230	.19 .0025	Combined GWA FUSION GWA
	12	116,982,161 36,281,317	SLC25A21	C/T	.377	.502	.609	.507	.393	.505		0.951-1.202	4.1 X 10 .26		0.912-1.151 0.933-1.178	.08	1.134		.0023	Combined GWA
	14	38.246.572	-	C/T	.540	.502	.584	.595	.562	.600		1.163-1.486			0.943-1.197	.42		1.084-1.284	1.3×10^{-4}	FUSION Imputed
	14	68,492,917	- ACTN1	G/A	.231	.242	.221	.221	.226	.231		0.920-1.216	.43		0.863-1.136	.32	1.020	0.926-1.124	.69	Combined Imputed
	15	56,417,311	-	T/G	.021	.045	.029	.032	.025	.039		1.541-3.127			0.800-1.539	.53	1.559		1.8 x 10 ⁻⁴	FUSION Imputed
	16	13,528,936		A/G	.206	.256	.228	.229	.217	.243		1.174-1.554			0.882-1.153	.90			.0028	FUSION GWA
	16	52,373,776	FTO	A/C	.403	.415	.361	.397	.381	.406		0.920-1.162	.58		1.046-1.329	.0070		1.019-1.203	.017	Combined GWA
	16	55,573,046	CETP	C/T	.667	.726	.705	.699	.687	.712		1.182-1.537	7.3 x 10 ⁻⁶		0.851-1.098	.60			.005	FUSION Imputed
	16	85,141,275	FLJ12998, FOXC2,	T/A	.895	.921	.915	.905	.905	.913	1.382	1.124-1.698	.002		0.728-1.092	.27	1.110	0.962-1.281	.15	FUSION Imputed
			MTHFSD																	1
rs7222308	17	25,301,167	CCDC55, EFCAB5,	T/C	.532	.553	.535	.552	.533	.553	1.094	0.973-1.229	.13	1.075	0.958-1.206	.22	1.086	1.001-1.179	.047	Combined GWA
			FLJ46247, SLC6A4,																	
			SSH2																	
rs17384005	18	1,565,020	-	A/G	.842	.859	.858	.859	.851	.859	1.147	0.974-1.351	.10	1.004	0.850-1.186	.96	1.074	0.956-1.206	.23	FUSION Imputed
	22	18,543,063	-	A/G	.490	.552	.538	.553	.515	.553		1.137-1.452			0.954-1.198	.25	1.165		2.9 x 10 ⁻⁴	FUSION Imputed
rs565979	22	19,353,500	DKFZp434N035,	C/T	.679	.730	.727	.709	.703	.720	1.295	1.139-1.472	7.0 x 10 ⁻⁵	0.929	0.816-1.056	.26	1.090	0.996-1.193	.060	FUSION GWA
			LOC150207,																	
			LOC645289,																	
22(722)	~~	25 200 745	PIK4CA, SERPIND1	0.00	(11		(20)	(10	(21		1.045	1 100 1 501	15 105	0.020	0.000 1.000			1 000 1 010	016	FUCIONI
rs2267339	22	35,290,742	CACNG2	G/T	.611	.674	.630	.618	.621	.646	1.341	1.182-1.521	4.5 x 10 ⁻⁶	0.939	0.832-1.060	.31	1.112	1.020-1.213	.016	FUSION Imputed

		Risk allele frequency in controls		FUSION S		FUSION S Genoty		Imputation measure	1 5	Observed	Maximum r ² with SNPs	
SNP	Genes	Imputed	Genotyped	p-value ^a	OR ^a	p-value	OR	Imputation consistency ^c	Estimated r^2 d	allelic	used for imputation	
rs12910827		.024	.021	2.5 x 10 ⁻⁶	2.57	6.3 x 10 ⁻⁶	2.20	.977	.720	.994	.39	
rs1449725		.544	.540	5.3 x 10 ⁻⁶	1.33	1.1 x 10 ⁻⁵	1.31	.989	.977	.990	.90	
rs17081352		.909	.905	7.3 x 10 ⁻⁶	1.70	5.5 x 10 ⁻⁶	1.68	.994	.954	1.000	.87	
rs11616188	SCNN1A/LTBR	.474	.426	1.5 x 10 ⁻⁵	1.40	4.8 x 10 ⁻⁵	1.27	.760	.585	.919	.27	
rs10837766		.840	.827	1.5 x 10 ⁻⁵	1.49	8.6 x 10 ⁻⁵	1.40	.975	.930	.975	.46	
rs11036627		.903	.912	1.7 x 10 ⁻⁵	1.67	1.9 x 10 ⁻⁵	1.66	.976	.901	.987	.75	
rs17384005		.811	.842	1.9 x 10 ⁻⁵	1.84	.10	1.15	.743	.309	.874	.11	
rs7750445		.116	.136	2.0 x 10 ⁻⁵	1.47	4.1 x 10 ⁻⁵	1.41	.986	.965	.977	.50	
rs2267339	CACNG2	.613	.611	2.8 x 10 ⁻⁵	1.33	4.5 x 10 ⁻⁶	1.34	.939	.873	.990	.72	
rs17356414		.551	.694	3.0 x 10 ⁻⁵	1.30	8.0 x 10 ⁻⁴	1.25	.944	.920	.878	.34	
rs1800774	CETP	.642	.667	3.9 x 10 ⁻⁵	1.39	7.3 x 10 ⁻⁶	1.35	.810	.617	.972	.29	
rs175200		.493	.490	6.6 x 10 ⁻⁵	1.28	5.5 x 10 ⁻⁵	1.28	.993	.976	.997	.85	
rs6103716		.342	.342	7.3 x 10 ⁻⁵	1.28	4.8 x 10 ⁻⁵	1.29	.993	.978	.999	.33	
rs13297268	NFIL3	.928	.924	7.5 x 10 ⁻⁵	1.72	9.0 x 10 ⁻⁵	1.65	.988	.916	.998	.28	
rs11646114	FOXC2/FLJ12998	.868	.895	9.1 x 10 ⁻⁵	1.66	.0020	1.38	.860	.512	.956	.13	
rs2021966	ENPP1	.584	.576	9.1 x 10 ⁻⁵	1.32	2.6 x 10 ⁻⁴	1.25	.846	.769	.937	.46	
rs1270874	SVIL	.745	.753	1.4 x 10 ⁻⁴	1.33	3.9 x 10 ⁻⁴	1.30	.983	.954	.988	.24	
rs4812831		.150	.116	1.6 x 10 ⁻⁴	1.53	.0055	1.28	.831	.516	.944	.45	
rs4402960	IGF2BP2	.290	.291	1.7 x 10 ⁻⁴	1.27	1.2 x 10 ⁻⁴	1.28	.997	1.026	.998	1.00	
rs2466291	SLC30A8	.399	.361	6.3 x 10 ⁻⁴	1.26	.0016	1.22	.874	.830	.935	.47	
rs1801282	PPARG	.816	.816	9.5 x 10 ⁻⁴	1.31	.0011	1.30	.999	1.002	1.000	1.00	
rs3802177	SLC30A8	.604	.605	9.9 x 10 ⁻⁴	1.23	.0012	1.22	.999	1.015	.999	1.00	
rs4506565	TCF7L2	.213	.214	.0015 ^b	1.26	.0017	1.26	.999	.965	1.000	.92	

Table S6: Comparison of T2D association results for SNPs that were imputed with a p-value < .001 and then genotyped in the FUSION stage 1 sample

 $\frac{\text{rs4506565}}{\text{almputation-based analysis restricted to individuals with successful genotypes for the same SNP; these results may differ from the imputed results in$ Table S2 which are based on all stage 1 individuals ^bImputed p-value = 7.0×10^{-4} in stage 1 sample

^cImputation consistency is the proportion of imputation iterations that agreed with the most likely genotype ^dThe estimated r² is the ratio of observed variance of dosage scores across samples to the expected variance given the imputed SNP allele frequency

Annotation	Weight
Maximum of:	
Frameshift	50
Stop codon	50
Critical splice site	50
Poly A signal	30
Any change to initial ATG signal	30
Non-synonymous coding:	
Identical amino acid seen in more than 75% of mammals	20
Similar amino acid seen in more than 75% of mammals	20
Non-conservative amino acid change	$6 \text{ to } 9^{a}$
Other non-synonymous	5
SNP in exon, includes 5' and 3' UTRs	2
Bonus:	
FUSION linkage LOD>1	1 to 3 ^b
SNP near candidate gene	1.5
SNP near gene over-expressed in tissue of interest	1.5
Conserved	1.2
Near any gene	1.2

Table S7. SNP annotation weights used in SNP picking for stage 2 genotyping

^a For non-conservative amino acid changes, the weight is 5 - x, where -4 < x < -1 is the BLOSUM62 score for the amino acid substitution (23)
^b For linkage, the weight is the T2D LOD score in the FUSION 1+2 families (2) if that LOD

score is >1

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