SUPPLEMENTARY INFORMATION

Subjects

The GWA study for T2D was performed with a three-stage design using the following Japanese samples. All study subjects were unrelated, and they provided written consent for participation. All methods of the study were approved by the ethics committees at the International Medical Center of Japan and the individual institutions involved in the present study.

1) Stage-1 and stage-2 samples

Cases and unaffected controls analyzed in stages 1 and 2 were enrolled according to the identical criteria and their baseline characteristics are shown in Supplementary Table S1. T2D cases were enrolled from the clinical practice or the annual medical checkup of university hospitals, medical institutions, and general practitioners that constitute the Study Group of the NIBIO GWA (the list of which is shown in acknowledgment) according to the 1999 WHO criteria [*Geneva, World Health Organization* (1999)]. Exclusion criteria for cases were individuals with diabetes due to: [1] liver dysfunction; [2] monogenic disorder known to cause diabetes; and [3] positive anti-GAD antibody. The inclusion criteria for controls were as follows: [1] no past history of urinary glucose or glucose intolerance; [2] HbA1c, <5.6% or a normal glucose (75g) tolerance test; and [3] age at examination, ≥55 years. Blood samples were drawn after an overnight fast to measure fasting blood glucose and HbA1c when applicable.

2) Stage-3 samples

Stage-3 samples comprised 4,000 T2D cases derived from the Biobank Japan project and a total of 12,569 subjects randomly selected from residents aged 50–74 years in the general population. From this population-based cohort, 4,889 controls were chosen for the genotype comparison with 4,000 T2D cases.

2-1. Biobank Japan samples

The BioBank Japan project (Reference 27; http://biobankjp.org/) was begun in 2003 for the collection of genomic DNA, serum, and clinical information from a total of >280,000 cases diagnosed with either of 47 diseases by a collaboration network of 66 hospitals in Japan. Patients gave written informed consent to participate in this project before information was collected. From the registered samples in the BioBank Japan, we selected 4,000 patients who were diagnosed as T2D.

2-2. Samples from general population cohort

The study subjects were participants in the baseline survey of the Kyushu University Fukuoka Cohort Study, which was designed to investigate lifestyle factors and genetic susceptibility of the so-called lifestyle-related diseases such as cardiovascular diseases, cancer, and diabetes mellitus. Eligible persons were residents of the East Ward of Fukuoka City aged 50 to 74 years. Some areas in the Ward were excluded because of potential emigration, sparse population, and remote distance. Of 53,927 persons who were contacted by mail, a total of 12,959 participated in the baseline survey during the period from February 2004 to August 2007. Brief description of the methods in the baseline survey is available elsewhere (51).

Excluding 8 for withdrawal, one for duplicate participation, and one for mental incompetence, the cohort comprised 12,949 persons. Of them, 12,629 gave informed consent to genetic analysis. For DNA extraction, 6 ml of venous blood was drawn into a vacuum tube containing EDTA-K2. Within at most 8 hours of blood sampling, 2 ml of plasma was taken after centrifugation, and the remaining blood sample added with 1 ml PBS was stored at –80 ˚C until DNA extraction. DNA was extracted from the peripheral leukocyte fraction using automatic nucleic acid isolation system NA-3000 (Kurabo, Tokyo, Japan) and stored at –80 ˚C until genotyping. A total of 12,569 subjects completed the questionnaire and also provided DNA for genotyping of SNPs.

As non-diabetic controls from the general population, we arbitrarily selected 4,889 subjects (2,259 men and 2,630 women) who met the following conditions: age, ≥55 years; HbA1c, ≤ 5.0%; no previous and/or current treatment for diabetes; and absence of renal failure (serum creatinine, <3.0 mg/dl).

The outline of the stage-3 analysis is shown in Figure 1. As for the SNPs detected by GWA scans (17 SNPs), which surpassed the stage-2 threshold and were taken forward in stage 3, 4,000 T2D cases (from the BioBank Japan project) and 4,889 controls were characterized for replication. On the other hand, as for the

previously-reported SNPs (6 SNPs apart from rs7754840 and rs7756992 in *CDKAL1* and rs10811661 in *CDKN2A/2B*), which were replicated in the stage 1+2 panel and were taken forward in stage 3, the same (stage 3) case-control panel was first characterized, of which the confirmed SNPs (5 of the 6 SNPs tested) were further genotyped in an additional panel of 7,680 population-based samples; these subjects plus 4,889 controls constitute the entire population-based panel (N = 12,569) in stage 3. Here, we took forward rs4712523 instead of rs7754840 and rs7756992 (*CDKAL1*), and rs2383208 instead of rs10811661 (*CDKN2A*/*2B*) in the stage-3 analysis to proceed with GWA scans from stage 1 to stage 3 by considering strong linkage disequilibrium (LD) between the SNPs in each of the corresponding loci. For the SNPs thus tested in the entire population-based panel, a total of 5,395 non-diabetic controls (≥50 years and no family history of diabetes in either of parents) were used for the stage-3 case-control analysis and meta-analysis. That is, 506 subjects were derived from the 7,680 population-based samples additionally characterized.

Since blood was drawn not strictly on the condition of overnight fast, HbA1c was measured in all participants to evaluate the impaired glucose metabolism (52). In Japan, stable HbA1c was standardized in the mid 1990s by the Japan Diabetes Society (JDS) and has been used to estimate the number of people with *probable* and *possible* diabetes in the Japan National Diabetes Survey (JNDS) [the survey data in 2002 are available at http://www.health-net.or.jp/data/menu05/toukei/tonyo_h14.pdf (in Japanese)]. In this survey, *probable* diabetes was defined as HbA1c ≥ 6.1 or under treatment of diabetes, and *possible* diabetes was defined as 5.6 ≤ HbA1c < 6.1 among those without treatment of diabetes. These cut-off points for HbA1c were chosen with respect to equivalent diagnostic cut-off points for fasting plasma glucose and 2-h plasma glucose in an oral glucose (75g) tolerance test for undiagnosed diabetes in the linear regression analysis (53). Moreover, the screening test properties of HbA1c for undiagnosed diabetes was assessed in the general population data (N = 1,904) according to the 1999-WHO criteria,

which further supported the JNDS cut-off points for HbA1c with respect to screening properties of undiagnosed diabetes in Japan (54).

For the assessment of combined risk of diabetes and pre-diabetes, all the general population samples (N = 12,569) were used. According to the ADA [http://www.diabetes.org/pre-diabetes.jsp], pre-diabetes can be defined as the condition that blood glucose levels are higher than normal but yet high not enough to be diagnosed as diabetes. Strictly, this definition of pre-diabetes is not identical to that of *possible* diabetes in the JNDS, but we arbitrarily used the cut-off point of 5.6≤ HbA1c < 6.1 among people without treatment of diabetes as 'pre-diabetes' and that for *probable* diabetes (i.e., HbA1c ≥ 6.1 or under treatment of diabetes) as 'diabetes' in our risk assessment in the general population.

Subjects with increased HbA1c levels include type 1 diabetes (T1D) as well as T2D. However, in the present study, overall, population-wide impacts of T1D seem to be negligible. Japan is known to have one of the lowest incidence rate of T1D in the world. According to population-based systems to detect childhood diabetes, the prevalence of T1D children has been estimated to be about 22.5 cases per 100,000 individuals. The prevalence of T1D in adults, on the other hand, appears more than twice that in childhood-onset patients (55), roughly indicating the T1D prevalence of ~0.05% in the general population. Thus, in Japan, T2D is common in diabetes mellitus in old age, and there are rarely elderly patients with T1D (56).

Stage-1 genome-wide scan and quality control

1) SNP genotyping

Genotyping was performed according to the manufacturer's protocol by labeling 750 ng of genomic DNA and hybridizing it to the Infinium HumanHap550 BeadArray (Illumina, San Diego, CA), which interrogated 555,352 SNPs. This set of SNP markers are reported to capture 87% of common SNPs with an LD coefficient of $r^2 > 0.8$ in the

HapMap Japanese and Chinese population (according to the manufacturer's brochure). Assay accuracy and reproducibility were measured using DNA from CEPH Utah samples (CEU) genotyped as part of the HapMap project (29). Genotype calling was performed using the BeadStudio software (Illumina), and genotype calls with the "GenTrain" Score < 0.53 were dropped from analysis. The "GenTrain" score measures the reliability of genotype calls based on the clustering of dye intensities [http://www.illumina.com/downloads/ GenCallTechSpotlight.pdf]. The average call rate was 96.9% in either of cases and controls.

2) Quality control of samples

Data cleaning and analysis were done using the PLINK software (28). Samples with genotype call rate less than 90% were excluded from analysis (N = 9). We looked for outlier samples with respect to the number of heterozygous SNPs, which could be caused by poor DNA quality. We found no such outliers in the stage-1 cohort after the removal of nine samples above.

In order to detect duplicate samples, relatives, and ethnic outliers among the subjects initially tested, similarity of DNA was evaluated for each pair of samples by the proportion of identity by state (IBS) alleles over all SNPs. Sample pairs with the IBS allele proportion > 0.99 were regarded as duplicates, in which case one each from such sample pairs was removed (N = 2). For each sample, the most similar pair could typically show the IBS allele proportion of ~0.77. We found no sample pairs with a significantly larger proportion of IBS alleles, in other words, no relatives were included in the stage-1 cohort. On the contrary, any samples showing significantly less similarity to the others in the IBS allele proportion (Z-score < –5) were removed as ethnic outliers (N = 2).

For the remaining 1,022 samples, we checked ethnicity by combining them with samples from the HapMap. The HapMap individuals comprised 17 Japanese in Tokyo

(JPT), 13 Han Chinese in Beijing (CHB), 52 of CEU, and 38 Yoruba in Ibadan (YRI). Multi-dimensional scaling analysis was applied to the pairwise IBS distance between the samples. Our study samples were clearly distinctive from the non-Asian samples (CEU and YRI) and clustered identically around the JPT samples, rather than around the CHB samples (see Supplementary Figure S8). Consequently, we adopted all of the 1,022 samples (519 cases and 503 controls) for further analysis.

3) Quality control of SNPs

Among 555,352 SNPs, we excluded SNPs for which [1] genotype call rate, <0.95; [2] genotype call rate, <0.99 and minor allele frequency (MAF), <0.05; [3] significant ($P < 10^{-6}$) deviation from the Hardy-Weinberg equilibrium in the controls; or [4] MAF, < 0.001. The remaining 482,625 SNPs were analyzed in the first stage scan of GWA study (Supplementary Table S2). Representative signal intensity plots are shown in Supplementary Figure S9 for nine SNPs that emerged at the end of the three-stage scan.

Evaluation and correction of population stratification

In order to detect and correct population stratification, we used the EIGENSTRAT software (30, 57). The software applies principal components analysis to genotype data and calculates eigenvalues, which are expected to include large values if the population is stratified. To infer population structure, *P*-values are calculated for eigenvalues under the null hypothesis of no stratification using TW statistics. Multiple correlated SNPs, for example, those in LD, also cause a large eigenvalue, and hence SNPs having a multiple correlation coefficient > 0.5 were pruned, in addition to excluding SNPs showing moderate case/control association ($P < 0.01$). In total, 117,598 SNPs were selected for the principal component analysis, and five eigenvalues were found to be significant ($P < 0.01$) as in Supplementary Table S12.

Each eigenvalue corresponds to an eigenvector that represents an axis of

population stratification. Only the first eigenvector was correlated with the case/control status (a correlation coefficient of –0.186), as illustrated in Supplementary Figure S10. Although cases and controls from the International Medical Center of Japan (379 cases and 503 controls genotyped) were distributed equally, the samples from Kyushu University were found slightly shifted to the left (140 cases alone). This could be due to genetic diversity among the subjects from different regions in Japan and/or some unnoticed differences in experimental setup between two genotyping facilities; samples typed in the International Medical Center of Japan were collected in Tokyo and Osaka, and their environs, and samples typed in Kyushu University were collected in the Kyushu region. Yet the regional genetic diversity appears to be small, because all samples in our study are clustered closely with the JPT samples among the HapMap populations (see Supplementary Figure S8).

Consequently, we corrected the Cochran-Armitage trend test statistic for each SNP according to the eigenvectors thus detected. The λ value of genomic-control (31) that could indicate the overall inflation of significance decreased from 1.047 to 1.032 by this EIGENSTRAT correction. The residual inflation was further removed by applying the genomic-control method. In order to boost the power of the GWA scan, the controls were augmented by additional genotype counts for 964 *random* controls (see below). The cumulative distribution of *P*-values in the first-stage scan after these corrections is plotted in Supplementary Figure S7.

The adjustment by EIGENSTRAT and genomic-control did not change the statistical significance of four SNPs that were identified by GWA study and confirmed in the subsequent stages: the raw and adjusted *P*-values were 2.3×10^{-4} and 1.7×10^{-4} for rs4712523 (*CDKAL1*), 2.0×10^{-6} and 6.1×10^{-6} for rs2383208 (*CDKN2A/2B*), 5.1×10^{-4} and 1.9×10^{-3} for rs2237892 (*KCNQ1*), and 1.5×10^{-5} and 1.4×10^{-5} for rs10425678 (*PEPD*).

Effect of genetic difference among geographical regions

The subjects in this study were collected at multiple institutions, and if a SNP tested for association has different frequency among regions in Japan, the test statistic can be skewed. To examine this possibility, we reorganized the samples according to regions and compared the allele frequency in controls for the confirmed SNPs in Table 1. As shown in Supplementary Table S13, all SNPs except rs2383208 had no significant regional difference, and the OR was similar whether stratified by regions and analyzed using Mantel-Haenszel methods, or simply pooled. Even when the OR by two methods is equal, the *P*-value for Mantel-Haenszel appears larger than the *P*-value for allele frequency test of the pooled count, because the number of cases and controls differs in each stratum. The SNP rs2383208 had significant regional difference in allele frequency ($P = 0.002$), and the OR decreased from 1.34 to 1.23 when adjusted using the Mantel-Haenszel methods, but still exhibited statistical significance of $P = 1.8 \times 10^{-7}$. For the analysis, the subjects were stratified into three regions. The subjects in 'Tokyo and multi-district' are from Tokyo, Nagoya, together with the BioBank samples from nationwide, since the residents in the capital city Tokyo generally originate from all over Japan. The 'Osaka' and 'Fukuoka' subjects are from the respective cities and their environs. We used the rmeta package for the R software (http://www.r-project.org).

Genotype results for 964 *random* controls from the public database

In addition to the samples genotyped in our study, we incorporated genotype frequencies in the Japanese general population to boost the power of the GWA scan, yet final results of the study were confirmed with our own data. In the relevant dataset, which was made publicly available from the Genome Medical Database of Japan (GeMDBJ; http://gemdbj.nibio.go.jp), a total of 964 samples were genotyped by the Infinium HumanHap550 BeadArray. We applied quality control of SNPs as adopted in

our study; we excluded SNPs for which [1] genotype call rate, <0.95; [2] genotype call rate, <0.99 and MAF, <0.05; [3] significant deviation ($P < 10^{-6}$) from the Hardy-Weinberg equilibrium; or [4] MAF, <0.001.

Stage-2 genotyping and analysis

A total of 1,811 SNPs surpassed the stage-1 threshold, and after removing SNPs mutually in strong LD ($r^2 > 0.9$) to avoid redundancy, 1,674 SNPs were subjected to the follow-up analysis in stage 2; 140 SNPs were genotyped by using the iPLEX assay (Sequenom, Cambridge, MA) and 1,534 SNPs by the Illumina GoldenGate Genotyping Assay (Illumina) according to the manufacturer's protocol.

We characterized 1,110 cases and 1,014 controls (2,124 in total) and adopted all samples in stage-2 analysis. Quality control criteria for markers were the same as in stage 1. After the quality control, we adopted 1,456 SNPs for stage-2 analysis (73 from iPLEX and 1,383 from GoldenGate). Association testing was performed using the Cochran-Armitage trend test statistic.

Significance level and power of the GWA scan

We aimed to identify disease-associated SNPs with an OR of 1.3 or 1.2 with a power of 50% or 10%, respectively. To assess the statistical power that represents the ratio of [true positives / (true positives + false negatives)] in our GWA scan, we simulated how frequently a disease-associated SNP could surpass the cut-off level of the first two stages (stages 1 and 2). Here, we regarded the stage-3 scan as a subsequent replication study. We assumed risk allele frequency (RAF) in the range of 0.2–0.7, the disease prevalence of 0.10 and an additive mode of inheritance. Since the sample size in each stage was pre-defined, we adjusted the significance level as follows: a cut-off level of $P < 0.0025$ was set in the first-stage scan to achieve a power of 53% and 17% for ORs of 1.3 and 1.2, respectively. Also, a cut-off level of $P < 7 \times 10^{-5}$ was set in the

second-stage scan to achieve a power of 49% and 11% for ORs of 1.3 and 1.2, respectively (see Supplementary Table S11).

Replication of previously-reported SNPs

In parallel with the GWA study, T2D association was tested in the stage 1 and 2 panels for 17 SNPs from 16 T2D candidate loci previously identified by GWA studies in European-descent populations (6–17). For stage-1 samples, 11 SNPs were included in the HumanHap550 array, and six SNPs were separately assayed by the TaqMan method. For stage-2 samples, ten SNPs were genotyped by the iPLEX assay additionally to 73 SNPs that were selected for the follow-up of GWA study, and seven SNPs were assayed by the TaqMan method. Eight SNPs showing significant ($P < 0.05$) association in the stage 1+2 samples were further studied in an additional panel of 4,000 T2D cases and 4,889 controls in stage 3. Apart from rs7578597 that did not show statistical significance at this point ($P > 0.05$ for all stages combined), the remaining seven SNPs were further studied in the entire 12,569 population-based sample including the 4,889 pre-selected controls.

Haplotype analysis in the associated loci detected by GWA study

In each loci identified by GWA study and/or replicated after the studies previously reported, we looked if more than one independent SNPs are associated with T2D. After adjusting for genotype effects of the SNP showing the lowest *P*-value in a locus, no other SNPs turned out to be significant ($P > 0.01$). When there were multiple significant SNPs mutually not in strong LD (coefficient $r^2 < 0.8$), we tested whether a haplotype class involving them could exert more significant effects than the individual SNPs. Here, haplotypes were inferred from genotype data in the NIBIO stage 1+2 combined panel (jointly for the 1,629 cases and 1,517 controls) and tested using the PLINK software.

In two associated loci, chromosome 6p22.3 (*CDKAL1*) and 19p13 (*PEPD*), a

haplotype class showed more significant association than an individual SNP as below.

In the *CDKAL1* locus, T2D association is found for two groups of SNPs: one group comprises rs4712523, rs7754840, rs10946398, rs9295475, and rs6906327 that are in strong LD to each other, and another group is rs7756992. The LD estimated between rs7754840 and rs7756992 is r^2 = 0.66 in Japanese, and 0.68 in European-derived populations. A risk haplotype class 'GG' showed more significant *P*-value ($P = 5.6 \times 10^{-11}$) than the individual SNPs constituting the haplotype (Supplementary Table S14A).

In the *PEPD* locus, four SNPs are grouped into two pairs of SNPs that are in complete LD (rs7250175 and rs3786920, r^2 = 0.99; rs10425678 and rs11880064, r^2 = 0.99; rs7250175 and rs10425678, r^2 = 0.46). A protective haplotype class 'CT' showed slightly more significant *P*-value ($P = 7.1 \times 10^{-5}$) than the individual SNPs constituting the haplotype (Supplementary Table S14B).

Assessment of combined risk of diabetes and pre-diabetes in the general population

We assessed the combined risk of diabetes by genetic and non-genetic (sex, age, and BMI) factors in a cohort of 12,569 individuals from general population.

We first assessed the effect size of each risk factor by multiple regression analysis with the logarithm of HbA1c (log HbA1c) as a response variable. Explanatory (predictor) variables were sex, age, BMI, and seven robustly-confirmed SNPs: rs4402960 (*IGF2BP2*), rs4712523 (*CDKAL1*), rs13266634 (*SLC30A8*), rs2383208 (*CDKN2A*/*2B*), rs1111875 (*HHEX*), rs7903146 (*TCF7L2*), and rs5219 (*KCNJ11*). SNP genotype was coded as 0, 1, or 2 according to the number of risk allele. A total of 12,372 samples with complete data were available for the analysis. The fitted multivariate regression is shown in Supplementary Table S9. R^2 denotes the variance of log HbA1c explained by each predictor variable, and it totals 5.3% for all variables included simultaneously in the regression.

Next, we examined how well the ‘actual diabetic state’ in each individual could be estimated by the risk factors of interest. Accumulated risk for each individual was assessed using the above-mentioned regression for HbA1c. We arranged the individuals in order of the risk estimated by multiple regression, sorted the whole population into 20 equal-sized groups (i.e., 5% each), and then examined the distribution of actual HbA1c value and disease status in each group. The diabetic state was assigned by questionnaire information and HbA1c values: individuals who answered in questionnaire to be diabetic or those with HbA1c $\geq$ 6.1 were classified as 'diabetes (DM)', and others with HbA1c 5.6–6.0 as 'pre-diabetes (pre-DM)' (see above). In Supplementary Figure S6, each group is represented as a vertical bar with the estimated risk increasing from the leftmost to the rightmost bar. Results for the lowest and the highest risk groups are also described in Table 2.

In the above analysis, we used the same set of samples both for the fitting of risk model by regression and for the assessment of actual diabetes prevalence using the resultant model. This may potentially cause overfitting of the model, although the possibility is small owing to the large sample size of 12,372. In order to avoid the overfitting, we also analyzed by randomly selecting half of the population for model fitting and the remaining half for model assessment. From 1,000 random trials, we computed the mean and 95% confidence interval for the prevalence of DM and pre-DM in each risk group. The figures for the highest and the lowest estimated risk groups in Supplementary Table S15 agree well with those in Table 2, suggesting the absence of overfitting.

The strength of association of a SNP and study power

We measured the explained variance of a SNP by the coefficient of determination (R^2) that represents the ability to detect association signals using the Cochran-Armitage trend test. We calculated R^2 for testing association by a linear regression (equivalent to

Cochran-Armitage trend test) with an independent variable x coding a genotype as 0, 1 or 2 according to the allele copy number, and a dependent variable y coding disease status as 1 (case) or 0 (control). The R^2 value equals the square of the correlation coefficient for the points (x, y). When testing a total of N samples under significance level α for a SNP with R^2, the power equals

$$\int_c^{\infty} F'(1, N-2, NR^2/(1-R^2))\,dx,$$

where $F'(1, N–2, \theta^2)$ is the probability density function for a F-distribution of df (degree of freedom) = 1 and N–2 and non-centrality parameter θ^2, and

$$\alpha = \int_c^{\infty} F(1, N-2)\,dx,$$

where $F(1, N–2)$ is the probability density function for a F-distribution of df = 1 and N–2 [Reference 58, Section 28.28] [Reference 59, Example 8.4]. When R^2 = 0.008, 0.004, and 0.002, the necessary sample size to achieve 80% power is N = 4,300, 8,600, and 17,200 for $\alpha = 5\times10^{-7}$, and N = 1,000, 2,000, and 3,900 for α = 0.05. The power for other combinations of N and α are listed in Supplementary Table S7. For the estimation of R^2 of a SNP from RAF and odds ratio (OR), we assumed additive mode-of-inheritance, 10% disease prevalence, and equal-sized cases and controls for a study.

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References up to number 50 are listed in the main text.

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Figure S1

Graphical summary of stage 1 association results. Horizontal axis is the physical position of each SNP on a chromosome, and the vertical axis is the minus logarithm to base 10 of *P*-value for the Cochran-Armitage trend test adjusted by EIGENSTRAT and genomic-control. The red SNPs examined in stage 2 had $P<0.0025$ either in trend test or its combination with linkage analysis. The red SNPs distributed lower in the plots showed modest association in trend test but were noticeable in linkage scan.

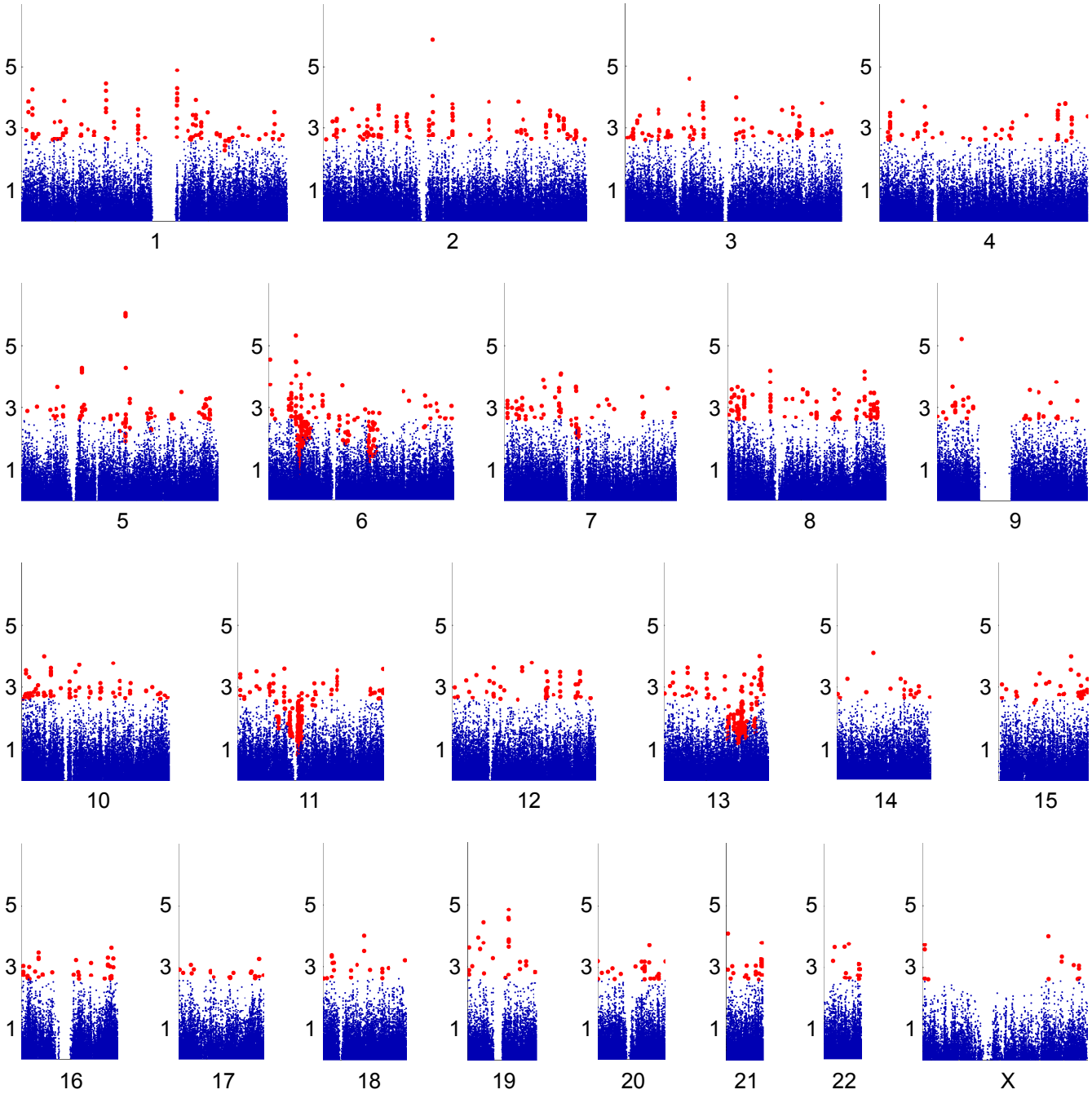
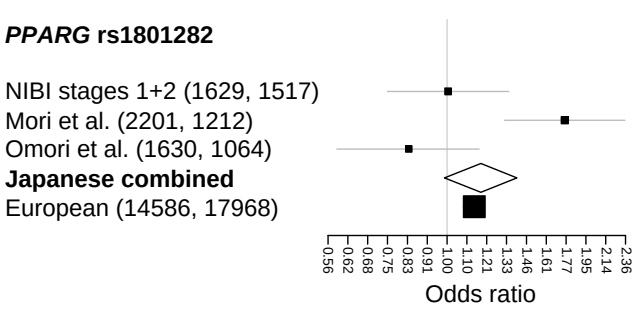
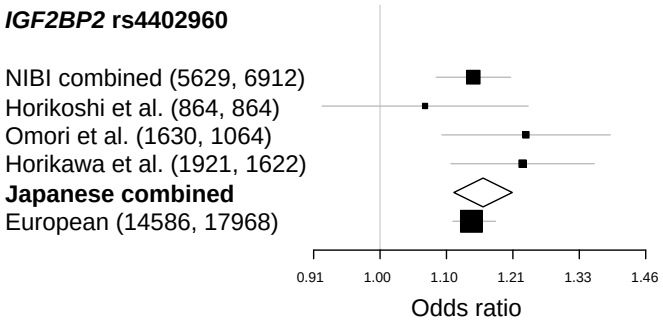
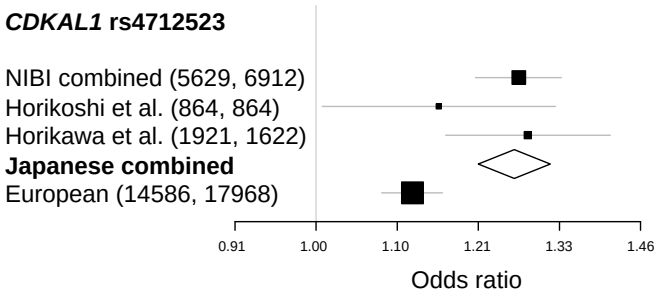


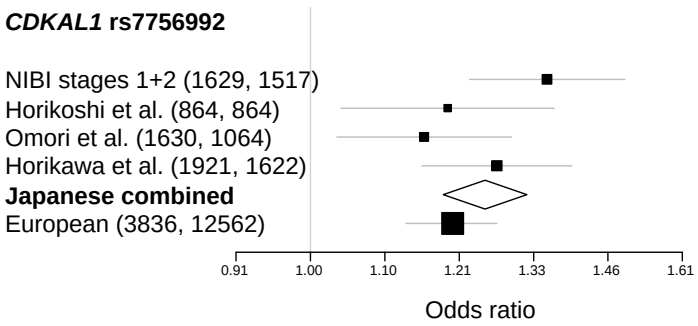
Figure S2

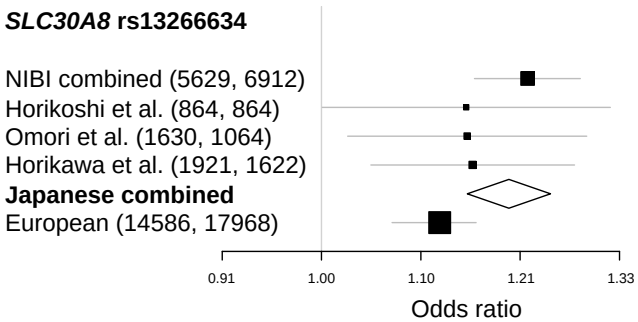
Meta-analysis of type 2 diabetes association in Japanese and European-derived populations. We performed meta-analysis with the previous studies by three groups in Japanese. The estimate and 95% confidence interval of odds ratio is illustrated in the forest plots. See Supplementary Information for detail. Genotype counts for each SNP is shown in Supplementary Table S4.











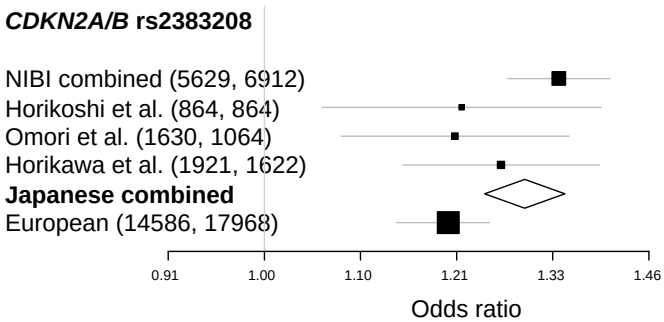


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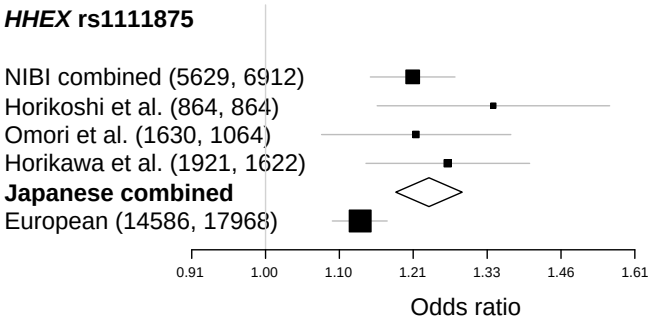
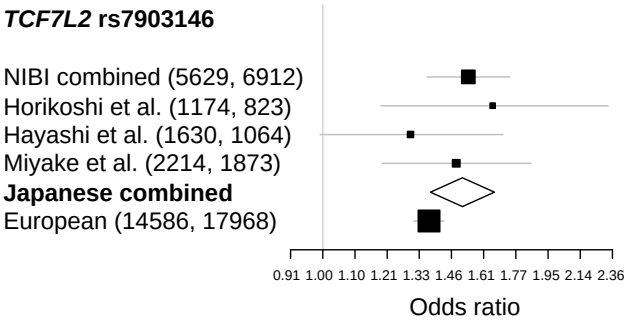
Figure S2 (continued)

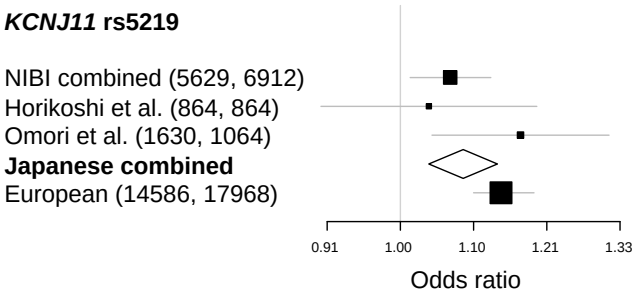
***HHEX* rs1111875**



***TCF7L2* rs7903146**



***KCNJ11* rs5219**



***FTO* rs8050136**

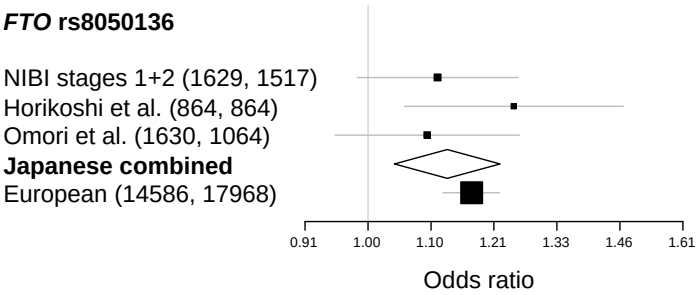


Figure S3

Linkage disequilibrium (LD) pattern in the European and Japanese populations at loci associated with type 2 diabetes. In the HapMap CEU (top) and JPT (bottom) populations, a red box indicates a SNP pair with r^2>0.5. A region of 200kb centered at the most significant SNP is plotted for the *IGF2BP2*, *SLC30A8*, *HHEX*, *TCF7L2* and *KCNJ11* loci.

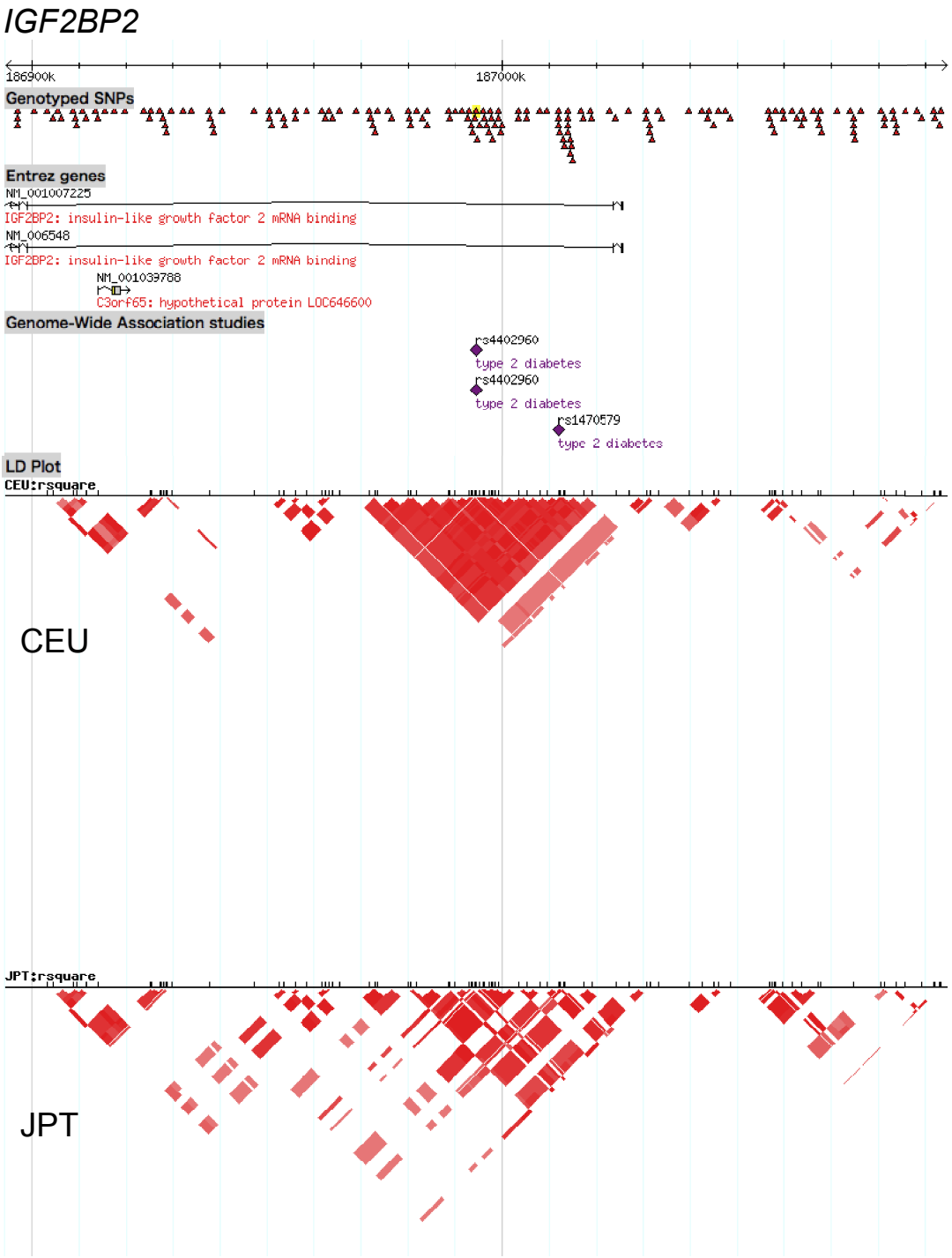


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Figure S3 (continued)

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Figure S3 (continued)

HHEX

(continues to next page)

Figure S3 (continued)

TCF7L2

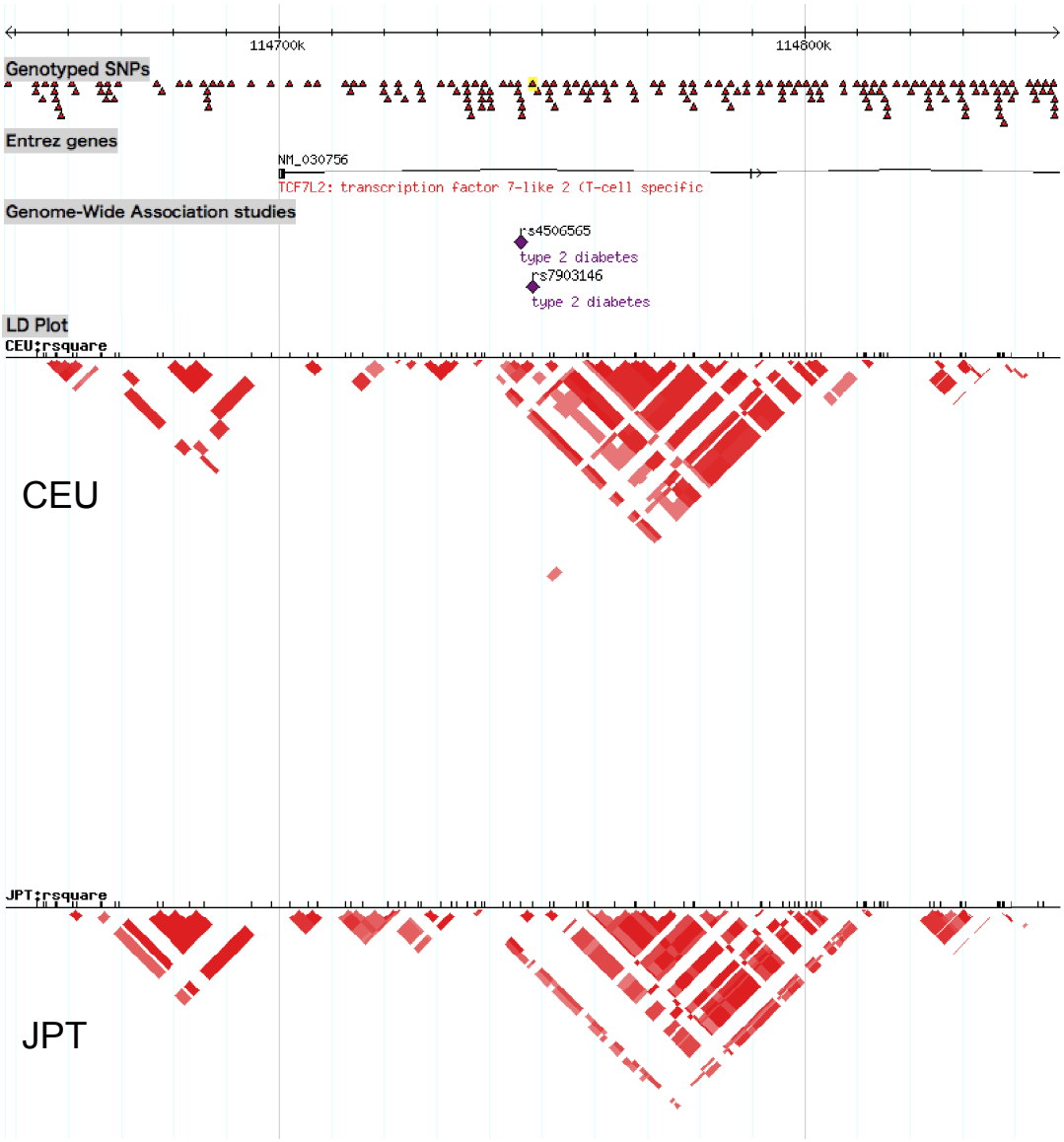

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Figure S3 (continued)

KCNJ11

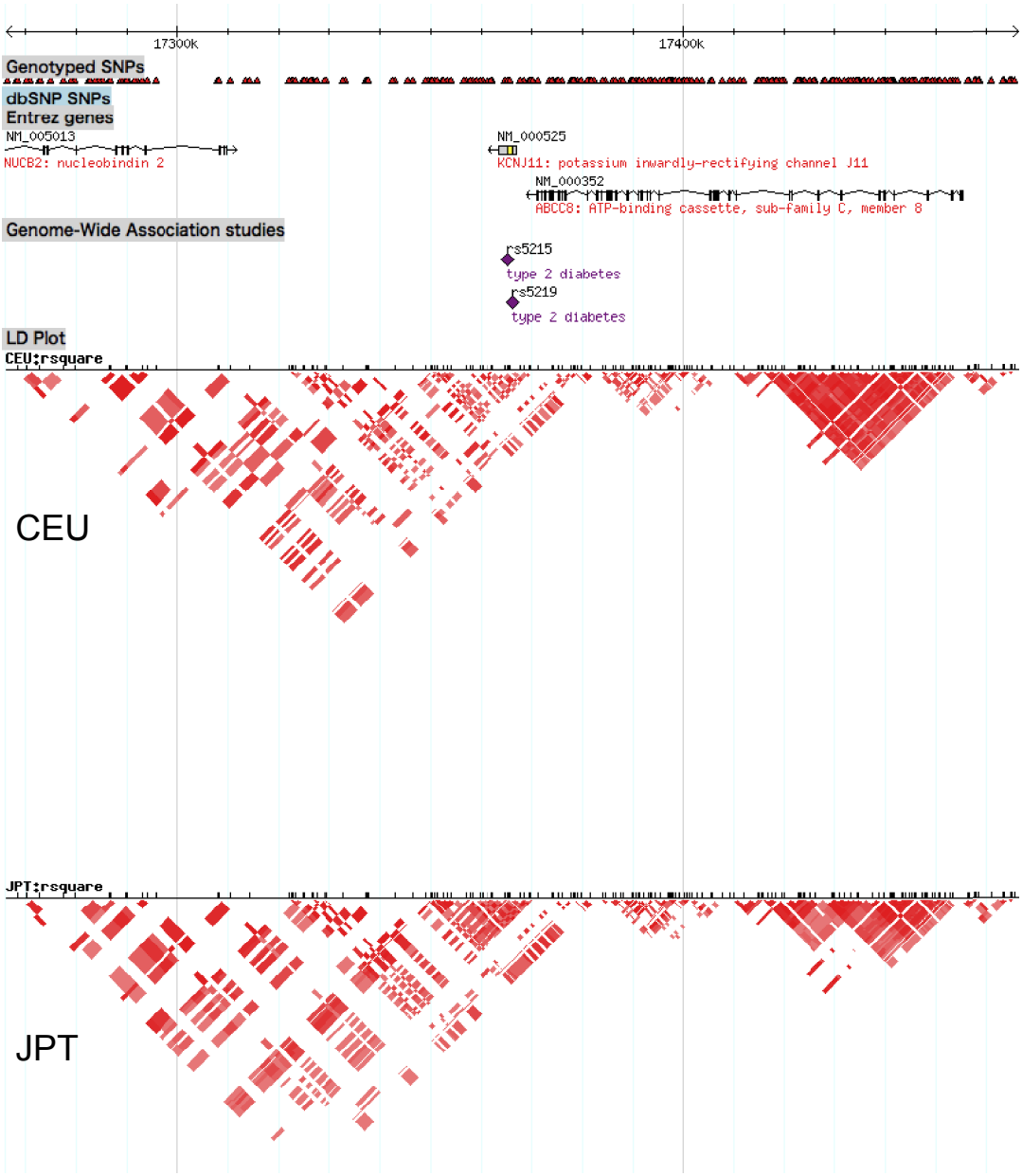
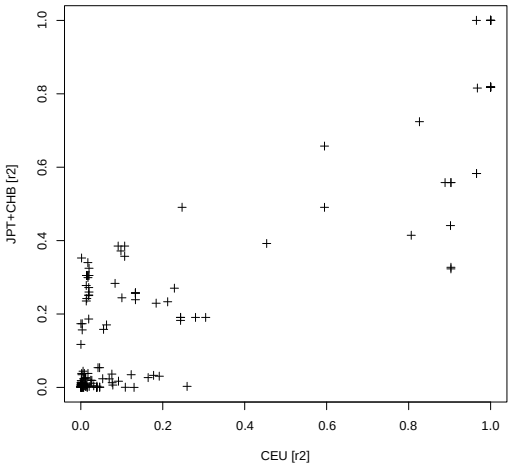


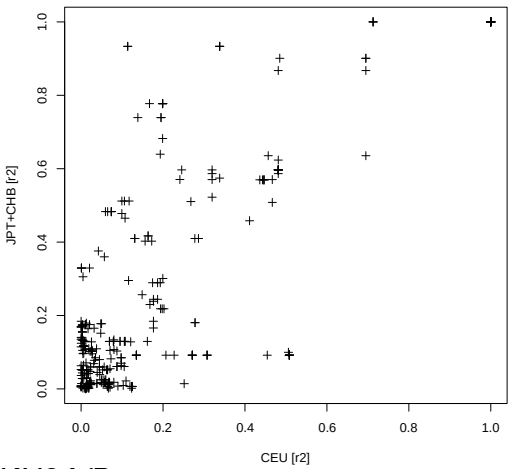
Figure S4

For each type 2 diabetes susceptibility locus, we compared the strength of linkage disequilibrium (LD) between HapMap CEU and JPT+CHB populations. LD is measured between the most significant index SNP in each locus and other SNPs within 200kb and with minor allele frequency at least 1%. Each non-index SNP is plotted by LD coefficient r^2 in 60 unrelated CEU (horizontal axis) and JPT+CHB (vertical axis). LD in *CDKAL1* and *KCNJ11* is stronger in JPT+CHB, whereas LD in *IGFBP2* and *HHEX* tends to be stronger in CEU. Also refer to Supplementary Figure S3.

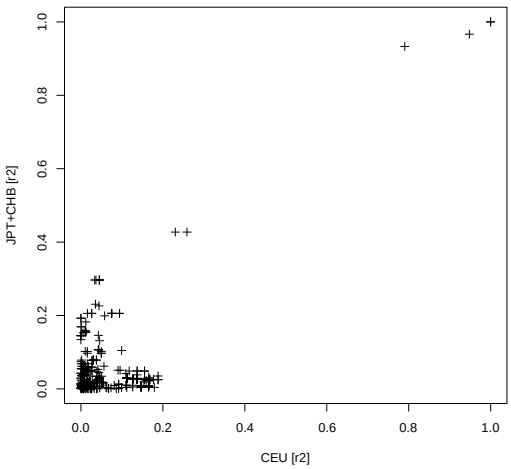
IGF2BP2 r2 between rs4402960 and SNPs within 200kb



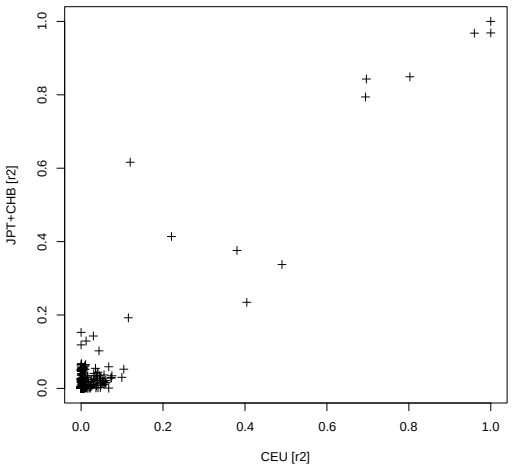
CDKAL1 r2 between rs4712523 and SNPs within 200kb



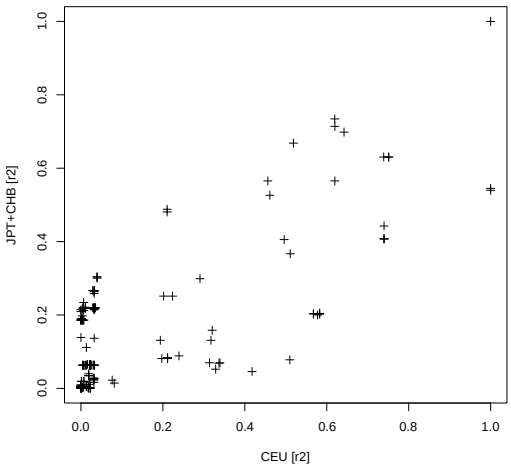
SLC30A8 r2 between rs13266634 and SNPs within 200kb



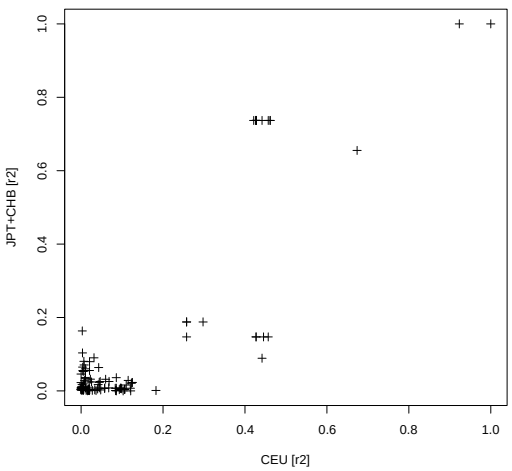
CDKN2A/B r2 between rs2383208 and SNPs within 200kb



HHEX r2 between rs1111875 and SNPs within 200kb



TCF7L2 r2 between rs7903146 and SNPs within 200kb



KCNJ11 r2 between rs5215 and SNPs within 200kb

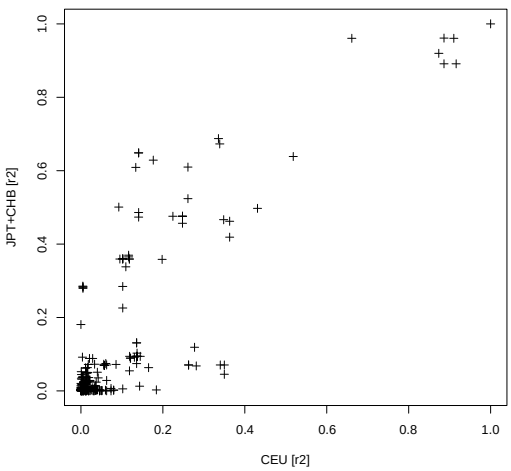


Figure S5

ROC curve for the prediction of type 2 diabetes risk with the use of seven susceptibility variants robustly associated in both our Japanese panel and Europeans. We used the same data as Figure 4. For various thresholds of predicted risk, specificity (horizontal axis) and sensitivity (vertical axis) are plotted. The area under the curve was 0.60. The black line is for prediction by random guess.

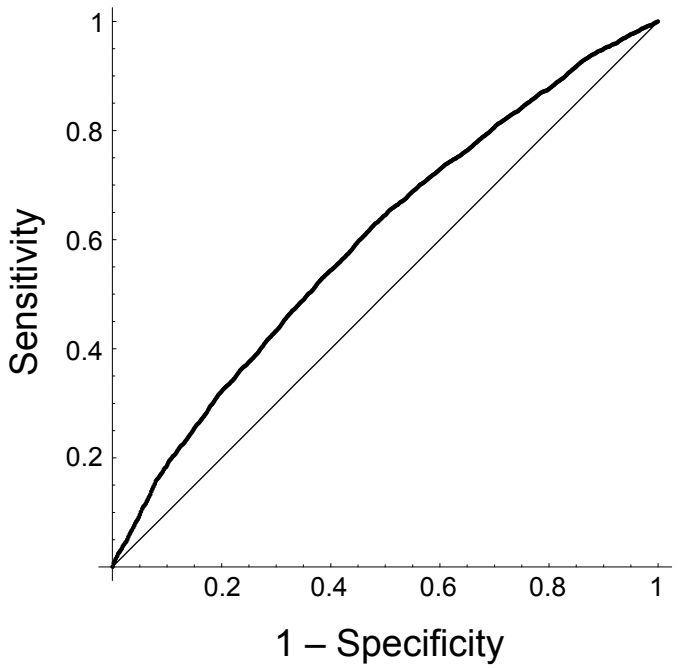


Figure S6

Assessment of risk for diabetes and pre-diabetes in the general population. Based on the regression of HbA1c value by SNP genotype, age and sex, the risk for high HbA1c was assessed for each individual using a predictor set of either 1) SNPs, 2) age and BMI, or 3) all. We sorted all individuals by their risk, divided the whole population into 20 equal-sized groups (i.e., 5% each) from low to high risk, and in each group, examined the distribution of actual HbA1c value (left figure) and diabetic status (right figure). Male and female are plotted separately.

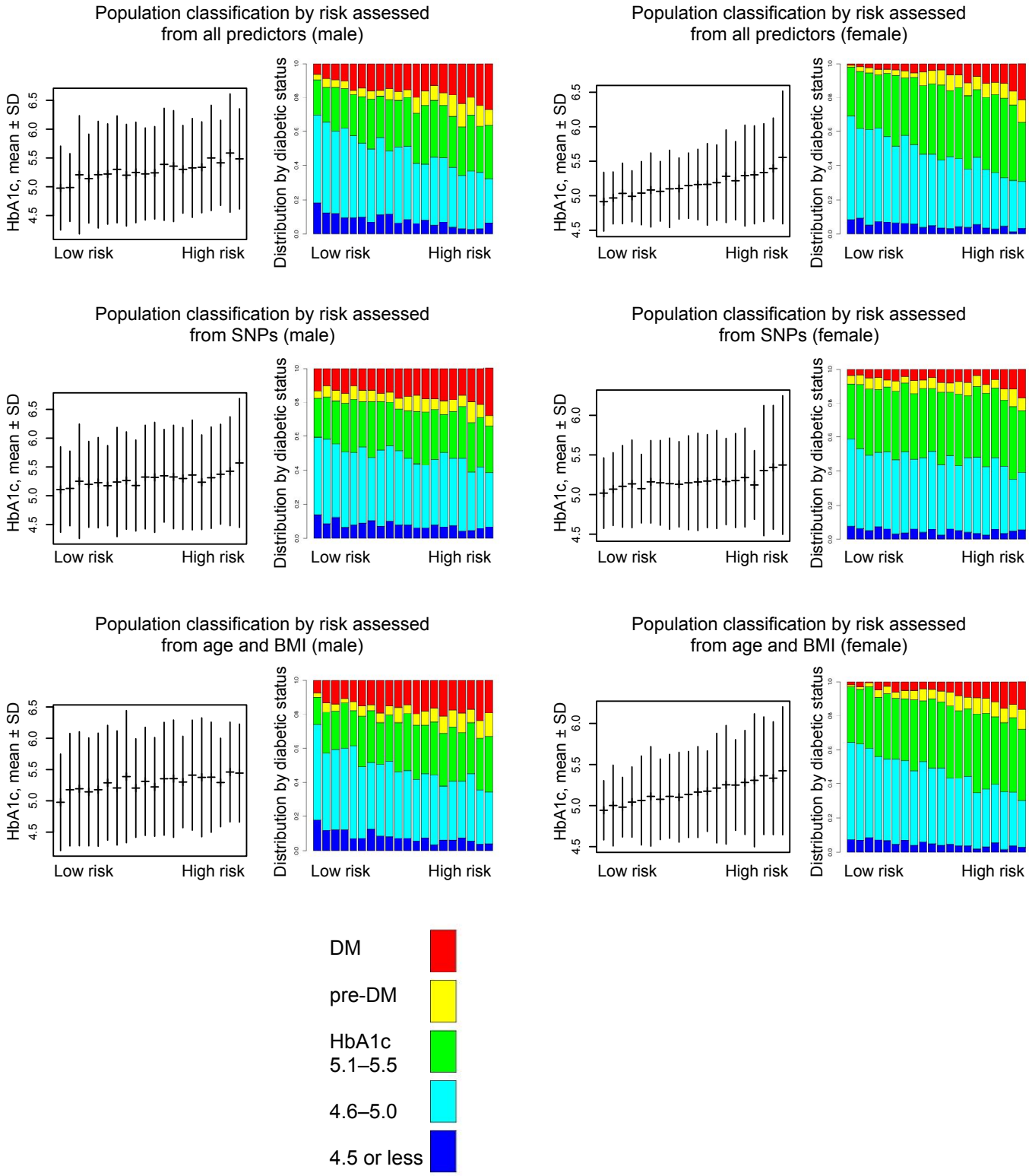


Figure S7

The cumulative distribution of P-values in the first stage scan after corrections by the EIGENSTRAT and genomic-control methods. Seven robustly-confirmed SNPs in Table 1 are marked in red and labeled. SNPs above the blue horizontal line were genotyped in stage 2 analysis.

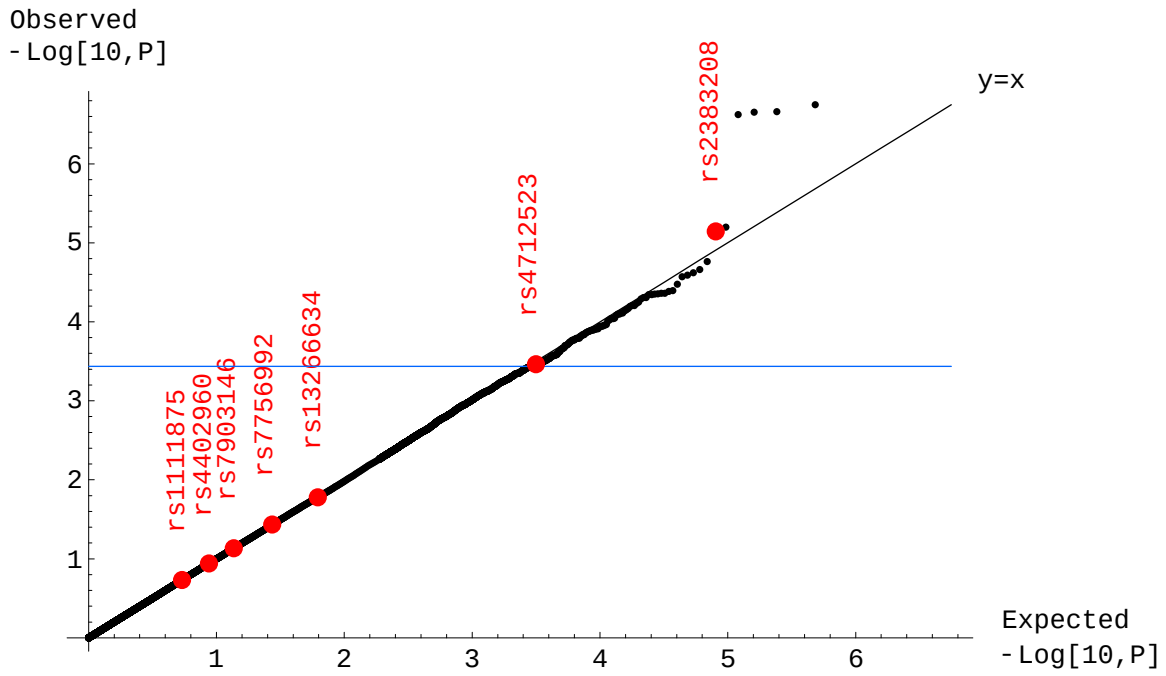


Figure S8

Ethnicity of stage 1 samples compared with HapMap populations. Each individual corresponds to a point in the multi-dimensional scaling plot which represents similarity between samples. The bottom plot zooms in around points for the stage 1 samples. Both the cases (DM) and controls (NDM) are clustered together with the Japanese in Tokyo (JPT) from HapMap.

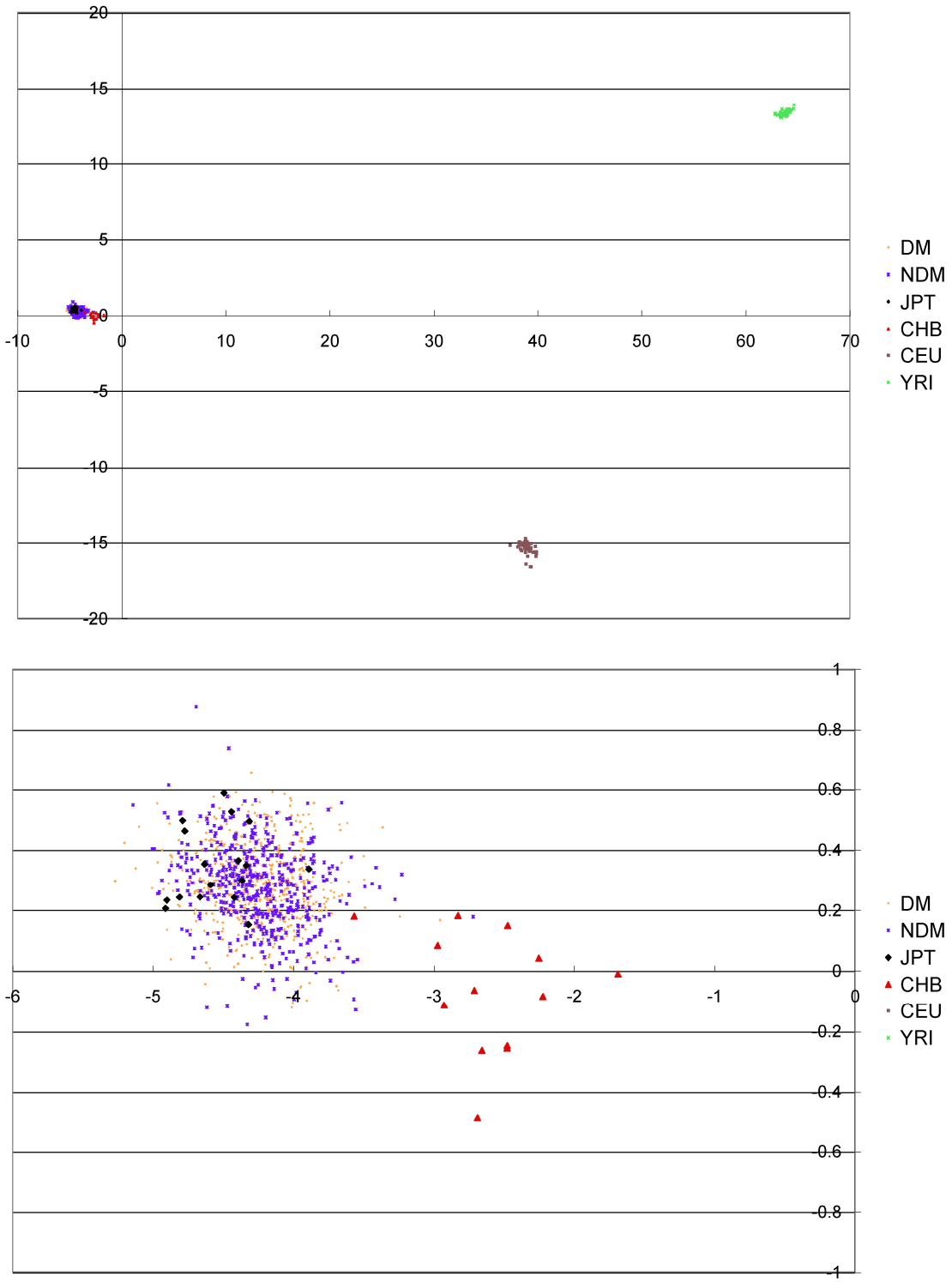


Figure S9

Representative signal intensity plots for nine SNPs that emerged at the end of the three stage scan. In each case of 8 SNPs genotyped with Illumina technology and 1 SNP (rs5219) additionally genotyped with TaqMan technology in the stage 1+2 cohort, the positions of data clouds (for three genotype classes) are demonstrated in the same plots, so as to visualize the ease of allelic discrimination.

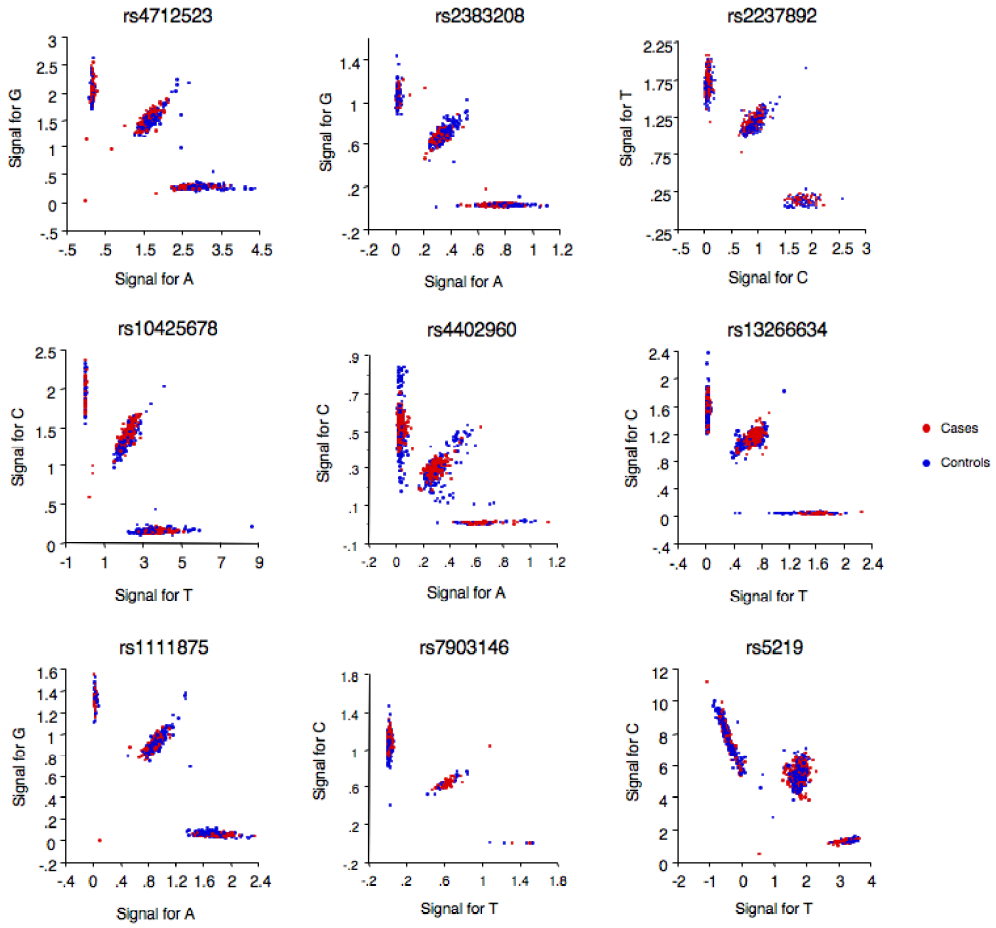
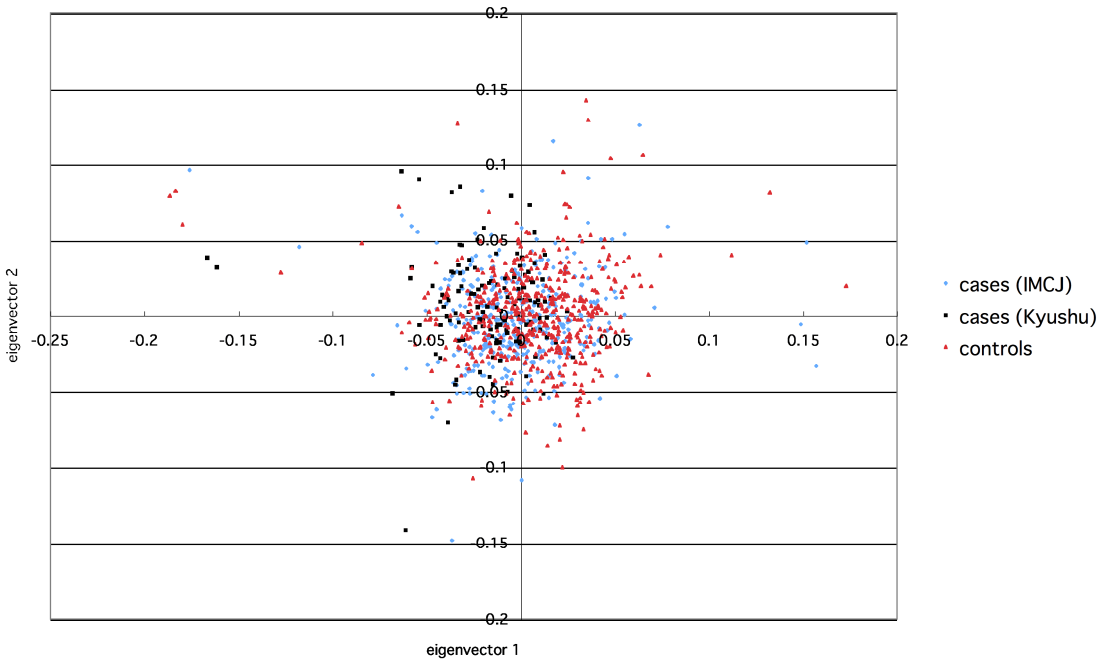


Figure S10

Plot of the first two eigenvectors from the EIGENSTRAT analysis of stage 1 genotyping.



Supplementary Table S1. Characteristics of stage1, stage 2 and stage 3 case and control samples

	Stage 1 [a]		Stage 2 [a]		Stage 3 [b]		
Variables	Cases	Controls	Cases	Controls	Cases	Controls	Population-based panel Whole subjects
Number	519	503	1,110	1,014	4,000	4,889	12,569
Sex Ratio (M / F)	315 / 204	264 / 239	613 / 497	542 / 472	2,526 / 1,474	2,259 / 2,630	5,671 / 6,898
Age at examination (yr)	66.6 ± 9.8	64.7 ± 6.8	62.7 ± 11.7	71.1 ± 9.6	62.3 ± 10.4	63.8 ± 5.8	62.6 ± 6.8
BMI (kg/m^2)	24.5 ± 3.6	23.3 ± 3.1	23.3 ± 3.9	23.0 ± 3.1	—	22.6 ± 2.8	23.1 ± 2.9
Fasting Plasma Glucose (mmol/l) [c]	8.44 ± 2.65	5.22 ± 0.46	8.96 ± 3.38	5.06 ± 0.47	—	—	—
HbA1c (%)	7.26 ± 1.25	5.20 ± 0.28	7.78 ± 1.85	5.40 ± 0.34	—	4.79 ± 0.20	5.23 ± 0.77

[a] Stage 1 and stage 2 case and control subjects were selected according to the identical criteria described in the methods.
Because of the pre-determined policy of collaborative study in analyzing the relevant samples, clinical characteristics other than T2D affection status are not provided for 140 cases in the stage 1 scan; therefore, the characteristics are shown for the remaining 379 samples out of 519.

[b] The stage 3 panel comprises T2D cases and a population-based panel; subjects in the population-based panel are participants of medical checkup in the epidemiological survey that has been organized by Kyushu University. Controls in the stage 3 panel are part of the population-based panel (see the methods section). Because of the pre-determined policy of collaborative study in analyzing the relevant samples, clinical characteristics other than T2D affection status and age are not provided for 4,000 case samples in the stage 3 scan, which have been collected as part of the Biobank Japan project (Nakamura, Y. *Clin. Adv. Hematol. Oncol.* **5**, 696-697 (2007)).

[c] Not fasting plasma glucose but HbA1c levels were measured for all subjects in the population-based panel of stage 3.

Supplementary Table S2. SNP genotyping in the present T2D study.

	Stage 1		Stage 2			Stage 3 [c]	
	519 cases / 503 controls		1,110 cases / 1,014 controls			4,000 cases / 12,569 general population (including 5,395 controls)	4,000 cases / 4,889 controls
Assay	HumanHap550	TaqMan [b]	iPLEX	GoldenGate	TaqMan	TaqMan	TaqMan
# of SNPs assayed	555,352	6	150	1534	7	7	16
SNPs typed successfully [a]							
Number	482,625	6	83	1383	7	7	16
Proportion to screened SNPs	87%	100%	55%	90%	100%	100%	100%
Avg. call rate	0.998	0.975	0.987	0.998	0.995	0.998	0.996
Std. dev. of call rate	0.006	0.002	0.011	0.005	0.002	0.001	0.002

[a] We removed SNPs with genotype call rate <0.95, or <0.99 and minor allele frequency (MAF) <0.05, or significant (P <1×10^{-6}) deviation from Hardy-Weinberg equilibrium in the controls, or MAF <0.001.

[b] Samples from Kyushu University (140 cases) are not included.

[c] For seven SNPs that were chosen for replication study and confirmed in both European-descent and Japanese populations, all the general population samples (n=12,569) were genotyped, whereas part of them (n=4,889) were genotyped as controls for 16 SNPs that survived after stages 1 and 2 scans.

Supplementary Table S3. Summary of association with T2D for SNPs surpassing stage 2 of GWA scan (Cochran-Armitage trend test *P*-value <7E-05 in stage 1+2 combined with Japanese general population)

					NIBI stage 2									NIBI stage 1+2									NIBI stage 1+2 combined with Japanese general population from GeMDBJ								
					Genotype count		Minor allele frequency							Genotype count		Minor allele frequency							Genotype count		Minor allele frequency						
CHR	POS	SNP[a]	Minor allele	Major allele	Case	Control	Case	Control	Odds ratio[b]	*P*trend[c]	*P*genotype	*P*dominant	*P*recessive	Case	Control	Case	Control	Odds ratio[b]	*P*trend	*P*genotype	*P*dominant	*P*recessive	Case	Control	Case	Control	Odds ratio[b]	*P*trend	*P*genotype	*P*dominant	*P*recessive
1	160570900	**rs347313**	G	A	27/304/642	48/342/618	0.18	0.22	0.81	4.2E-03	1.9E-02	3.1E-02	2.1E-02	40/446/1006	70/511/930	0.18	0.22	0.78	1.2E-04	4.4E-04	7.7E-04	4.4E-03	40/446/1006	108/846/1521	0.18	0.21	0.78	3.1E-05	1.6E-04	1.5E-04	6.8E-03
1	221925811	**rs1419310**	A	G	4/52/920	2/34/973	0.03	0.02	1.65	1.1E-02	NA	NA	NA	4/86/1404	2/52/1458	0.03	0.02	1.72	1.8E-03	NA	NA	NA	4/86/1404	2/82/2392	0.03	0.02	1.84	6.4E-05	NA	NA	NA
2	100945886	rs12622050	G	A	135/441/397	161/474/372	0.37	0.40	0.88	2.8E-02	1.6E-01	7.8E-02	1.9E-01	203/665/620	242/728/539	0.36	0.40	0.84	9.6E-04	2.8E-03	8.3E-04	6.5E-02	203/665/620	399/1215/859	0.36	0.41	0.82	3.2E-05	5.5E-05	1.3E-05	3.4E-02
2	100957875	**rs2305159**	T	G	79/376/520	105/428/475	0.27	0.32	0.81	1.8E-03	1.4E-02	5.7E-03	7.6E-02	119/577/798	158/657/695	0.27	0.32	0.79	3.3E-05	1.4E-04	5.1E-05	1.8E-02	119/577/798	246/1091/1137	0.27	0.32	0.80	9.6E-06	2.5E-05	5.3E-06	3.7E-02
2	100961667	rs1542179	T	C	82/388/504	106/433/469	0.28	0.32	0.84	6.5E-03	4.5E-02	2.0E-02	1.1E-01	126/588/779	163/665/683	0.28	0.33	0.80	9.8E-05	4.0E-04	1.3E-04	2.9E-02	126/588/779	258/1109/1108	0.28	0.33	0.80	1.2E-05	2.8E-05	6.0E-06	4.0E-02
2	221789700	rs12476870	T	C	92/401/481	76/402/530	0.30	0.27	1.13	3.9E-02	1.9E-01	1.5E-01	1.3E-01	134/631/728	101/594/816	0.30	0.26	1.21	1.1E-03	4.8E-03	4.0E-03	1.9E-02	134/631/728	161/954/1360	0.30	0.26	1.24	2.7E-05	1.5E-04	1.6E-04	4.1E-03
2	221790225	rs13025789	G	A	92/404/479	76/404/529	0.30	0.28	1.14	3.6E-02	1.8E-01	1.4E-01	1.3E-01	134/629/725	101/596/815	0.30	0.26	1.20	1.2E-03	5.0E-03	4.5E-03	1.8E-02	134/629/725	161/956/1359	0.30	0.26	1.24	2.7E-05	1.5E-04	1.7E-04	3.6E-03
2	221794575	**rs6751269**	C	A	144/442/390	123/450/436	0.37	0.34	1.14	3.0E-02	1.5E-01	1.4E-01	9.4E-02	216/694/584	172/666/673	0.38	0.33	1.21	6.0E-04	2.8E-03	2.5E-03	1.2E-02	216/694/584	273/1084/1118	0.38	0.33	1.23	1.8E-05	1.0E-04	1.8E-04	1.5E-03
5	169026257	**rs6883997**	T	C	75/362/536	49/369/589	0.26	0.23	1.18	1.2E-02	2.4E-02	1.3E-01	9.1E-03	124/567/801	74/534/902	0.27	0.23	1.29	2.8E-05	5.8E-05	8.2E-04	1.7E-04	124/567/801	122/908/1444	0.27	0.23	1.24	5.8E-05	2.5E-05	4.0E-03	1.9E-05
6	1775830	**rs3823276**	A	G	51/296/629	31/296/680	0.20	0.18	1.19	2.0E-02	4.1E-02	1.5E-01	1.6E-02	75/477/943	51/418/1040	0.21	0.17	1.28	2.9E-04	1.4E-03	7.2E-04	2.5E-02	75/477/943	82/689/1702	0.21	0.17	1.27	4.8E-05	2.5E-04	2.0E-04	7.7E-03
6	20603525	rs10946384	T	C	48/289/638	54/358/596	0.20	0.23	0.82	5.5E-03	1.4E-02	3.8E-03	6.6E-01	66/452/966	91/540/879	0.20	0.24	0.78	9.3E-05	4.0E-04	1.1E-04	5.3E-02	66/452/966	152/877/1442	0.20	0.24	0.78	1.7E-05	8.3E-05	2.6E-05	2.3E-02
6	20739932	rs2328529	A	C	175/440/358	107/447/454	0.41	0.33	1.40	2.7E-07	1.2E-06	1.9E-04	2.7E-06	272/672/546	172/651/680	0.41	0.33	1.39	1.7E-09	7.4E-09	1.7E-06	1.6E-07	272/672/546	292/1096/1077	0.41	0.34	1.33	3.4E-09	5.4E-09	1.3E-05	2.3E-08
6	20756741	rs9460540	G	A	125/443/486	141/484/378	0.33	0.38	0.79	2.1E-04	5.5E-04	1.1E-04	1.4E-01	185/663/724	230/711/564	0.33	0.39	0.77	1.1E-06	3.8E-06	1.4E-06	4.3E-03	185/663/724	362/1172/935	0.33	0.38	0.79	5.5E-07	1.0E-06	2.5E-07	8.8E-03
6	20765543	**rs4712523**	G	A	275/514/318	159/487/358	0.48	0.40	1.38	1.6E-07	4.7E-07	6.5E-04	3.2E-07	404/755/466	245/720/540	0.48	0.40	1.38	8.0E-10	1.5E-09	1.6E-05	3.3E-09	404/755/466	412/1197/860	0.48	0.41	1.34	3.1E-10	1.6E-10	3.8E-05	1.5E-10
6	20769229	*rs7754840*	C	G	248/464/299	152/484/373	0.47	0.39	1.41	6.1E-08	1.4E-07	4.2E-04	9.4E-08	338/636/399	235/712/559	0.48	0.39	1.42	1.7E-10	3.6E-10	4.6E-06	1.4E-09	338/636/399	235/712/559	0.48	0.39	1.42	1.7E-10	3.6E-10	4.6E-06	1.4E-09
6	20770102	rs979614	C	T	126/458/499	141/490/378	0.33	0.38	0.79	1.2E-04	3.3E-04	6.6E-05	1.1E-01	187/678/737	231/717/564	0.33	0.39	0.77	5.8E-07	2.1E-06	8.6E-07	3.2E-03	187/678/737	362/1179/935	0.33	0.38	0.78	3.5E-07	6.9E-07	1.7E-07	7.1E-03
6	20787688	*rs7756992*	G	A	328/516/260	194/498/312	0.53	0.44	1.43	5.8E-09	2.8E-08	1.0E-04	3.4E-08	463/773/387	310/729/467	0.52	0.45	1.35	4.6E-09	2.9E-08	7.0E-06	2.6E-07	463/773/387	509/1213/748	0.52	0.45	1.33	3.5E-10	1.3E-09	6.8E-06	5.7E-09
6	20802863	rs2206734	A	G	235/449/292	140/478/390	0.47	0.38	1.48	1.6E-09	4.3E-09	3.9E-05	6.8E-09	349/692/454	225/694/591	0.46	0.38	1.43	4.7E-11	2.0E-10	4.5E-07	3.9E-09	349/692/454	381/1159/934	0.46	0.39	1.37	4.8E-11	7.7E-11	2.3E-06	3.9E-10
7	25261871	**rs916893**	A	G	185/489/301	223/513/273	0.44	0.48	0.87	1.3E-02	8.6E-02	6.1E-02	8.5E-02	248/674/421	346/743/415	0.44	0.48	0.85	1.7E-03	5.2E-03	2.8E-02	2.9E-03	248/674/421	587/1222/656	0.44	0.49	0.82	2.5E-05	1.1E-04	1.9E-03	1.4E-04
7	50670014	**rs2329487**	C	T	157/434/384	123/439/446	0.38	0.34	1.21	2.5E-03	1.6E-02	2.8E-02	1.3E-02	235/707/552	202/652/657	0.39	0.35	1.21	4.4E-04	1.0E-03	2.6E-04	6.6E-02	235/707/552	328/1074/1073	0.39	0.35	1.21	9.1E-05	2.5E-04	7.0E-05	3.0E-02
7	50706457	rs2244480	A	G	123/426/424	105/388/515	0.35	0.30	1.25	7.0E-04	3.3E-03	8.1E-04	1.2E-01	186/689/614	152/617/730	0.36	0.31	1.25	6.3E-05	1.7E-04	4.1E-05	4.2E-02	186/689/614	243/1047/1172	0.36	0.31	1.22	3.9E-05	1.9E-04	9.7E-05	1.0E-02
7	101812662	**rs6976282**	A	G	80/420/474	72/393/544	0.30	0.27	1.17	1.3E-02	6.3E-02	1.9E-02	3.7E-01	138/628/727	103/579/830	0.30	0.26	1.24	2.1E-04	1.0E-03	6.7E-04	1.4E-02	138/628/727	172/950/1354	0.30	0.26	1.23	6.8E-05	3.6E-04	2.5E-04	9.0E-03
9	22122076	**rs2383208**	G	A	151/503/453	173/476/352	0.36	0.41	0.82	9.7E-04	8.2E-03	6.6E-03	2.1E-02	208/751/667	262/749/493	0.36	0.42	0.76	1.6E-07	1.0E-06	1.8E-06	2.9E-04	208/751/667	422/1242/804	0.36	0.42	0.76	6.0E-09	2.9E-08	3.6E-08	1.9E-04
9	22124094	*rs10811661*	C	T	160/503/428	193/494/322	0.38	0.44	0.78	5.8E-05	5.6E-04	4.7E-04	6.3E-03	208/667/578	294/751/461	0.37	0.44	0.74	2.2E-08	1.2E-07	1.8E-07	1.6E-04	208/667/578	294/751/461	0.37	0.44	0.74	2.2E-08	1.2E-07	1.8E-07	1.6E-04
11	2796327	**rs2237892**	T	C	130/488/492	164/452/398	0.34	0.38	0.81	7.6E-04	4.2E-03	1.8E-02	2.9E-03	185/724/720	240/696/581	0.34	0.39	0.80	2.3E-05	9.3E-05	7.9E-04	2.5E-04	185/724/720	385/1165/931	0.34	0.39	0.79	7.4E-07	4.7E-06	2.0E-05	1.6E-04
11	2803645	rs163184	G	T	209/477/278	192/484/331	0.46	0.43	1.14	1.9E-02	1.1E-01	5.3E-02	1.5E-01	334/732/415	280/736/491	0.47	0.43	1.19	9.7E-04	4.3E-03	6.7E-03	7.2E-03	334/732/415	439/1213/819	0.47	0.42	1.22	1.8E-05	8.9E-05	7.7E-04	2.4E-04
12	22201720	**rs918130**	A	G	119/480/377	109/426/474	0.37	0.32	1.24	5.7E-04	8.4E-04	1.7E-04	3.3E-01	210/699/585	164/646/702	0.37	0.32	1.26	2.3E-05	1.1E-04	5.6E-05	7.7E-03	210/699/585	264/1072/1140	0.37	0.32	1.25	3.3E-06	1.9E-05	2.2E-05	1.4E-03
16	27950998	**rs398889**	C	T	33/301/642	47/367/594	0.19	0.23	0.78	7.3E-04	5.7E-03	1.6E-03	1.5E-01	46/446/999	73/540/898	0.18	0.23	0.75	6.6E-06	3.8E-05	1.7E-05	1.4E-02	46/446/999	131/842/1502	0.18	0.22	0.77	6.4E-06	2.9E-05	6.6E-05	1.1E-03
16	82878275	**rs11865624**	C	T	56/316/604	70/373/565	0.22	0.25	0.82	5.3E-03	2.9E-02	8.3E-03	2.7E-01	88/490/917	113/573/825	0.22	0.26	0.80	2.3E-04	7.6E-04	1.8E-04	8.1E-02	88/490/917	184/943/1348	0.22	0.26	0.80	3.6E-05	1.1E-04	2.2E-05	6.1E-02
17	67903781	**rs7212633**	T	C	0/32/943	0/20/989	0.02	0.01	1.67	3.5E-02	NA	NA	NA	0/51/1443	0/26/1486	0.02	0.01	2.00	3.3E-03	NA	NA	NA	0/51/1443	0/37/2439	0.02	0.01	2.31	6.9E-05	NA	NA	NA
19	38656021	rs11880064	C	T	97/433/563	61/407/540	0.29	0.26	1.13	3.8E-02	4.8E-02	3.4E-01	1.4E-02	144/660/808	91/585/835	0.29	0.25	1.23	3.7E-04	1.1E-03	4.1E-03	2.1E-03	144/660/808	140/965/1369	0.29	0.25	1.24	2.1E-05	2.8E-05	1.1E-03	5.8E-05
19	38669236	**rs10425678**	C	T	99/438/572	64/403/539	0.29	0.26	1.12	4.9E-02	8.4E-02	3.6E-01	2.7E-02	146/669/813	94/581/834	0.30	0.25	1.23	3.6E-04	1.3E-03	2.8E-03	3.9E-03	146/669/813	146/958/1369	0.30	0.25	1.24	2.1E-05	5.2E-05	6.7E-04	1.9E-04
19	38680322	rs7250175	T	C	53/374/665	38/316/652	0.22	0.19	1.16	2.3E-02	1.4E-01	6.4E-02	2.3E-01	78/564/969	50/458/1000	0.22	0.19	1.27	1.6E-04	8.2E-04	3.6E-04	3.2E-02	78/564/969	84/744/1643	0.22	0.18	1.27	1.7E-05	9.4E-05	3.7E-05	2.1E-02
19	38686257	rs3786920	C	T	50/384/665	38/325/648	0.22	0.20	1.14	4.0E-02	2.1E-01	9.0E-02	3.6E-01	75/574/969	50/467/997	0.22	0.19	1.25	3.2E-04	1.5E-03	5.6E-04	5.7E-02	75/574/969	84/755/1639	0.22	0.19	1.26	3.2E-05	1.6E-04	4.7E-05	4.4E-02

SNPs clustered in chromosomal position are consecutively highlighted by yellow or pink.

[a] SNPs genotyped in stage 3 are indicated by bold font. Among the SNPs chosen to replicate association signals previously reported, three SNPs in italic, rs7754840 and rs7756992 (CDKAL1 region) and rs10811661 (CDKN2A/B region), also surpassed the GWA scan threshold, and are listed in the table for reference.
In the 7p region, rs2329487 was genotyped in substitution for rs2244480, because these two SNPs were in LD (r2=0.64) to each other and modest T2D association (p=0.033) was shown for rs2329487 in DIAGRAM data.

[b] Odds ratio of case incidence for minor allele.

[c] One-tailed test for association was performed in the direction consistent with stage 1 data.

Supplementary Table S4. T2D association of SNPs detailed for each stage in our study, other studies, and combined analysis.

rs#	Chr	Position (bp)	Region	Risk allele / protective allele	Panel (cases, controls)	Genotype count						Genotype frequency						Risk allele frequency		Odds ratio	(95% CI)	*P* trend[a]	*P* genotype	*P* dominant[b]	*P* recessive[c]	R^2	note
						cases			controls			cases			controls			cases	control								
						RR	RP	PP	RR	RP	PP	RR	RP	PP	RR	RP	PP										
rs10923931	1	120,230,001	*NOTCH2-AD*	T / G	NIBI stage 1 (519, 503)	0	26	493	1	19	483	0.000	0.050	0.950	0.002	0.038	0.960	0.025	0.021	1.21	(0.67 2.16)	5.3E-01	3.2E-01	4.5E-01	4.9E-01	0.0004	rs1493694 (r2=1)
					NIBI stage 2 (1110, 1014)	3	43	1057	1	37	972	0.003	0.039	0.958	0.001	0.037	0.962	0.022	0.019	1.15	(0.75 1.77)	5.2E-01	7.4E-01	6.6E-01	6.3E-01	0.0002	
					NIBI stages 1+2 (1629, 1517)	3	69	1550	2	56	1455	0.002	0.043	0.956	0.001	0.037	0.962	0.023	0.020	1.17	(0.83 1.65)	3.8E-01	6.7E-01	4.2E-01	1.0E+00	0.0002	
rs7578597	2	43,644,474	*THADA*	T / C	NIBI stage 1 (519, 503)	513	4	0	494	4	0	0.992	0.008	0.000	0.992	0.008	0.000	0.996	0.996	1.04	(0.26 4.16)	9.6E-01	1.0E+00	1.0E+00	1.0E+00	2.8E-06	
					NIBI stage 2 (1110, 1014)	1098	11	0	988	21	1	0.990	0.010	0.000	0.978	0.021	0.001	0.995	0.989	2.31	(1.12 4.75)	2.2E-02	4.0E-02	4.8E-01	3.4E-02	0.0025	
					NIBI stages 1+2 (1629, 1517)	1611	15	0	1482	25	1	0.991	0.009	0.000	0.983	0.017	0.001	0.995	0.991	1.95	(1.03 3.67)	3.9E-02	6.7E-02	4.8E-01	5.8E-02	0.0014	
					NIBI replication (4000, 5395)	3910	86	0	4782	99	2	0.978	0.022	0.000	0.979	0.020	0.000	0.989	0.989	0.98	(0.73 1.31)	8.9E-01	5.6E-01	5.0E-01	8.2E-01	0.0000	
					NIBI combined (5629, 6912)	5521	101	0	6264	124	3	0.982	0.018	0.000	0.980	0.019	0.000	0.991	0.990	1.13	(0.87 1.47)	3.5E-01	3.0E-01	2.5E-01	4.6E-01	0.0001	
rs1801282	3	12,368,125	*PPARG*	C / G	NIBI stage 1 (519, 503)	343	20	0	465	34	0	0.945	0.055	0.000	0.932	0.068	0.000	0.972	0.966	1.25	(0.71 2.18)	4.4E-01	4.8E-01	1.0E+00	4.8E-01	0.0007	Risk allele according to Mori et al.
					NIBI stage 2 (1110, 1014)	1038	70	1	953	61	0	0.936	0.063	0.001	0.940	0.060	0.000	0.968	0.970	0.92	(0.65 1.31)	6.5E-01	8.9E-01	1.0E+00	7.2E-01	9.5E-05	
					NIBI stages 1+2 (1629, 1517)	1381	90	1	1418	95	0	0.938	0.061	0.001	0.937	0.063	0.000	0.969	0.969	1.00	(0.75 1.34)	9.7E-01	8.2E-01	4.9E-01	9.4E-01	3.5E-07	
					Mori et al. (2201, 1212)	2097	103	1	1114	96	2	0.953	0.047	0.000	0.919	0.079	0.002	0.976	0.959	1.76	(1.32 2.35)	5.5E-05	1.5E-04	2.9E-01	1.0E-04	0.005	Diabetes 2001; PMID 11289058
					Omori et al. (1630, 1064)	1511	98	3	1001	53	2	0.937	0.061	0.002	0.948	0.050	0.002	0.968	0.973	0.83	(0.59 1.17)	2.8E-01	4.7E-01	1.0E+00	2.7E-01	0.0004	
					Japanese combined (5460, 3793)	4989	291	5	3533	244	4	0.944	0.055	0.001	0.934	0.065	0.001	0.972	0.967	1.18	(0.99 1.40)	6.2E-02	1.6E-01	1.0E+00	6.0E-02	0.0004	
					European (14586, 17968)														0.82	1.14	(1.08 1.20)						
rs4607103	3	64,686,944	*ADAMTS9*	C / T	NIBI stage 1 (519, 503)	195	243	79	192	238	73	0.377	0.470	0.153	0.382	0.473	0.145	0.612	0.618	0.97	(0.81 1.16)	7.8E-01	9.4E-01	7.9E-01	9.0E-01	0.0001	rs7638389 (r2=0.75)
					NIBI stage 2 (1110, 1014)	421	514	165	338	496	173	0.383	0.467	0.150	0.336	0.493	0.172	0.616	0.582	1.15	(1.02 1.31)	2.3E-02	6.4E-02	1.9E-01	2.6E-02	0.0025	
					NIBI stages 1+2 (1629, 1517)	616	757	244	530	734	246	0.381	0.468	0.151	0.351	0.486	0.163	0.615	0.594	1.09	(0.99 1.21)	9.0E-02	2.1E-01	3.8E-01	8.8E-02	0.0009	
rs4402960	3	186,994,389	*IGF2BP2*	T / G	NIBI stage 1 (519, 503)	69	228	219	56	198	240	0.134	0.442	0.424	0.113	0.401	0.486	0.355	0.314	1.20	(1.00 1.45)	5.8E-02	1.4E-01	5.8E-02	3.4E-01	0.004	
					NIBI stage 2 (1110, 1014)	118	487	460	95	431	466	0.111	0.457	0.432	0.096	0.434	0.470	0.339	0.313	1.13	(0.99 1.29)	6.9E-02	1.9E-01	9.2E-02	2.8E-01	0.002	
					NIBI stages 1+2 (1629, 1517)	187	715	679	151	629	706	0.118	0.452	0.429	0.102	0.423	0.475	0.344	0.313	1.15	(1.04 1.28)	9.8E-03	3.1E-02	1.2E-02	1.5E-01	0.002	
					NIBI replication (4000, 5395)	449	1784	1750	537	2251	2600	0.113	0.448	0.439	0.100	0.418	0.483	0.337	0.309	1.14	(1.07 1.21)	5.0E-05	1.4E-04	3.7E-05	4.4E-02	0.002	
					NIBI combined (5629, 6912)	636	2499	2429	688	2880	3306	0.114	0.449	0.437	0.100	0.419	0.481	0.339	0.310	1.14	(1.08 1.21)	1.0E-06	3.0E-06	7.9E-07	1.1E-02	0.002	
					Horikoshi et al. (864, 864)	84	380	384	86	348	407	0.099	0.448	0.453	0.102	0.414	0.484	0.323	0.309	1.07	(0.92 1.24)	3.8E-01	3.6E-01	2.1E-01	8.7E-01	0.0004	
					Omori et al. (1630, 1064)	190	718	717	88	437	522	0.117	0.442	0.441	0.084	0.417	0.499	0.338	0.293	1.23	(1.09 1.39)	5.9E-04	2.5E-03	4.2E-03	6.4E-03	0.004	
					Horikawa et al. (1921, 1622)	230	835	787	143	675	759	0.124	0.451	0.425	0.091	0.428	0.481	0.350	0.305	1.23	(1.11 1.36)	8.1E-05	3.7E-04	1.1E-03	1.7E-03	0.005	
					Japanese combined (10044, 10462)	1140	4432	4317	1005	4340	4994	0.115	0.448	0.437	0.097	0.420	0.483	0.339	0.307	1.16	(1.11 1.21)	4.8E-12	2.7E-11	3.6E-11	3.2E-05	0.002	
					European (14586, 17968)														0.30	1.14	(1.11 1.18)						
rs734312	4	6,421,426	*WFS1*	A / G	NIBI stage 1 with general population (519, 1467)	394	120	5	1080	358	27	0.759	0.231	0.010	0.737	0.244	0.018	0.875	0.859	1.14	(0.93 1.41)	2.1E-01	3.1E-01	2.2E-01	3.5E-01	0.0008	
rs4712523	6	20,765,543	*CDKAL1*	G / A	NIBI stage 1 (519, 503)	129	241	148	86	233	182	0.249	0.465	0.286	0.172	0.465	0.363	0.482	0.404	1.37	(1.15 1.63)	6.2E-04	2.5E-03	9.0E-03	2.7E-03	0.011	
					NIBI stage 1 with general population (519, 1467)	129	242	148	253	711	502	0.249	0.466	0.285	0.173	0.485	0.342	0.482	0.415	1.31	(1.14 1.51)	2.3E-04	4.1E-04	1.7E-02	2.2E-04	0.007	
					NIBI stage 2 (1110, 1014)	275	514	318	159	487	358	0.248	0.464	0.287	0.158	0.485	0.357	0.481	0.401	1.38	(1.22 1.56)	3.3E-07	4.7E-07	7.7E-04	2.9E-07	0.012	
					NIBI stages 1+2 (1629, 1517)	404	755	466	245	720	540	0.249	0.465	0.287	0.163	0.478	0.359	0.481	0.402	1.38	(1.25 1.52)	8.0E-10	1.5E-09	1.8E-05	3.1E-09	0.012	
					NIBI stages 1+2 with general population (1629, 2481)	404	755	466	412	1197	860	0.249	0.465	0.287	0.167	0.485	0.348	0.481	0.409	1.34	(1.22 1.46)	3.1E-10	1.6E-10	4.2E-05	2.4E-10	0.010	
					NIBI replication (4000, 5395)	899	1867	1224	906	2591	1892	0.225	0.468	0.307	0.168	0.481	0.351	0.459	0.409	1.23	(1.16 1.30)	8.0E-12	2.6E-12	6.7E-06	5.3E-12	0.005	
					NIBI combined (5629, 6912)	1303	2622	1690	1151	3311	2432	0.232	0.467	0.301	0.167	0.480	0.353	0.466	0.407	1.27	(1.21 1.33)	7.2E-20	5.8E-21	9.3E-10	9.7E-20	0.007	
					Horikoshi et al. (864, 864)	179	434	239	158	423	280	0.210	0.509	0.281	0.184	0.491	0.325	0.465	0.429	1.16	(1.01 1.32)	3.5E-02	9.8E-02	4.6E-02	1.8E-01	0.003	rs10946398 (r2 = 0.95)
					Horikawa et al. (1921, 1622)	446	881	543	262	781	538	0.239	0.471	0.290	0.166	0.494	0.340	0.474	0.413	1.28	(1.16 1.41)	4.5E-07	3.3E-07	1.7E-03	1.2E-07	0.007	rs7754840 (r2 = 0.95)
					Japanese combined (8414, 9398)	1928	3937	2472	1571	4515	3250	0.231	0.472	0.297	0.168	0.484	0.348	0.467	0.410	1.26	(1.21 1.32)	1.1E-26	5.2E-28	2.6E-13	1.1E-25	0.006	
					European (14586, 17968)														0.36	1.12	(1.08 1.16)						rs10946398 WTCCC/UKT2D, rs7754840 others (r2 = 0.95)
rs7754840	6	20,769,229	*CDKAL1*	C / G	NIBI stage 1 (519, 503)	90	172	100	83	228	186	0.249	0.475	0.276	0.167	0.459	0.374	0.486	0.396	1.44	(1.19 1.75)	3.0E-04	1.4E-03	2.7E-03	3.4E-03	0.015	
					NIBI stage 2 (1110, 1014)	248	464	299	152	484	373	0.245	0.459	0.296	0.151	0.480	0.370	0.475	0.390	1.41	(1.25 1.60)	1.2E-07	1.4E-07	4.7E-04	1.0E-07	0.014	
					NIBI stages 1+2 (1629, 1517)	338	636	399	235	712	559	0.246	0.463	0.291	0.156	0.473	0.371	0.478	0.392	1.42	(1.28 1.57)	1.7E-10	3.6E-10	5.2E-06	1.5E-09	0.014	
					European (14586, 17968)														0.36	1.12	(1.08 1.16)						rs10946398 WTCCC/UKT2D, rs7754840 others (r2 = 0.95)
rs7756992	6	20,787,688	*CDKAL1*	G / A	NIBI stage 1 (519, 503)	135	257	127	116	231	155	0.260	0.495	0.245	0.231	0.460	0.309	0.508	0.461	1.21	(1.01 1.43)	3.9E-02	7.0E-02	2.5E-02	3.1E-01	0.004	
					NIBI stage 2 (1110, 1014)	328	516	260	194	498	312	0.297	0.467	0.236	0.193	0.496	0.311	0.531	0.441	1.43	(1.27 1.62)	1.2E-08	2.8E-08	1.1E-04	3.4E-08	0.015	
					NIBI stages 1+2 (1629, 1517)	463	773	387	310	729	467	0.285	0.476	0.238	0.206	0.484	0.310	0.523	0.448	1.35	(1.23 1.50)	4.6E-09	2.9E-08	8.1E-06	2.6E-07	0.011	
					Horikoshi et al. (864, 864)	238	426	188	191	450	216	0.279	0.500	0.221	0.223	0.525	0.252	0.529	0.485	1.19	(1.04 1.37)	9.3E-03	2.1E-02	1.4E-01	7.4E-03	0.004	
					Omori et al. (1630, 1064)	430	782	398	238	508	293	0.267	0.486	0.247	0.229	0.489	0.282	0.510	0.474	1.16	(1.03 1.29)	1.1E-02	3.8E-02	5.1E-02	2.8E-02	0.002	
					Horikawa et al. (1921, 1622)	537	876	442	330	818	438	0.289	0.472	0.238	0.208	0.516	0.276	0.526	0.466	1.27	(1.15 1.40)	9.8E-07	2.3E-07	1.2E-02	4.2E-08	0.007	
					Japanese combined	1668	2857	1415	1069	2505	1414	0.281	0.481	0.238	0.214	0.502	0.283	0.521	0.465	1.25	(1.19 1.32)	3.5E-16	2.5E-16	7.8E-08	1.2E-15	0.006	
					European (3836, 12562)	352	1514	1888	852	4716	6869	0.094	0.403	0.503	0.069	0.379	0.552	0.295	0.258	1.20	(1.13 1.27)	2.1E-10	7.2E-10	1.1E-07	4.5E-07	0.002	Steinthorsdottir 2007 Nat Genet 39:770; controls from general population
rs864745	7	27,953,796	*JAZF1*	T / C	NIBI stage 1 (519, 503)	335	159	25	309	164	30	0.645	0.306	0.048	0.614	0.326	0.060	0.799	0.777	1.14	(0.92 1.40)	2.5E-01	5.1E-01	4.9E-01	3.3E-01	0.0013	rs1635852 (r2=1)
					NIBI stage 2 (1110, 1014)	715	346	46	630	338	37	0.646	0.313	0.042	0.627	0.336	0.037	0.802	0.795	1.05	(0.90 1.22)	5.6E-01	4.7E-01	6.5E-01	3.7E-01	0.0002	
					NIBI stages 1+2 (1629, 1517)	1050	505	71	939	502	67	0.646	0.311	0.044	0.623	0.333	0.044	0.801	0.789	1.08	(0.95 1.22)	2.5E-01	3.9E-01	9.3E-01	1.8E-01	0.0004	
rs13266634	8	118,253,964	*SLC30A8*	C / T	NIBI stage 1 (519, 503)	192	246	81	160	230	113	0.370	0.474	0.156	0.318	0.457	0.225	0.607	0.547	1.28	(1.07 1.53)	7.1E-03	1.4E-02	5.3E-03	8.7E-02	0.007	
					NIBI stage 2 (1110, 1014)	384	571	149	338	492	181	0.348	0.517	0.135	0.334	0.487	0.179	0.606	0.578	1.13	(1.00 1.27)	5.2E-02	2.0E-02	5.8E-03	5.2E-01	0.002	
					NIBI stages 1+2 (1629, 1517)	576	817	230	498	722	294	0.355	0.503	0.142	0.329	0.477	0.194	0.607	0.567	1.18	(1.06 1.30)	1.5E-03	4.1E-04	8.5E-05	1.3E-01	0.003	
					NIBI replication (4000, 5395)	1535	1898	561	1731	2667	973	0.384	0.475	0.140	0.322	0.497	0.181	0.622	0.571	1.24	(1.17 1.31)	1.2E-12	1.0E-11	1.3E-07	5.4E-10	0.005	
					NIBI combined (5629, 6912)	2111	2715	791	2229	3389	1267	0.376	0.483	0.141	0.324	0.492	0.184	0.618	0.570	1.22	(1.16 1.28)	1.8E-14	1.1E-13	7.8E-11	1.3E-09	0.005	
					Horikoshi et al. (864, 864)	328	383	149	293	394	172	0.381	0.445	0.173	0.341	0.459	0.200	0.604	0.570	1.15	(1.00 1.32)	5.3E-02	1.5E-01	1.6E-01	8.8E-02	0.002	
					Omori et al. (1630, 1064)	651	740	223	381	491	173	0.403	0.458	0.138	0.365	0.470	0.166	0.633	0.600	1.15	(1.03 1.29)	1.6E-02	5.4E-02	5.8E-02	4.6E-02	0.002	
					Horikawa et al. (1921, 1622)	690	806	334	522	725	327	0.377	0.440	0.183	0.332	0.461	0.208	0.597	0.562	1.16	(1.05 1.27)	4.5E-03	1.5E-02	6.8E-02	6.4E-03	0.002	
					Japanese combined (10044, 10462)	3780	4644	1497	3425	4999	1939	0.381	0.468	0.151	0.331	0.482	0.187	0.615	0.572	1.20	(1.15 1.25)	1.1E-18	1.3E-17	6.1E-12	6.3E-14	0.004	
					European (14586, 17968)														0.61	1.12	(1.07 1.16)						
rs2383208	9	22,122,076	*CDKN2A/B*	A / G	NIBI stage 1 (519, 503)	214	248	57	141	273	89	0.412	0.478	0.110	0.280	0.543	0.177	0.651	0.552	1.52	(1.27 1.81)	2.0E-06	1.0E-05	2.3E-03	1.0E-05	0.022	
					NIBI stage 1 with general population (519, 1467)	214	248	57	452	766	249	0.412	0.478	0.110	0.308	0.522	0.170	0.651	0.569	1.41	(1.22 1.64)	2.0E-06	1.1E-05	1.1E-03	1.9E-05	0.011	
					NIBI stage 2 (1110, 1014)	453	503	151	352	476	173	0.409	0.454	0.136	0.352	0.476	0.173	0.636	0.589	1.22	(1.08 1.38)	1.9E-03	8.2E-03	2.2E-02	7.1E-03	0.005	
					NIBI stages 1+2 (1629, 1517)	667	751	208	493	749	262	0.410	0.462	0.128	0.328	0.498	0.174	0.641	0.577	1.31	(1.18 1.45)	1.6E-07	1.0E-06	3.1E-04	2.1E-06	0.009	
					NIBI stages 1+2 with general population (1629, 2481)	667	751	208	804	1242	422	0.410	0.462	0.128	0.326	0.503	0.171	0.641	0.577	1.31	(1.19 1.43)	6.0E-09	2.9E-08	2.0E-04	3.9E-08	0.008	
					NIBI replication (4000, 5395)	1516	1877	591	1597	2689	1101	0.381	0.471	0.148	0.296	0.499	0.204	0.616	0.546	1.33	(1.26 1.42)	9.6E-22	9.3E-21	2.3E-12	1.8E-17	0.010	
					NIBI combined (5629, 6912)	2183	2628	799	2090	3438	1363	0.389	0.468	0.142	0.303	0.499	0.198	0.623	0.553	1.34	(1.27 1.41)	2.1E-29	2.2E-28	3.1E-16	1.9E-23	0.010	
					Horikoshi et al. (864, 864)	324	408	129	290	398	176	0.376	0.474	0.150	0.336	0.461	0.204	0.613	0.566	1.22	(1.06 1.40)	5.5E-03	9.8E-03	3.7E-03	7.9E-02	0.004	rs10811661 (r2 = 1)
					Omori et al. (1630, 1064)	603	757	256	329	520	200	0.373	0.468	0.158	0.314	0.496	0.191	0.607	0.561	1.21	(1.08 1.35)	9.3E-04	3.5E-03	3.5E-02	1.8E-03	0.004	rs10811661 (r2 = 1)
					Horikawa et al. (1921, 1622)	683	891	283	486	770	326	0.368	0.480	0.152	0.307	0.487	0.206	0.608	0.551	1.26	(1.15 1.39)	1.9E-06	9.1E-06	4.4E-05	2.0E-04	0.007	rs10811661 (r2 = 1)
					Japanese combined (10044, 10462)	3793	4684	1467	3195	5126	2065	0.381	0.471	0.148	0.308	0.494	0.199	0.617	0.554	1.29	(1.24 1.35)	2.8E-37	4.4E-36	4.4E-22	1.7E-28	0.008	
					European (14586, 17968)														0.85	1.20	(1.14 1.25)						rs10811661 WTCCC/UKT2D (r2 = 1)
rs10811661	9	22,124,094	*CDKN2A/B*	T / C	NIBI stage 1 (519, 503)	150	164	48	139	257	101	0.414	0.453	0.133	0.280	0.517	0.203	0.641	0.538	1.53	(1.26 1.86)	1.9E-05	7.2E-05	8.0E-03	4.2E-05	0.021	
					NIBI stage 2 (1110, 1014)	428	503	160	322	494	193	0.392	0.461	0.147	0.319	0.490	0.191	0.623	0.564	1.28	(1.13 1.44)	1.2E-04	5.6E-04	7.2E-03	5.3E-04	0.007	
					NIBI stages 1+2 (1629, 1517)	578	667	208	461	751	294	0.398	0.459	0.143	0.306	0.499	0.195	0.627	0.555	1.35	(1.21 1.49)	2.2E-08	1.2E-07	1.6E-04	1.9E-07	0.011	
					European (14586, 17968)														0.85	1.20	(1.14 1.25)						rs10811661 WTCCC/UKT2D (r2 = 1)
rs12779790	10	12,368,016	*CDC123-CAI*	G / A	NIBI stage 1 (519, 503)	8	99	256	12	133	341	0.022	0.273	0.705	0.025	0.274	0.702	0.158	0.162	0.98	(0.75 1.27)	8.6E-01	9.7E-01	9.4E-01	1.0E+00	3.6E-05	
					NIBI stage 2 (1110, 1014)	22	277	805	24	247	740	0.020	0.251	0.729	0.024	0.244	0.732	0.145	0.146	1.00	(0.84 1.18)	9.6E-01	8.0E-01	9.2E-01	5.5E-01	1.1E-06	
					NIBI stages 1+2 (1629, 1517)	30	376	1061	36	380	1081	0.020	0.256	0.723	0.024	0.254	0.722	0.149	0.151	0.98	(0.85 1.13)	8.0E-01	8.0E-01	9.7E-01	5.4E-01	2.2E-05	

rs1111875	10	94,452,862	*HHEX*	C / T	NIBI stage 1 (519, 503)	50	229	240	38	212	252	0.096	0.441	0.462	0.076	0.422	0.502	0.317	0.287	1.15 (0.95 1.39)	1.3E-01	3.2E-01	2.1E-01	2.7E-01	0.002	
					NIBI stage 2 (1110, 1014)	117	486	503	71	435	508	0.106	0.439	0.455	0.070	0.429	0.501	0.325	0.285	1.21 (1.06 1.38)	3.4E-03	6.3E-03	3.7E-02	4.6E-03	0.004	
					NIBI stages 1+2 (1629, 1517)	167	715	743	109	647	760	0.103	0.440	0.457	0.072	0.427	0.501	0.323	0.285	1.19 (1.07 1.33)	1.1E-03	2.5E-03	1.4E-02	2.4E-03	0.003	
					NIBI replication (4000, 5395)	359	1760	1866	397	2140	2855	0.090	0.442	0.468	0.074	0.397	0.529	0.311	0.272	1.21 (1.13 1.29)	5.2E-09	1.7E-08	4.9E-09	4.0E-03	0.004	
					NIBI combined (5629, 6912)	526	2475	2609	506	2787	3615	0.094	0.441	0.465	0.073	0.403	0.523	0.314	0.275	1.21 (1.15 1.28)	6.7E-12	5.1E-11	9.7E-11	3.8E-05	0.004	
					Horikoshi et al. (864, 864)	95	371	394	57	342	461	0.110	0.431	0.458	0.066	0.398	0.536	0.326	0.265	1.34 (1.16 1.56)	9.1E-05	3.5E-04	1.5E-03	1.6E-03	0.009	
					Omori et al. (1630, 1064)	174	702	739	84	425	535	0.108	0.435	0.458	0.080	0.407	0.512	0.325	0.284	1.21 (1.07 1.37)	1.6E-03	6.8E-03	6.1E-03	2.2E-02	0.004	
					Horikawa et al. (1921, 1622)	212	784	852	132	603	828	0.115	0.424	0.461	0.084	0.386	0.530	0.327	0.277	1.27 (1.14 1.41)	1.4E-05	7.9E-05	6.7E-05	3.6E-03	0.006	
					Japanese combined (10044, 10462)	1007	4332	4594	779	4157	5439	0.101	0.436	0.462	0.075	0.401	0.524	0.319	0.275	1.23 (1.18 1.29)	2.7E-22	3.3E-21	1.5E-18	4.0E-11	0.005	
					European (14586, 17968)														0.52	1.13 (1.09 1.17)						
rs7903146	10	114,748,339	*TCF7L2*	T / C	NIBI stage 1 (519, 503)	2	51	466	4	27	472	0.004	0.098	0.898	0.008	0.054	0.938	0.053	0.035	1.55 (1.01 2.39)	5.5E-02	1.5E-02	2.2E-02	4.4E-01	0.004	
					NIBI stage 2 (1110, 1014)	3	91	982	0	68	946	0.003	0.085	0.913	0.000	0.067	0.933	0.045	0.034	1.36 (0.99 1.87)	5.5E-02	6.6E-02	8.6E-02	2.5E-01	0.002	
					NIBI stages 1+2 (1629, 1517)	5	142	1448	4	95	1418	0.003	0.089	0.908	0.003	0.063	0.935	0.048	0.034	1.42 (1.10 1.84)	7.3E-03	1.7E-02	6.3E-03	1.0E+00	0.002	
					NIBI replication (4000, 5395)	17	409	3568	12	360	5018	0.004	0.102	0.893	0.002	0.067	0.931	0.055	0.036	1.59 (1.38 1.83)	1.1E-10	7.2E-10	1.4E-10	9.1E-02	0.004	
					NIBI combined (5629, 6912)	22	551	5016	16	455	6436	0.004	0.099	0.897	0.002	0.066	0.932	0.053	0.035	1.54 (1.36 1.74)	7.6E-12	4.4E-11	7.5E-12	1.1E-01	0.004	
					Horikoshi et al. (1174, 823)	4	119	1051	2	51	770	0.003	0.101	0.895	0.002	0.062	0.936	0.054	0.033	1.65 (1.19 2.33)	2.3E-03	4.6E-03	1.7E-03	1.0E+00	0.005	Diabetologia. 2007 Apr;50(4):747-51
					Hayashi et al. (1630, 1064)	4	165	1450	2	85	980	0.002	0.102	0.896	0.002	0.080	0.918	0.053	0.042	1.30 (0.99 1.70)	5.1E-02	1.5E-01	5.1E-02	1.0E+00	0.001	Diabetologia. 2007 May;50(5):980-4
					Miyake et al. (2214, 1873)	5	228	1921	1	137	1696	0.002	0.106	0.892	0.001	0.075	0.925	0.055	0.038	1.48 (1.19 1.85)	2.4E-04	5.3E-04	3.7E-04	2.3E-01	0.003	J Hum Genet. 2008;53(2):174-80
					Japanese combined (10647, 10672)	35	1063	9438	21	728	9882	0.003	0.101	0.896	0.002	0.068	0.930	0.054	0.036	1.51 (1.38 1.66)	5.0E-18	3.2E-17	2.8E-18	6.1E-02	0.004	
					European (14586, 17968)														0.18	1.37 (1.31 1.43)						
rs11196218	10	114,830,484	*TCF7L2*	G / A	NIBI stage 1 (519, 503)	319	173	25	300	174	28	0.617	0.335	0.048	0.598	0.347	0.056	0.784	0.771	1.08 (0.88 1.33)	4.6E-01	7.7E-01	5.3E-01	5.9E-01	0.001	
					Miyake et al. (2214, 1873)	1331	730	93	1115	617	100	0.618	0.339	0.043	0.609	0.337	0.055	0.787	0.777	1.06 (0.95 1.18)	2.7E-01	2.4E-01	1.0E-01	5.6E-01	0.000	J Hum Genet. 2008;53(2):174-80
rs2237892	11	2,796,327	*KCNQ1*	C / T	NIBI stage 1 (519, 503)	228	236	55	183	244	76	0.439	0.455	0.106	0.364	0.485	0.151	0.667	0.606	1.30 (1.08 1.56)	4.3E-03	1.7E-02	3.2E-02	1.5E-02	0.008	
					NIBI stage 1 with general population (519, 1467)	228	236	55	533	713	221	0.439	0.455	0.106	0.363	0.486	0.151	0.667	0.606	1.30 (1.12 1.51)	5.1E-04	2.4E-03	1.2E-02	2.3E-03	0.006	
					NIBI stage 2 (1110, 1014)	492	488	130	398	452	164	0.443	0.440	0.117	0.393	0.446	0.162	0.663	0.615	1.23 (1.08 1.39)	1.5E-03	4.2E-03	1.8E-02	2.9E-03	0.005	
					NIBI stages 1+2 (1629, 1517)	720	724	185	581	696	240	0.442	0.444	0.114	0.383	0.459	0.158	0.664	0.612	1.25 (1.13 1.39)	2.3E-05	9.3E-05	7.9E-04	2.5E-04	0.006	
					NIBI stages 1+2 with general population (1629, 2481)	720	724	185	931	1165	385	0.442	0.444	0.114	0.375	0.470	0.155	0.664	0.610	1.26 (1.15 1.39)	7.4E-07	4.7E-06	2.0E-05	1.6E-04	0.006	
					NIBI replication (4000, 4889)	1740	1785	465	1695	2345	838	0.436	0.447	0.117	0.347	0.481	0.172	0.660	0.588	1.36 (1.28 1.45)	1.6E-22	2.0E-21	2.1E-13	1.8E-17	0.011	
					NIBI combined (5629, 6406)	2460	2509	650	2276	3041	1078	0.438	0.447	0.116	0.356	0.476	0.169	0.661	0.594	1.33 (1.27 1.41)	1.1E-26	1.4E-25	4.9E-20	1.7E-16	0.010	
rs5219	11	17,366,148	*KCNJ11*	T / C	NIBI stage 1 (519, 503)	46	185	131	55	226	215	0.127	0.511	0.362	0.111	0.456	0.433	0.383	0.339	1.21 (0.99 1.48)	5.5E-02	1.1E-01	4.1E-02	5.2E-01	0.004	
					NIBI stage 2 (1110, 1014)	186	531	389	133	472	407	0.168	0.480	0.352	0.131	0.466	0.402	0.408	0.365	1.20 (1.06 1.36)	3.7E-03	1.4E-02	1.7E-02	2.1E-02	0.004	
					NIBI stages 1+2 (1629, 1517)	232	716	520	188	698	622	0.158	0.488	0.354	0.125	0.463	0.412	0.402	0.356	1.22 (1.09 1.35)	2.5E-04	1.2E-03	1.2E-03	9.8E-03	0.005	
					NIBI replication (4000, 5395)	536	1795	1662	702	2423	2261	0.134	0.450	0.416	0.130	0.450	0.420	0.359	0.355	1.02 (0.96 1.08)	6.0E-01	8.5E-01	7.3E-01	6.0E-01	2.9E-05	
					NIBI combined (5629, 6912)	768	2511	2182	890	3121	2883	0.141	0.460	0.400	0.129	0.453	0.418	0.371	0.355	1.07 (1.01 1.13)	1.5E-02	5.1E-02	3.7E-02	6.3E-02	0.0005	
					Horikoshi et al. (864, 864)	131	393	334	113	417	332	0.153	0.458	0.389	0.131	0.484	0.385	0.382	0.373	1.04 (0.90 1.19)	6.0E-01	3.6E-01	8.8E-01	2.1E-01	0.0002	rs5215 (r2 = 0.995)
					Omori et al. (1630, 1064)	259	763	613	118	512	423	0.158	0.467	0.375	0.112	0.486	0.402	0.392	0.355	1.17 (1.04 1.31)	6.7E-03	3.2E-03	1.7E-01	7.7E-04	0.003	
					Japanese combined (8123, 8840)	1158	3667	3129	1121	4050	3638	0.146	0.461	0.393	0.127	0.460	0.413	0.376	0.357	1.09 (1.04 1.13)	3.4E-04	7.8E-04	1.0E-02	5.5E-04	0.0008	
					European (14586, 17968)														0.46	1.14 (1.10 1.19)						rs5215 WTCCC/UKT2D (r2 = 0.995)
rs3740878	11	44,214,378	*EXT2*	A / G	NIBI stage 1 (519, 503)	149	168	46	187	238	73	0.410	0.463	0.127	0.376	0.478	0.147	0.642	0.614	1.12 (0.92 1.37)	2.4E-01	5.1E-01	4.3E-01	3.2E-01	0.002	
					NIBI stage 2 (1110, 1014)	450	484	161	417	467	130	0.411	0.442	0.147	0.411	0.461	0.128	0.632	0.642	0.96 (0.85 1.09)	5.2E-01	4.2E-01	2.3E-01	1.0E+00	0.0002	
					NIBI stages 1+2 (1629, 1517)	599	652	207	604	705	203	0.411	0.447	0.142	0.399	0.466	0.134	0.634	0.633	1.01 (0.91 1.12)	8.8E-01	5.6E-01	5.6E-01	5.5E-01	7.1E-06	
					Horikoshi et al. (864, 864)	352	403	106	318	418	125	0.409	0.468	0.123	0.369	0.485	0.145	0.643	0.612	1.14 (0.99 1.31)	5.9E-02	1.7E-01	2.0E-01	1.0E-01	0.002	
					Omori et al. (1630, 1064)	685	712	218	431	474	144	0.424	0.441	0.135	0.411	0.452	0.137	0.645	0.637	1.03 (0.92 1.16)	5.7E-01	7.9E-01	8.6E-01	5.2E-01	0.0001	rs11037909 (r2 = 1)
					Japanese combined (4123, 3445)	1636	1767	531	1353	1597	472	0.416	0.449	0.135	0.395	0.467	0.138	0.640	0.629	1.05 (0.98 1.13)	1.4E-01	2.0E-01	7.3E-01	7.8E-02	0.0003	
					European (3278, 3508)	1866	1227	166	1837	1363	272	0.573	0.376	0.051	0.529	0.393	0.078	0.761	0.725	1.20 (1.11 1.30)	2.4E-06	1.9E-06	5.1E-06	3.5E-04	0.003	Sladek (2007) Nature
rs7961581	12	69,949,369	*TSPAN8-LGI*	C / T	NIBI stage 1 (519, 503)	18	128	226	10	161	307	0.048	0.344	0.608	0.021	0.337	0.642	0.220	0.189	1.21 (0.96 1.54)	1.0E-01	7.3E-02	3.2E-01	3.2E-02	0.003	rs4760920 (r2=1)
					NIBI stage 2 (1110, 1014)	65	360	679	49	324	638	0.059	0.326	0.615	0.048	0.320	0.631	0.222	0.209	1.08 (0.93 1.25)	3.1E-01	5.1E-01	4.7E-01	3.4E-01	0.0005	
					NIBI stages 1+2 (1629, 1517)	83	488	905	59	485	945	0.056	0.331	0.613	0.040	0.326	0.635	0.222	0.202	1.12 (0.99 1.27)	7.5E-02	8.7E-02	2.4E-01	3.9E-02	0.0011	
rs8050136	16	52,373,776	*FTO*	A / C	NIBI stage 1 (519, 503)	25	185	309	18	156	325	0.048	0.356	0.595	0.036	0.313	0.651	0.226	0.192	1.23 (0.99 1.52)	5.8E-02	1.6E-01	7.0E-02	3.5E-01	0.004	
					NIBI stage 2 (1110, 1014)	55	370	677	50	321	640	0.050	0.336	0.614	0.049	0.318	0.633	0.218	0.208	1.06 (0.91 1.23)	4.5E-01	6.6E-01	3.9E-01	1.0E+00	0.0003	
					NIBI stages 1+2 (1629, 1517)	80	555	986	68	477	965	0.049	0.342	0.608	0.045	0.316	0.639	0.221	0.203	1.11 (0.98 1.26)	9.2E-02	2.1E-01	7.7E-02	6.1E-01	0.0009	
					Horikoshi et al. (864, 864)	37	334	486	38	269	554	0.043	0.390	0.567	0.044	0.312	0.643	0.238	0.200	1.25 (1.06 1.47)	6.8E-03	3.3E-03	1.3E-03	1.0E+00	0.004	
					Omori et al. (1630, 1064)	84	505	1027	36	339	685	0.052	0.313	0.636	0.034	0.320	0.646	0.208	0.194	1.09 (0.95 1.26)	2.1E-01	8.8E-02	5.9E-01	2.8E-02	0.0006	
					Japanese combined (4123, 3445)	201	1394	2499	142	1085	2204	0.049	0.340	0.610	0.041	0.316	0.642	0.219	0.200	1.13 (1.04 1.22)	3.0E-03	1.2E-02	4.4E-03	1.2E-01	0.001	
					European (14586, 17968)														0.38	1.17 (1.12 1.22)						
rs7501939	17	33,175,269	*TCF2*	T / C	NIBI stage 1 with general population (519, 1467)	64	235	217	142	606	712	0.124	0.455	0.421	0.097	0.415	0.488	0.352	0.305	1.24 (1.07 1.44)	5.7E-03	2.1E-02	8.9E-03	9.4E-02	0.004	
rs10425678	19	38,669,236	*PEPD*	C / T	NIBI stage 1 (519, 503)	47	231	241	30	178	295	0.091	0.445	0.464	0.060	0.354	0.586	0.313	0.237	1.47 (1.21 1.79)	1.1E-04	3.7E-04	1.0E-04	7.5E-02	0.015	
					NIBI stage 1 with general population (519, 1467)	47	231	241	82	555	830	0.091	0.445	0.464	0.056	0.378	0.566	0.313	0.245	1.40 (1.20 1.64)	1.5E-05	8.6E-05	7.8E-05	9.2E-03	0.009	
					NIBI stage 2 (1110, 1014)	99	438	572	64	403	539	0.089	0.395	0.516	0.064	0.401	0.536	0.287	0.264	1.12 (0.98 1.28)	9.8E-02	8.4E-02	3.6E-01	2.8E-02	0.001	
					NIBI stages 1+2 (1629, 1517)	146	669	813	94	581	834	0.090	0.411	0.499	0.062	0.385	0.553	0.295	0.255	1.23 (1.10 1.37)	3.6E-04	1.3E-03	3.0E-03	4.7E-03	0.004	
					NIBI stages 1+2 with general population (1629, 2481)	146	669	813	146	958	1369	0.090	0.411	0.499	0.059	0.387	0.554	0.295	0.253	1.24 (1.12 1.37)	2.1E-05	5.2E-05	7.0E-04	2.4E-04	0.004	
					NIBI replication (4000, 4889)	324	1590	2075	347	1850	2675	0.081	0.399	0.520	0.071	0.380	0.549	0.281	0.261	1.10 (1.03 1.18)	4.0E-03	1.6E-02	7.0E-03	8.3E-02	0.0009	
					NIBI combined (5629, 6406)	470	2259	2888	441	2431	3509	0.084	0.402	0.514	0.069	0.381	0.550	0.285	0.260	1.14 (1.07 1.20)	1.4E-05	7.7E-05	9.4E-05	3.0E-03	0.002	
					NIBI combined with general population (5629, 7370)	470	2259	2888	493	2808	4044	0.084	0.402	0.514	0.067	0.382	0.551	0.285	0.258	1.14 (1.08 1.21)	2.1E-06	1.1E-05	4.0E-05	3.9E-04	0.002	Control includes 964 Japanese general population from GeMDBJ

[a]Genotypes are denoted RR, RP and PP, where 'R' is the risk allele, and 'P' is the protective allele.

[b]P-value for two tailed test. For replication, the value should be halved if association is set to be in same direction as stages 1+2.

[c]Dominant for risk allele.

[d]Recessive for risk allele.

Supplementary Table S5. Logistic regression of T2D status by SNP genotype adjusted for BMI.

	Stage 1				Stage 2				Stage 3				Stage 1+2				Stage 1+2+3			
	OR	(95% CI)		*P*	OR	(95% CI)		*P*	OR	(95% CI)		*P*	OR	(95% CI)		*P*	OR	(95% CI)		*P*
rs4712523	1.42	(1.18	1.72)	2.4E-04	1.37	(1.21	1.54)	3.7E-07	1.22	(1.15	1.30)	8.7E-12	1.38	(1.25	1.53)	4.4E-10	1.26	(1.20	1.33)	7.5E-20
rs4712523	1.47	(1.22	1.79)	8.1E-05	1.38	(1.22	1.56)	2.6E-07					1.40	(1.27	1.55)	1.2E-10				
BMI	1.13	(1.08	1.18)	1.3E-08	1.02	(1.00	1.05)	7.8E-02					1.05	(1.02	1.07)	3.3E-05				
rs4712523	1.45	(1.19	1.75)	1.6E-04	1.37	(1.22	1.55)	3.8E-07	1.25	(1.18	1.33)	8.0E-13	1.40	(1.26	1.55)	2.0E-10	1.29	(1.23	1.36)	7.9E-22
BMIge25	2.29	(1.72	3.07)	2.0E-08	1.06	(0.87	1.29)	5.6E-01	2.78	(2.53	3.06)	2.8E-97	1.32	(1.13	1.56)	7.2E-04	2.30	(2.12	2.50)	8.9E-88
rs2383208	0.60	(0.49	0.74)	1.2E-06	0.82	(0.73	0.93)	2.0E-03	0.75	(0.71	0.79)	1.3E-21	0.75	(0.68	0.84)	1.4E-07	0.75	(0.71	0.78)	6.5E-29
rs2383208	0.59	(0.48	0.73)	9.3E-07	0.82	(0.72	0.93)	1.6E-03					0.75	(0.67	0.83)	7.6E-08				
BMI	1.13	(1.08	1.18)	3.4E-08	1.02	(0.99	1.04)	1.5E-01					1.04	(1.02	1.06)	1.6E-04				
rs2383208	0.62	(0.50	0.76)	5.9E-06	0.82	(0.72	0.93)	1.6E-03	0.73	(0.68	0.78)	5.5E-23	0.75	(0.67	0.83)	1.1E-07	0.73	(0.69	0.77)	1.9E-30
BMIge25	2.16	(1.62	2.89)	2.0E-07	1.04	(0.85	1.27)	7.1E-01	2.78	(2.53	3.06)	1.7E-96	1.29	(1.10	1.52)	2.2E-03	2.28	(2.10	2.48)	9.1E-86
rs4402960	1.18	(0.97	1.43)	9.5E-02	1.13	(0.99	1.29)	6.9E-02	1.14	(1.07	1.21)	5.1E-05	1.14	(1.03	1.27)	1.6E-02	1.14	(1.08	1.20)	1.9E-06
rs4402960	1.14	(0.94	1.39)	1.9E-01	1.15	(1.00	1.31)	4.6E-02					1.15	(1.03	1.28)	1.3E-02				
BMI	1.12	(1.08	1.17)	4.9E-08	1.02	(1.00	1.05)	9.8E-02					1.04	(1.02	1.07)	6.3E-05				
rs4402960	1.15	(0.94	1.40)	1.8E-01	1.15	(1.00	1.31)	4.4E-02	1.14	(1.07	1.22)	4.7E-05	1.15	(1.03	1.29)	1.1E-02	1.15	(1.08	1.21)	1.4E-06
BMIge25	2.24	(1.68	2.99)	4.6E-08	1.07	(0.87	1.30)	5.3E-01	2.74	(2.49	3.02)	5.7E-95	1.33	(1.13	1.56)	6.9E-04	2.28	(2.10	2.48)	2.9E-86
rs13266634	0.81	(0.67	0.98)	2.9E-02	0.88	(0.78	1.00)	5.2E-02	0.81	(0.76	0.86)	1.3E-12	0.86	(0.77	0.95)	3.1E-03	0.82	(0.78	0.86)	4.0E-14
rs13266634	0.80	(0.66	0.97)	2.0E-02	0.89	(0.79	1.01)	8.3E-02					0.86	(0.77	0.95)	4.2E-03				
BMI	1.13	(1.08	1.17)	3.3E-08	1.02	(0.99	1.04)	1.5E-01					1.04	(1.02	1.06)	1.3E-04				
rs13266634	0.80	(0.67	0.97)	2.5E-02	0.90	(0.79	1.02)	9.0E-02	0.80	(0.75	0.85)	1.3E-12	0.86	(0.77	0.95)	4.8E-03	0.81	(0.77	0.86)	6.8E-14
BMIge25	2.25	(1.69	3.00)	3.4E-08	1.03	(0.84	1.25)	8.0E-01	2.77	(2.52	3.05)	2.6E-96	1.29	(1.10	1.51)	2.1E-03	2.28	(2.10	2.47)	1.1E-85
rs1111875	1.07	(0.87	1.32)	5.2E-01	1.22	(1.07	1.39)	3.5E-03	1.21	(1.14	1.29)	5.4E-09	1.18	(1.05	1.32)	3.9E-03	1.21	(1.14	1.27)	4.0E-11
rs1111875	1.08	(0.88	1.34)	4.5E-01	1.23	(1.08	1.41)	2.3E-03					1.20	(1.07	1.34)	2.0E-03				
BMI	1.12	(1.08	1.17)	4.3E-08	1.02	(1.00	1.05)	1.1E-01					1.04	(1.02	1.07)	1.0E-04				
rs1111875	1.08	(0.87	1.34)	4.8E-01	1.23	(1.07	1.41)	2.8E-03	1.24	(1.16	1.33)	5.7E-10	1.19	(1.07	1.34)	2.3E-03	1.23	(1.16	1.31)	1.2E-12
BMIge25	2.23	(1.68	2.98)	4.1E-08	1.05	(0.86	1.27)	6.5E-01	2.78	(2.52	3.06)	5.2E-97	1.30	(1.11	1.53)	1.4E-03	2.29	(2.11	2.48)	8.3E-87
rs7903146	1.51	(0.98	2.36)	6.5E-02	1.36	(0.99	1.88)	5.6E-02	1.57	(1.37	1.81)	1.6E-10	1.40	(1.09	1.81)	1.0E-02	1.52	(1.35	1.72)	1.2E-11
rs7903146	1.51	(0.97	2.38)	7.0E-02	1.31	(0.95	1.82)	9.9E-02					1.38	(1.06	1.79)	1.6E-02				
BMI	1.12	(1.08	1.17)	4.5E-08	1.02	(1.00	1.05)	9.3E-02					1.04	(1.02	1.07)	5.6E-05				
rs7903146	1.47	(0.94	2.32)	9.0E-02	1.30	(0.95	1.81)	1.1E-01	1.60	(1.39	1.86)	1.7E-10	1.37	(1.06	1.78)	1.8E-02	1.54	(1.35	1.74)	2.7E-11
BMIge25	2.22	(1.67	2.96)	5.0E-08	1.07	(0.87	1.30)	5.3E-01	2.75	(2.50	3.02)	2.5E-95	1.32	(1.13	1.55)	7.1E-04	2.28	(2.10	2.48)	2.0E-86
rs2237892	0.81	(0.66	0.98)	3.3E-02	0.82	(0.72	0.93)	1.5E-03	0.74	(0.69	0.78)	2.3E-22	0.81	(0.73	0.90)	1.0E-04	0.75	(0.72	0.80)	1.7E-25
rs2237892	0.78	(0.64	0.96)	1.8E-02	0.81	(0.72	0.92)	1.4E-03					0.81	(0.73	0.90)	7.1E-05				
BMI	1.13	(1.08	1.18)	2.6E-08	1.02	(0.99	1.04)	1.4E-01					1.04	(1.02	1.06)	1.1E-04				
rs2237892	0.78	(0.64	0.96)	1.9E-02	0.82	(0.72	0.92)	1.4E-03	0.74	(0.69	0.79)	3.7E-20	0.81	(0.73	0.90)	8.3E-05	0.75	(0.71	0.80)	8.9E-24
BMIge25	2.27	(1.70	3.03)	2.4E-08	1.03	(0.85	1.26)	7.4E-01	2.77	(2.51	3.06)	2.4E-91	1.30	(1.10	1.53)	1.5E-03	2.26	(2.08	2.46)	2.3E-81
rs5219	1.22	(1.00	1.50)	5.6E-02	1.20	(1.06	1.36)	3.7E-03	1.02	(0.96	1.08)	6.0E-01	1.22	(1.10	1.35)	2.6E-04	1.07	(1.01	1.12)	1.5E-02
rs5219	1.25	(1.01	1.54)	3.8E-02	1.20	(1.06	1.36)	5.2E-03					1.22	(1.09	1.36)	3.0E-04				
BMI	1.13	(1.08	1.18)	1.9E-08	1.02	(0.99	1.04)	1.5E-01					1.04	(1.02	1.06)	1.3E-04				
rs5219	1.24	(1.01	1.53)	4.0E-02	1.20	(1.06	1.36)	5.2E-03	1.03	(0.97	1.10)	3.6E-01	1.22	(1.10	1.36)	2.6E-04	1.08	(1.03	1.14)	3.6E-03
BMIge25	2.32	(1.73	3.11)	1.6E-08	1.04	(0.86	1.27)	6.9E-01	2.75	(2.50	3.02)	1.3E-95	1.31	(1.11	1.54)	1.3E-03	2.27	(2.09	2.47)	8.9E-86
rs10425678	1.44	(1.16	1.79)	8.5E-04	1.12	(0.98	1.28)	9.8E-02	1.10	(1.03	1.17)	6.9E-03	1.21	(1.08	1.35)	1.2E-03	1.13	(1.06	1.19)	6.9E-05
rs10425678	1.46	(1.17	1.82)	8.1E-04	1.13	(0.98	1.29)	9.0E-02					1.21	(1.08	1.36)	1.1E-03				
BMI	1.12	(1.08	1.17)	4.2E-08	1.02	(0.99	1.04)	1.5E-01					1.04	(1.02	1.06)	1.8E-04				
rs10425678	1.44	(1.16	1.80)	1.1E-03	1.13	(0.98	1.29)	8.9E-02	1.11	(1.03	1.19)	4.2E-03	1.21	(1.08	1.36)	1.2E-03	1.14	(1.07	1.21)	3.7E-05
BMIge25	2.23	(1.67	2.98)	5.0E-08	1.03	(0.85	1.26)	7.5E-01	2.76	(2.49	3.05)	1.4E-86	1.29	(1.10	1.51)	2.1E-03	2.24	(2.06	2.44)	1.1E-76

The predictor variable for a SNP genotype is coded by the copy number of minor allele. The predictor variable of 'BMI' takes a raw BMI value, and 'BMIge25' is a categorical variable indicating if BMI is greater or equal to 25. We tested three models of regression with the predictor(s) as SNP alone, SNP with BMI, and SNP with BMIge25. The models are separated by horizontal lines in the table. Results are shown for an individual stage or their combinations, separately by columns. The raw BMI value was not available for the samples in Stage 3; therefore, the corresponding results are omitted. The P-value for a given SNP tends to decrease by the adjustment for BMI (or BMIge25) in the logistic regression. This may indicate that the estimate of OR for the relevant SNP would become more accurate after subtracting the variance explained by these confounding factors (BMI or BMIge25). No significant interaction was detected between SNP genotype and BMI (P >0.01). We did not adjust for sex and age, because these were not matched between cases and controls; it has to be noted that age ≥55 years (in stage 1 and 2 cohort) and age ≥50 years are set to be the enrollment criteria for controls (Supplementary Table S1).

Supplementary Table S6. Comparison of T2D Association of 19 SNPs between Japanese and European-decent populations.

rs#	Chr	Position (bp)	Region	Risk allele / non-risk allele	Japanese [a]							European-decent							$P_{heterogeneity}$ [e]	Proxy SNPs
					Control risk allele freq.	OR (95% CI)	*P* trend	Sample size		R^2	Population attributable risk	Control risk allele freq.	OR (95% CI)	*P* trend	Sample size	R^2	Population attributable risk	Reference		
								Actual [b]	Required [c]						Actual					
Replicated in both populations																				
rs4402960	3	186,994,389	*IGF2BP2*	T / G	0.310	1.16 (1.11–1.21)	4.8E-12	20,506	3,400	0.0024	0.08	0.300	1.14 (1.11–1.18)	8.9E-16	32,554	0.0018	0.07	Scott, Zeggini, DGI	0.519	
rs4712523	6	20,765,543	*CDKAL1*	G / A	0.407	1.26 (1.21–1.32)	1.1E-26	17,812	1,300	0.0065	0.17	0.360	1.12 (1.08–1.16)	4.1E-11	32,554	0.0015	0.07	Scott, Zeggini, DGI	4.1E-05	rs10946398 WTCCC/UKT2D, rs7754840 other Europeans (r^2 = 0.95)
rs13266634	8	118,253,964	*SLC30A8*	C / T	0.570	1.20 (1.15–1.25)	1.1E-18	20,506	2,100	0.0038	0.18	0.610	1.12 (1.07–1.16)	5.3E-08	32,554	0.0015	0.12	Scott, Zeggini, DGI	0.020	
rs2383208	9	22,122,076	*CDKN2A/B*	A / G	0.553	1.29 (1.24–1.35)	2.8E-37	20,506	1,000	0.0080	0.25	0.850	1.20 (1.14–1.25)	7.8E-15	32,554	0.0021	0.26	Scott, Zeggini, DGI	0.024	rs10811661 WTCCC/UKT2D (r^2 = 1)
rs1111875	10	94,452,862	*HHEX*	C / T	0.275	1.23 (1.18–1.29)	2.7E-22	20,506	1,700	0.0046	0.11	0.520	1.13 (1.09–1.17)	5.7E-10	32,554	0.0019	0.11	Scott, Zeggini, DGI	0.004	
rs7903146	10	114,748,339	*TCF7L2*	T / C	0.035	1.51 (1.38–1.66)	5.0E-18	21,319	2,300	0.0035	0.03	0.180	1.37 (1.31–1.43)	1.0E-48	32,554	0.0072	0.11	Scott, Zeggini, DGI	0.062	
rs2237892	11	2,796,327	*KCNQ1*	C / T	0.594	1.33 (1.27–1.41)	1.1E-26	12,035	900	0.0095	0.30	0.926	1.23 (1.14–1.33)	6.6E-08	25,099	0.0014	0.32	Zeggini (2008) DIAGRAM and Yasuda,Unoki (2008) Nat Genet [d]	0.100	rs2283228 Danish (r^2 = 1)
rs5219	11	17,366,148	*KCNJ11*	T / C	0.355	1.09 (1.04–1.13)	3.4E-04	16,963	10,300	0.0008	0.06	0.460	1.14 (1.10–1.19)	6.7E-11	32,554	0.0021	0.11	Scott, Zeggini, DGI	0.124	rs5215 WTCCC/UKT2D (r^2 = 0.995)
rs8050136	16	52,373,776	*FTO*	A / C	0.200	1.13 (1.04–1.22)	3.0E-03	7,568	6,800	0.0012	0.05	0.380	1.17 (1.12–1.22)	1.3E-12	32,554	0.0029	0.11	Scott, Zeggini, DGI	0.451	
rs7501939	17	33,175,269	*TCF2*	T / C	0.305	1.24 (1.07–1.44)	5.7E-03	1,986	2,100	0.0039	0.12	0.582	1.10 (1.06–1.15)	9.2E-07	33,023	0.0011	0.10	Gudmundsson (2007) Nat Genet	0.127	
Not significant (P>0.05) in Japanese, yet OR consistent with or larger than that in European-decent populations																				
rs10923931	1	120,230,001	*NOTCH2-ADAM30*	T / G	0.020	1.17 (0.83–1.65)	0.382	3,146	32,200	0.0002	0.01	0.106	1.13 (1.08–1.17)	4.1E-08	58,667	0.0007	0.02	Zeggini (2008) DIAGRAM	0.844	
rs7578597	2	43,644,474	*THADA*	T / C	0.990	1.13 (0.87–1.47)	0.350	12,541	>100,000	0.0001	0.21	0.902	1.15 (1.10–1.20)	1.1E-09	60,832	0.0009	0.22	Zeggini (2008) DIAGRAM	0.897	
rs1801282	3	12,368,125	*PPARG*	C / G	0.967	1.18 (0.99–1.40)	0.062	9,253	20,400	0.0004	0.27	0.820	1.14 (1.08–1.20)	1.7E-06	32,554	0.0013	0.19	Scott, Zeggini, DGI	0.709	
rs4607103	3	64,686,944	*ADAMTS9*	C / T	0.594	1.09 (0.99–1.21)	0.090	3,146	8,600	0.0009	0.09	0.761	1.09 (1.06–1.12)	1.2E-08	62,387	0.0007	0.12	Zeggini (2008) DIAGRAM	1.000	
rs734312	4	6,421,426	*WFS1*	A / G	0.859	1.14 (0.93–1.41)	0.210	1,986	10,000	0.0008	0.20	0.717	1.09 (1.05–1.14)	2.0E-05	20,992	0.0008	0.11	Sandhu (2007) Nat Genet	0.679	
rs864745	7	27,953,796	*JAZF1*	T / C	0.789	1.08 (0.95–1.22)	0.246	3,146	18,300	0.0004	0.11	0.501	1.10 (1.07–1.13)	5.0E-14	59,617	0.0011	0.09	Zeggini (2008) DIAGRAM	0.779	
rs7961581	12	69,949,369	*TSPAN8-LGR5*	C / T	0.202	1.12 (0.99–1.27)	0.075	3,146	7,400	0.0011	0.04	0.269	1.09 (1.06–1.12)	1.1E-09	62,301	0.0007	0.04	Zeggini (2008) DIAGRAM	0.677	
Association weaker in Japanese than in European-decent populations																				
rs12779790	10	12,368,016	*CDC123-CAMK1D*	G / A	0.151	0.98 (0.85–1.13)	0.798	3,146	opposite to European	–	–	0.183	1.11 (1.07–1.14)	1.2E-10	62,366	0.0008	0.04	Zeggini (2008) DIAGRAM	0.094	
rs3740878	11	44,214,378	*EXT2*	A / G	0.629	1.05 (0.98–1.13)	0.144	7,568	27,000	0.0003	0.05	0.725	1.20 (1.11–1.30)	2.4E-06	6,786	0.0033	0.23	Sladek (2007) Nature	0.014	

Results of T2D association are compared between Japanese and European-derived populations for a total of 19 SNPs with significant evidence for association, which has been reported originally in large-scale European-derived populations except for *KCNQ1*.

[a] See Supplementary Table S4 for details.

[b] In the control group, 964 random controls from the GeMDBJ (http://gemdbj.nibio.go.jp) are included for the association test at each locus, additionally to the samples actually genotyped and/or meta-analysed. For example, as for *TCF2* and *WFS1*, the stage 1 panel (*N*=1,022) plus 964 subjects are used for the combined analysis in this table.

[c] Required sample size to detect significant (P <0.05) association with 80% power, where the OR observed in Japanese is assumed to represent a true genetic impact.

[d] Association results (OR and *P* trend) for rs2237892 in the *KCNQ1* locus are calculated by meta-analysis of data in DIAGRAM and those presented by Yasuda et al. and Unoki et al. (2008), from which the control risk allele frequency in European-decent populations is derived.

[e] Woolf's test of heterogeneity for OR in Japanese and European-decent populations.

Supplementary Table S7. Power for testing a SNP with coeffecient of determination R^2 in N samples, half cases and half controls, under a significance level of α (see Supplementary Information for details).

R^2	Odds Ratio			Corresponding SNP from meta-analysis in Japanese	Significance threshold (α)							
	Risk allele frequency				$5x10^{-7}$				0.05			
					Sample size (N)				Sample size (N)			
	0.2	0.5	0.8		1,000	3,000	10,000	20,000	1,000	3,000	10,000	20,000
0.008	1.34	1.29	1.41		0.014	0.453	1.000	1.000	0.810	0.998	1.000	1.000
0.004	1.24	1.20	1.27		0.001	0.059	0.904	1.000	0.517	0.934	1.000	1.000
0.002	1.16	1.13	1.18		0.0001	0.005	0.290	0.904	0.293	0.688	0.994	1.000
0.001	1.12	1.09	1.12	*FTO*, rs8050136	2.8E-05	0.0005	0.031	0.290	0.170	0.410	0.886	0.994
0.0004	1.07	1.06	1.07	*PPARG*, rs1801282	5.5E-06	4.2E-05	0.001	0.014	0.097	0.195	0.516	0.808
0.0003	1.06	1.05	1.06	*EXT2*, rs3740878	3.7E-06	2.3E-05	0.0005	0.005	0.085	0.158	0.410	0.688

For the reader's reference, the observed power of <0.5, i.e., an aribitrarily defined level of insufficient study power, is obscured in gray for a series of representative situations in the table.

Supplementary Table S8. Results of T2D association of 7 previously-reported SNPs with suggestive evidence in Japanese [from Yasuda *et al.* (2008) Nat Genet 40:1092, Table 1]

Original SNP rs#*	Chr	SNP rs#	Position (bp)	Minor allele frequency		Odds ratio	(95% CI)	*P* trend	
				Case	Control				
rs2250402	15	rs2250402	38109844	0.229	0.213	1.10	(0.89 – 1.36)	0.376	
rs2307027	12	rs2307027	51490881	0.201	0.194	1.04	(0.82 – 1.32)	0.749	
rs3741872 (r^2=0.839)	12	rs2293040	31346021	0.257	0.229	1.17	(0.95 – 1.43)	0.141	
rs574628	20	rs574628	840948	0.393	0.389	1.02	(0.85 – 1.22)	0.842	
rs2233647 (r^2=0.889)	6	rs11758426	34611316	0.132	0.145	0.90	(0.70 – 1.15)	0.404	
rs3785233 (r^2=0.781)	16	rs7204945	7608397	0.201	0.195	1.04	(0.83 – 1.29)	0.734	
rs2075931 (r^2=1)	1	rs1883109	34562006	0.349	0.309	1.20	(1.00 – 1.44)	0.061	OR, opposite direction

The results were derived from the stage 1 panel in the present GWA study (519 cases vs. 503 controls).

*In case the identical SNPs were not genotyped in the stage 1 of GWA study, the results for the alternative SNPs in high LD are shown.

Supplementary Table S9. Multiple regression of the logarithm of HbA1c in the general population.

	Regression coefficient, assuming multiplicative effect on HbA1c (95%CI)						*P*-value	R^2
Sex (male)	1.011	(	1.006	–	1.015	)	7.8E-07	0.0047
Age	1.002	(	1.002	–	1.002	)	3.9E-41	0.0143
BMI	1.006	(	1.005	–	1.007	)	5.5E-54	0.0172
rs4712523	1.010	(	1.007	–	1.013	)	2.2E-11	0.0036
rs2383208	1.011	(	1.008	–	1.014	)	1.6E-13	0.0042
rs4402960	1.007	(	1.004	–	1.010	)	1.9E-05	0.0014
rs13266634	1.009	(	1.006	–	1.012	)	7.7E-09	0.0026
rs1111875	1.006	(	1.003	–	1.010	)	2.4E-04	0.0010
rs7903146	1.024	(	1.017	–	1.032	)	4.8E-10	0.0029
rs5219	1.005	(	1.002	–	1.008	)	2.4E-03	0.0007

Supplementary Table S10. Effects of control selection criteria and study basis (meta-analysis and origin) on the odds ratio in case-control comparison

rs#	Region	OR (95% CI)			
		Nested case-control comparison (vs. 740 diabetic cases) within the same population		Meta-analysis in JPN	Case/control study in Chinese & Korean (ref.23)
		Non-diabetics controls (*N*=4,889)	Control subjects excl. diabetics (*N*=11,829)	Combined controls (*N*=8,840-10,672)	Combined controls (*N*=3,678)
rs4402960	*IGF2BP2*	1.27 (1.13 – 1.43)	1.23 (1.10 – 1.38)	1.16 (1.11 – 1.21)	1.14 (1.06 – 1.23)
rs4712523	*CDKAL1*	1.36 (1.21 – 1.52)	1.27 (1.14 – 1.41)	1.26 (1.21 – 1.32)	1.28 (1.19 – 1.37)
rs13266634	*SLC30A8*	1.27 (1.13 – 1.43)	1.19 (1.07 – 1.33)	1.20 (1.15 – 1.25)	1.13 (1.05 – 1.21)
rs2383208	*CDKN2A/B*	1.37 (1.22 – 1.54)	1.29 (1.15 – 1.44)	1.29 (1.24 – 1.35)	1.29 (1.20 – 1.38)
rs1111875	*HHEX*	1.21 (1.07 – 1.36)	1.18 (1.05 – 1.32)	1.23 (1.18 – 1.29)	1.16 (1.07 – 1.24)
rs7903146	*TCF7L2*	2.04 (1.61 – 2.58)	1.94 (1.56 – 2.40)	1.54 (1.36 – 1.74)	1.35 (1.10 – 1.67)
rs5219	*KCNJ11*	1.17 (1.04 – 1.31)	1.14 (1.02 – 1.27)	1.09 (1.04 – 1.13)	N/A (–)

From the population-based subjects in stage 3 (*N*=12,569), the controls were chosen as either (1) non-diabetics with HbA1c ≤5.0 or (2) the remaining subjects after excluding diabetics. These controls were compared with diabetic cases (N=740) who were under medication or HbA1c ≥7.0. Here, the diabetic cases in this general population were not included in the meta-analysis in Japanese.

Even when relatively generous criteria were adopted for control selection, i.e., simply excluding diabetics from the entire population (in the middle columns), the ORs were almost comparable to those calculated by meta-analysis in Japanese (in the right columns) (see Supplementary Figure S2 and Supplementary Table S4). Increased and decreased ORs (differences ≥0.5) were colored in red and blue, respectively.

When compared to the ORs reported by Ng et al. (*N*=6,719, reference 23), no significant differences were detected between the two studies by Woolf's method ($P > 0.05$), while the ORs tended to be smaller for SLC30A8 and TCF7L2 in the study by Ng et al., where rs7754840 for CDKAL1 and rs10811661 for CDKN2A/B were used.

Supplementary Table S11A. Power of the first stage in the present GWA study.

RAF	OR		
	1.3	1.2	1.15
0.2	0.53	0.17	0.08
0.3	0.66	0.26	0.11
0.4	0.73	0.30	0.16
0.5	0.74	0.29	0.13
0.6	0.68	0.29	0.12
0.7	0.58	0.20	0.11

Samples comprised of 519 cases, and 1,467 (= 503+964) controls; a cut-off level was set at P <0.0025.

Supplementary Table S11B. Power of the second stage in the present GWA study.

RAF	OR		
	1.3	1.2	1.15
0.2	0.49	0.11	0.03
0.3	0.65	0.18	0.05
0.4	0.72	0.24	0.08
0.5	0.73	0.23	0.06
0.6	0.67	0.22	0.07
0.7	0.56	0.14	0.05

Samples comprised of 1,629 cases, and 2,481 (= 1,517+964) controls; a cut-off level was set at P <7×10^{-5}.

Supplementary Table S12. Eigenvalues from the EIGENSTRAT analysis in the stage 1 genotyping.

Number	Eigenvalue	TW Statistics	TW *P*-value
1	1.340	75.072	2.27E-190
2	1.251	8.866	1.86E-09
3	1.247	6.068	1.63E-06
4	1.242	3.024	1.63E-03
5	1.240	2.213	7.22E-03
6	1.239	1.817	0.014
7	1.236	0.347	0.113
8	1.234	-0.852	0.372
9	1.232	-1.977	0.719
10	1.231	-2.174	0.773

Supplementary Table S13. Association of SNPs listed in Table 1, stratified by geographical regions.

rs#	Region	Risk allele / protective allele	Risk allele frequency								Heterozygosity of allele frequency in controls (*P*)	Heterozygosity of odds ratio (*P*)[a]	Mantel-Haenszel[a]		Pooled	
			Tokyo and multi-district		Osaka		Fukuoka		Pooled				Odds ratio (95% CI)	*P* allele	Odds ratio (95% CI)	*P* allele
			cases (4837)	controls (1107)	cases (652)	controls (410)	cases (140)	controls (5395)	cases (5629)	controls (6912)						
rs4712523	*CDKAL1*	G / A	0.463	0.405	0.492	0.393	0.446	0.409	0.466	0.407	0.684	0.182	1.29 (1.20, 1.40)	1.2E-10	1.27 (1.21, 1.33)	1.7E-20
rs2383208	*CDKN2A/B*	A / G	0.620	0.588	0.652	0.548	0.618	0.546	0.623	0.553	0.002	0.010	1.23 (1.14, 1.34)	1.8E-07	1.34 (1.27, 1.41)	1.9E-29
rs4402960	*IGF2BP2*	T / G	0.337	0.314	0.349	0.313	0.359	0.309	0.339	0.310	0.885	0.634	1.14 (1.05, 1.24)	2.1E-03	1.14 (1.08, 1.21)	8.9E-07
rs13266634	*SLC30A8*	C / T	0.619	0.577	0.605	0.543	0.625	0.571	0.618	0.570	0.235	0.714	1.22 (1.13, 1.32)	8.2E-07	1.22 (1.16, 1.28)	2.5E-14
rs1111875	*HHEX*	C / T	0.311	0.286	0.329	0.284	0.361	0.272	0.314	0.275	0.353	0.094	1.19 (1.09, 1.29)	7.7E-05	1.21 (1.15, 1.28)	9.7E-12
rs7903146	*TCF7L2*	T / C	0.055	0.035	0.037	0.032	0.050	0.036	0.053	0.035	0.835	0.501	1.52 (1.25, 1.87)	4.3E-05	1.54 (1.36, 1.74)	3.9E-12
rs2237892	*KCNQ1*	C / T	0.659	0.615	0.668	0.605	0.696	0.588	0.661	0.594	0.049	0.113	1.27 (1.17, 1.37)	7.6E-09	1.33 (1.27, 1.41)	1.1E-26
rs5219	*KCNJ11*	T / C	0.366	0.363	0.408	0.336	NA	0.355	0.371	0.355	0.386	*0.005*	*1.08 (0.99, 1.17)*	*8.8E-02*	1.07 (1.01, 1.13)	1.4E-02
rs10425678	*PEPD*	C / T	0.282	0.266	0.292	0.226	0.329	0.261	0.285	0.260	0.065	0.031	1.18 (1.07, 1.28)	2.9E-04	1.14 (1.07, 1.20)	1.4E-05

[a]The data for rs5219 is based on two strata 'Tokyo and multi-district' and 'Osaka', because the genotype for the cases in 'Fukuoka' stratum is missing. The corresponding figures are denoted in italic font.

Supplementary Table S14A. Association of haplotypes in the *CDKAL*1 locus.

SNP	Chr	Position	Minor allele	Major allele	Minor allele frequency		*P*-value	OR
					Cases	Controls		
rs4712523	6	20765543	G	A	0.481	0.402	3.4E-10	1.38
rs7756992	6	20787688	G	A	0.523	0.448	2.3E-09	1.35

SNPs constituting haplotype	Haplotype class	Haplotype class freuqency		*P*-value
		Cases	Controls	
rs4712523 | rs7756992	GG	0.454	0.372	5.6E-11
rs4712523 | rs7756992	AG	0.070	0.077	0.27
rs4712523 | rs7756992	GA	0.027	0.030	0.38
rs4712523 | rs7756992	AA	0.450	0.521	2.2E-08

Supplementary Table S14B. Association of haplotypes in the *PEPD* locus.

SNP	Chr	Position	Minor allele	Major allele	Minor allele frequency		*P*-value	OR
					Cases	Controls		
rs7250175	19	38680322	T	C	0.224	0.185	0.00017	1.27
rs10425678	19	38669236	C	T	0.295	0.255	0.00035	1.23

SNPs constituting haplotype	Haplotype class	Haplotype class freuqency		*P*-value
		Cases	Controls	
rs7250175 | rs10425678	TC	0.196	0.162	0.0006
rs7250175 | rs10425678	CC	0.099	0.091	0.33
rs7250175 | rs10425678	TT	0.028	0.022	0.17
rs7250175 | rs10425678	CT	0.678	0.724	7.1E-05

Supplementary Table S15. Combined risk of diabetes and pre-diabetic status corrected for overfitting.

	Prevalence of DM (95% CI)	Prevalence of pre-DM (95% CI)	Prevalence of DM or pre-DM (95% CI)
Male			
Highest risk group (5%) predicted by			
All variables	0.26 (0.21 , 0.32)	0.09 (0.05 , 0.13)	0.35 (0.29 , 0.42)
SNP genotypes	0.27 (0.22 , 0.34)	0.06 (0.03 , 0.10)	0.34 (0.27 , 0.40)
Age and BMI	0.19 (0.14 , 0.24)	0.14 (0.10 , 0.18)	0.33 (0.27 , 0.39)
Lowest risk group (5%) predicted by			
All variables	0.08 (0.04 , 0.12)	0.04 (0.01 , 0.06)	0.12 (0.08 , 0.16)
SNP genotypes	0.11 (0.06 , 0.15)	0.05 (0.02 , 0.08)	0.15 (0.11 , 0.20)
Age and BMI	0.08 (0.05 , 0.12)	0.03 (0.01 , 0.04)	0.11 (0.06 , 0.15)
Female			
Highest risk group (5%) predicted by			
All variables	0.22 (0.17 , 0.27)	0.12 (0.08 , 0.16)	0.34 (0.28 , 0.40)
SNP genotypes	0.16 (0.12 , 0.20)	0.08 (0.05 , 0.11)	0.24 (0.19 , 0.28)
Age and BMI	0.16 (0.12 , 0.20)	0.12 (0.08 , 0.16)	0.28 (0.23 , 0.33)
Lowest risk group (5%) predicted by			
All variables	0.01 (0.00 , 0.02)	0.01 (0.00 , 0.02)	0.02 (0.01 , 0.04)
SNP genotypes	0.03 (0.01 , 0.05)	0.05 (0.02 , 0.08)	0.08 (0.05 , 0.11)
Age and BMI	0.02 (0.01 , 0.05)	0.01 (0.00 , 0.02)	0.04 (0.01 , 0.06)