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Discovering missing heritability and early risk prediction for type 2 diabetes: a new perspective for genome-wide association study analysis with the Nurses' Health Study and the Health Professionals' Follow-Up Study

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Background/aim: Despite the rise in type 2 diabetes prevalence worldwide, we do not have a method for early risk prediction. The predictive ability of genetic models has been found to be little or negligible so far. In this study, we aimed to develop a better early risk prediction method for type 2 diabetes.

Materials and methods: We used phenotypic and genotypic data from the Nurses' Health Study and Health Professionals' Follow-up Study cohorts and analyzed them by using binary logistic regression.

Results: Phenotypic variables yielded 70.7% overall correctness and an area under the curve (AUC) of 0.77. With regard to genotype, 798 single nucleotide polymorphisms with P-values of lower than 1.0E-3 yielded 90.0% correctness and an AUC of 0.965. This is the highest score in the literature, even including the scores obtained with phenotypic variables. The additive contributions of phenotype and genotype increased the overall correctness to 92.9% and the AUC to 0.980.

Conclusion: Our results showed that genotype could be used to obtain a higher score, which could enable early risk prediction. These findings present new possibilities for genome-wide association study analysis in terms of discovering missing heritability. These results should be confirmed by follow-up studies.

Key words: Type 2 diabetes, genome-wide association study, single nucleotide polymorphism, Affymetrix, binary logistic regression, ROC curve

1. Introduction

Type 2 diabetes is a complex disease that is characterized by insulin resistance in peripheral tissues and dysfunction in insulin secretion. Type 2 diabetes is a major public health problem, and its prevalence is increasing at an alarming rate worldwide. It has been estimated that 371 million people are already affected by type 2 diabetes, and the number is projected to reach 552 million by 2030 (1).

The development of type 2 diabetes is caused by a combination of lifestyle and genetic factors (2,3). Some risk factors, such as diet and obesity, are under personal control; however, genetic factors are not (4). Although the rise in type 2 diabetes prevalence can be mostly attributed to changes in diet and lifestyle, there is strong evidence of a genetic basis for type 2 diabetes (2). However, genetic risk factors have been found to have lower predictive values when compared to phenotype variables such as body mass index (BMI), familial diabetes history (FAMDB), high blood pressure (HBP), and cholesterol (CHOL) (5,6). Furthermore, the additive contribution of genetic studies using single nucleotide polymorphisms (SNPs) to phenotype variables was found to be almost negligible in several studies (5–12). Because numerous genetic and nongenetic risk factors interact in the causation of type 2 diabetes, the predictive ability of genetic models will likely remain modest.

At present, the clinical use of genetic testing for type 2 diabetes prediction in adults is not recommended (13). Phenotypic risk factors have a higher predictive ability with area under the curve (AUC) values of 0.70–0.90, but these are in middle or later ages when the reversibility of factors is low. Therefore, a model to predict the risk score for type 2 diabetes in the early stages is needed. Additionally, as prediabetic individuals usually remain undiagnosed and

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untreated, identifying new methods using the genotype for the screening and prediction of risk factors is very important. The early prediction of risk factors may help patients to make lifestyle modifications in connection with preventable risk factors, such as obesity (14).

Genome-wide association studies (GWASs) have been widely used to investigate the role of the genotype in the development of diseases. Although many studies have been conducted to uncover the heritability of type 2 diabetes, only a small proportion of genetic heritability can be explained by the variants identified. GWASs have shown significant genome-wide associations with type 2 diabetes at 44 susceptibility loci so far (15). The current type 2 diabetes risk variants explain only about 5%–10% of the genetic basis of type 2 diabetes; much of the genetic basis remains unexplained (16,17).

Most of these studies used logistic regression for the analysis of genetic variables. However, the maximum number of SNPs used was 42, and C-statistics results (AUC) for the genotype were lower than 0.60 (5–12). In the course of our GWAS analysis of Nurses' Health Study (NHS) and Health Professionals' Follow-up Study (HPFS) data, we realized that sensitivity, specificity, and C-statistics increased with the number of SNPs. As we used genotype data for the whole genome instead of a finite number of SNPs, unlike previous studies, a high number of SNPs were included in the analysis. The highest prediction risk scores and AUCs for type 2 diabetes in the literature, even when phenotype studies are included, were achieved in this study using the 798 SNPs selected with P-values of less than 1.0E-3 for the model. Our findings demonstrate the importance of genotype in the prediction of type 2 diabetes, which has been previously disregarded.

2. Materials and methods

2.1. Study population

The NHS and HPFS are well-characterized cohorts of nurses and health professionals, conducted in order to identify novel genetic factors that contribute to type 2 diabetes through large-scale, GWASs and to investigate the role of environmental exposure on the development of type 2 diabetes. The NHS and HPFS cohorts are part of the Gene Environment Association Studies initiative (GENEVA, http://www.genevastudy.org). The NHS was established in 1976, and the HPFS study was started in 1986. Participants of the NHS and HPFS completed a mailed questionnaire on their medical history and lifestyle. Blood was collected in 1989–1990 for the NHS and in 1993–1995 for the HPFS. Genotyping was completed in December 2008 for the NHS and in March 2009 for the HPFS. Lifestyle factors, including smoking, menopausal status and postmenopausal hormone therapy, and body weight, have been updated by validated questionnaires every 2 years.

Participants meeting the following criteria were excluded from the study: 1) those with other types of diabetes (65 NHS, 68 HPFS); 2) those belonging to races other than white (61 NHS, 100 HPFS); 3) HapMap controls (45 NHS, 29 HPFS); and 4) first-degree relatives (15 NHS, 14 HPFS). The final sample included 3248 (1769 controls and 1479 cases) for the NHS and 2391 (1277 controls and 1114 cases) for the HPFS. The current analysis includes SNPs mapped to chromosomes 1 through 23, as annotated based on the Affymetrix Genome-Wide Human SNP Array 6.0 (GeneChip 6.0).

2.2. Phenotypic variables

BMI has been shown to be the most important phenotypic variable in risk prediction of type 2 diabetes. BMI data were continuous in our study, and we converted them to binary using threshold levels that were calculated separately for males and females using the Youden Index (YI = sensitivity + specificity – 1) against the status of diabetes. We found BMI threshold levels of 26.3 kg/m^2 for females and 27.1 kg/m^2 for males that maximized the YI. Other phenotypic data including FAMDB, CHOL, and HBP were binary.

We also analyzed other phenotypic variables. While sex, polyunsaturated fat intake, trans fat intake, and magnesium intake were statistically not important, smoking, activity levels, postmenopausal hormonal status, alcohol, cereal fiber intake, heme iron intake, and glycemic load were found to be significantly related to diabetic status (data not shown). However, since these variables mostly depend on individual declaration, they are subjective. The contribution of these variables to classification and the AUC were negligible; therefore, we excluded them from the analysis for clarity.

2.3. Software

Analyses were conducted using PLINK and SPSS 15.0 for Windows. Amelia software was used to fill in missing values, and R was used for graphical presentation of quantile plots and Manhattan plots (www.r-project.org).

PLINK version 1.07 was used to analyze genome-wide data (http://pngu.mgh.harvard.edu/~purcell/plink). We merged NHS and HPFS data first. SNPs that met any of the following criteria were excluded from the analysis: 1) minor allele frequencies (MAF) of <0.05; 2) call rate of <95%; 3) P for Hardy–Weinberg equilibrium of <0.001; and 4) missing rates 0.1. After applying the QC filter, 642,576 SNPs remained for the analyses.

2.4. Binary logistic regression

We performed binary logistic regression (BLR) using NHS and HPFS genotypic and phenotypic data via SPSS to test the associations of the genotypic and phenotypic risk scores with diabetes. We coded genotypes for common allele homozygotes, heterozygotes, and rare allele

homozygotes separately for analysis. We evaluated model discrimination by using C-statistics (areas under receiver operating characteristic curves, ROC-AUCs), which were calculated for the predicted risk of the logistic regression model.

We used SNPs with P-values of less than 1.0E-3. There were 886 SNPs with P-values below this level. However, we excluded SNPs if the missing allele number was greater than 50 (patients), except for rs10739592, since it had the lowest P-value (2.08E-14). It had 99 missing alleles. To fill in the missing alleles, we used the Amelia toolbox for imputation (18). The result of the imputation was validated by comparing 'before' and 'after' P-values of SNPs and observing the relative distribution density of the original data set and the imputed data set.

3. Results

3.1. The clinical characteristics of the participants

The clinical characteristics of the study populations are presented in Table 1. We performed a genome-wide analysis of NHS and HPFS participants. The frequency distribution of the P-value of the SNPs is given in Table 2. The P-values of 886 SNPs were less than 1.0E-03. The distribution of P-values for all SNPs (642,576) versus chromosomal distribution is shown as a Manhattan plot in Figure 1. Chromosomes, P-values, odds ratios, and MAF values of 798 SNPs are provided in the Appendix (on the journal's website). Quantile–quantile (QQ) plots of P-values of SNPs are given against the expected P-values in Figure 2. We accepted 1.0E-3 as the threshold level to determine which SNPs would be included in the analysis (Figure 2). Initially, 886 SNPs were considered; after a quality check for missing criteria, 798 SNPs were used.

3.2. BLR analysis of phenotype

The analysis results of phenotype variables of the NHS and HPFS data sets are presented in Table 2. The summary of BMI is also listed in Table 3 as a continuous variable. As noted in Section 2, BMI was converted to a binary form before BLR analysis. Type 2 diabetes patients had significantly higher BMIs than the controls. BMI was strongly associated with type 2 diabetes; the odds ratio for BMI was 3.86. Other important phenotypes were FAMDB, HBP, and CHOL. Their P-values and odds ratios are also given in Table 4. The combined effect of these 4 phenotype variables yielded an overall classification of 70.7% and an AUC of 0.77. We also compared rs10739592, which had the lowest P-value in GWAS analysis, with phenotypic variables. It should be noted that rs10739592 alone (OR: 1.34, P-value: 2.08E-14) increased the overall prediction by only 2.84%. The composite effect of phenotypic variables was less than the sum of the individual effects of each variable alone due to the effect of overlap.

We were able to predict individual risk scores using the following formula with constants obtained from logistic regression analyses of familial diabetes history, high blood pressure, cholesterol, and BMI.

Table 1. Clinical characteristics of the participants. Data presented as mean ± SD.

	Type 2 diabetes	Control subjects
n (male/female)	1114/1479	1277/1769
Age (years)	57.42 ± 7.72	57.12 ± 7.66
BMI (kg/m^2)		
Female	29.91 ± 5.76	25.39 ± 4.83
Male	27.89 ± 4.14	25.21 ± 2.82

Table 2. P-value distribution of SNPs (before filtering of missing alleles, see Section 2).

P-value	Cumulative frequency	Frequency
<1.0E-11	1	1
1.0E-10	6	5
1.0E-09	6	0
1.0E-08	6	0
1.0E-07	10	4
1.0E-06	29	19
1.0E-05	132	103
1.0E-04	886	754

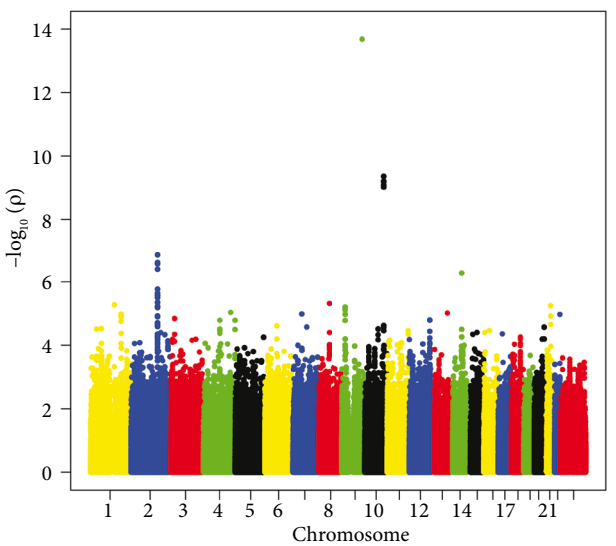

Figure 1. Manhattan plot of the point-wise P-values for the 642,576 SNP loci of the NHS and HPFS data sets.

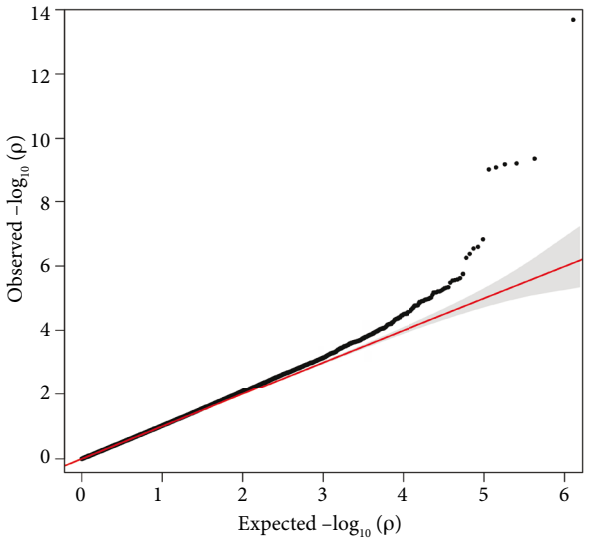

Figure 2. Quantile-quantile plots of SNP P-values in (NHS+HPFS) GWAS analysis. The x-axis is $-\log^{10}$ of the expected P-values and the y-axis is $-\log^{10}$ of the observed P-values. Detaching point from the expected $-\log^{10}$ is nearly 1.0E-3.

$$P=\frac{exp^{(-1,579+famdb+1,132+hbp\times 0,862+chol\times 0,556+BMI\times 1,351}}{1+exp^{(-1,579+famdb+1,132+hbp\times 0,862+chol\times 0,556+BMI\times 1,351}}$$

The C-statistics (AUC) value for the 4 phenotype variables was found to be 0.77 ± 0.003.

3.3. BLR analysis of genotype

Because the number of SNPs (798) is high and is unusual for BLR, as reported in the literature, we used a different approach to evaluate the effect of genotype on prediction scores and AUC. First, we grouped SNPs according to their P-values. Three groups of SNPs with P-values of less than 1.0E-4 yielded a maximum prediction score of 67.4% and an AUC of 0.735; 680 SNPs with P-values between 1.0E-04 and 1.0E-03 yielded a prediction score of 87.7% and an AUC of 0.947. When we used an incremental approach, the first 3 groups containing 118 SNPs with P-values of less than 1.0E-4 yielded prediction scores that were lower than that of the fourth group (Table 5). This showed that more SNPs should be included for higher prediction rates and explained why previous studies in the literature that used a maximum of 40 SNPs obtained lower predictive values. In addition, we tested how various threshold levels in BLR analysis affected the prediction score and AUC (Table 6). The threshold level was chosen to be 0.5 by default in BLR analysis. When the threshold level increases, negative predictive value increases, positive predictive value decreases, and AUC does not change (Table 6).

We also investigated the additive contribution of phenotypes to the model built from genotyping data. The addition of 4 phenotypes (BMI, FAMDB, CHOL, and HBP) increased the prediction score from 90.0% to 92.9% and the AUC from 0.965 to 0.980 (Figure 3).

In addition, we found important differences between females and males in SNPs corresponding to the transcription factor-7–like 2 (*TCF7L2*) gene (Table 7). We found that the *TCF7L2* gene was more determinative in males than in females. Although the *TCF7L2* gene is one of the most significant genetic marker associated with type 2 diabetes mellitus risk (19), there is no information in the literature about the relationship between the TCF7L2 gene and sex. This finding is important when interpreting literature on interethnic differences that do not mention sex.

4. Discussion

Development of genotype-based prediction will help us in the early prediction, identification, and prevention of type 2 diabetes. We showed that genotype-based predictions for type 2 diabetes yielded as high a score as phenotype-based methods. We obtained 90.0% prediction correctness, and the AUC was 0.965 with only genotype (SNP) variables. According to our knowledge, this is the highest score reported in the literature for risk prediction of type 2 diabetes.

GWAS has facilitated the understanding of the genetic basis of complex traits; it is a powerful method for the detection of genetic variations that predispose individuals

Table 3. Body mass index values of males and females in the control and diabetic groups. Data presented as mean ± SD.

	Male	n	Female	n	Average	n
Control	25.21 ± 2.82	1277	25.39 ± 4.83	1769	25.31 ± 4.11	3046
Diabetes	27.89 ± 4.14[a]	1114	29.91 ± 5.76[b]	1479	29.04 ± 5.22[c]	2593
Average	26.45 ± 3.74	2391	27.44 ± 5.73	3248	27.03 ± 5.01	5639

[a] Independent sample t-test, 3.72E-115.
[b] Independent sample t-test, 1.52E-68.
[c] Independent sample t-test, 1.85E-174.

Table 4. P-value, odds ratio, net reclassification improvement (NRI) percentage, overall prediction percentage, and AUC of phenotypic variables (n/a, not applicable).

Phenotype	P-value	Odds ratio	NRI %	Overall prediction %	AUC
Baseline	n/a	n/a	n/a	54	n/a
Body mass index	5.21E-108	3.86	13.99	68.0	0.68[a]
Familial diabetes history	4.32E-69	3.10	9.70	63.7	0.63[b]
High blood pressure	3.25E-39	2.37	9.68	63.7	0.62[b]
Cholesterol	7.76E-15	1.74	4.40	58.4	0.56
Four phenotypes (BMI+FAMDB+HBP+CHOL)	1.56E-187	n/a	16.70	70.7	0.77[c]
rs10739592	2.08E-14	1.34	2.84	56.9	0.55

[a] $P < 0.001$, significantly higher than other groups except BMI+FAMDB+HBP+CHOL.
[b] $P < 0.001$, significantly higher than cholesterol and rs10739592.
[c] $P < 0.001$, significantly higher than others.
BMI: Body mass index, FAMDB: familial diabetes history, HBP: high blood pressure, CHOL: cholesterol.

Table 5. Additive binary logistic regression analysis of SNPs grouped according to their P-values obtained in GWAS analysis.
NPV: Negative predictive value, PPV: positive predictive value, AUC: area under curve.

SNP groups according to their P-values	Number of SNPs (n)	NPV (percentage correct for control)	PPV (percentage correct for diabetes)	Overall %	AUC
<1.0E-06	10	75.0	38.7	58.3	0.602
<1.0E-05	27 (10+17)	72.8	45.3	60.2	0.636
<1.0E-04	118 (91+27)	74.3	59.3	67.4	0.735
<1.0E-03	798 (680+118)	90.7	89.1	90.0	0.965

Table 6. Effects of cut-off value on classification correctness and AUC.

ROC cutoff value	SNPs (n)	NPV	PPV	Overall %	AUC
0.5	798	90.7	89.1	90.0	0.965 ± 0.002
0.6	798	94.0	83.7	89.3	0.965 ± 0.002
0.7	798	96.8	76.8	87.6	0.965 ± 0.002
0.8	798	98.4	67.5	84.2	0.965 ± 0.002
0.9	798	99.3	52.6	77.8	0.965 ± 0.002

NPV: Negative predictive value, PPV: positive predictive value, AUC: area under curve.

to complex chronic diseases. GWAS has provided many useful insights into the pathophysiology of type 2 diabetes by enabling the identification of novel susceptibility loci that were not identified by classical approaches. However, for most of the identified type 2 diabetes susceptibility loci, the causal variants and molecular mechanisms for diabetes risk are unknown. Our findings do not reject the importance of susceptibility loci for causal variants, but rather provide more accurate risk prediction. It is also important to remember that the effect sizes found for SNPs thus far are not a reflection of their biological or clinical significance. Although their individual predictive values may be small, SNPs as a profile might point to important biological pathways that could be targeted for therapeutic intervention.

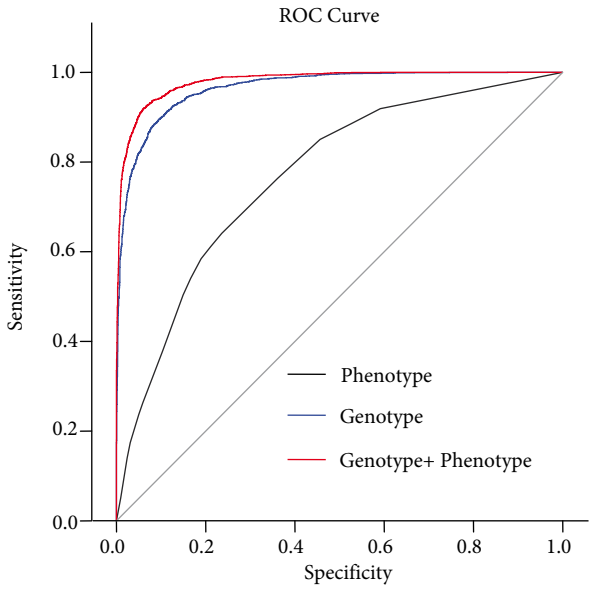

Figure 3. ROC plot for the BLR model containing type 2 diabetes and 4 phenotype variants, body mass index, familial diabetes history, high blood pressure, and cholesterol (black line, AUC = 0.77), for the 798 SNP variants (red line, AUC = 0.965) and genotype plus phenotype (blue line, AUC = 0.980).

Table 7. SNPs corresponding to the *TCF7L2* gene in our GWAS analysis. The P-values of some SNPs differ between males and females.

SNP	P-value		
	General	NHS (Female)	HPFS (Male)
rs12255372	4.37E-10	9.72E-05	5.52E-07
rs12243326	6.12E-10	1.80E-04	3.47E-07
rs4132670	6.53E-10	2.56E-04	1.94E-07
rs7901695	8.18E-10	1.53E-04	5.83E-07
rs4506565	9.48E-10	1.67E-04	5.92E-07
rs11196208	2.40E-05	3.67E-03	2.08E-03
rs10885409	2.71E-05	5.33E-03	1.50E-03
rs11196205	3.49E-05	5.59E-03	1.91E-03
rs4074720	1.30E-04	1.22E-02	3.29E-03
rs7077039	1.35E-04	1.50E-02	2.77E-03
rs10787472	1.38E-04	1.36E-02	3.09E-03
rs6585201	3.96E-04	3.57E-02	2.95E-03
rs4073288	3.88E-03	>0.05	1.40E-02
rs7901275	4.71E-03	>0.05	2.25E-03
rs11196212	7.30E-03	4.39E-02	>0.05
rs7917983	7.76E-03	>0.05	2.62E-03
rs11196181	2.67E-02	>0.05	>0.05
rs12266632	3.28E-02	4.17E-02	>0.05
rs11196203	3.39E-02	>0.05	1.64E-02

Fortunately, the incidence of type 2 diabetes can be delayed or prevented by maintaining healthy lifestyle behaviors (14). The early identification of population subgroups that are at particularly high risk for type 2 diabetes might facilitate the targeting of prevention efforts to those who might benefit from them the most. Until these findings, genetic associations have not appeared to improve type 2 diabetes risk prediction, which has already been achieved through clinical risk predictors alone.

In the time since the first GWAS data were published in 2007 by the Wellcome Trust Case Control Consortium (20), significant progress has been made and much information has been obtained from GWASs. However, GWAS-based studies to improve clinical decisions are still in their initial stages (21). Previous studies have focused mostly on causative loci rather than the entire risk prediction approach. In addition, the results of risk prediction models are not satisfactory for type 2 diabetes. Nearly 40 susceptible loci have been identified in European and Asian populations, but the heritability of type 2 diabetes remains largely unexplained (22). Only ~10% of the known type 2 diabetes heritability could be explained by the results of a European twin study (23). This evidence suggests that information on a large portion of heritability is missing. Since a statistical P-value of 5×10^{-8} is generally accepted for genome-wide significance (24), previous studies did not use SNPs that had P-values greater than this. Several limitations of the current approach for GWASs in revealing the missing heritability information have been proposed. One limitation is that the accepted importance threshold level for GWASs ($P < 5 \times 10^{-8}$) may produce type 2 errors (false-negative results). Therefore, many important loci could be obscured among other loci having only borderline associations. In addition, Imamura et al. suggested that the other reason for the low percentage of genetic contribution might be the omission of susceptibility variants that have an MAF value of less than 1% (22). However, our findings do not agree with these suggestions. In this study, we used SNPs that had P-values of greater than 5×10^{-8}, accepted 5% as the threshold for MAF, and thereby obtained a higher risk prediction score. The most important reason for the low genetic contribution reported so far is that the use of a small number of SNPs for analysis fails to yield a sufficient composite risk score. We proposed that SNPs that have P-values of less than the detaching point of a distribution (in QQ plot), 1.0E-3 in our study, could contribute to risk prediction. Furthermore, Imamura et al. (22) suggested

that genome-wide exon (exome) sequencing by next-generation sequencers might help explain the missing heritability. Our findings suggest that this might not be necessary in order to obtain a high risk-prediction score. However, next-generation sequencing technology may help find the exact causative loci near or encompassing the newly discovered SNPs.

Because individual SNPs do not yield adequate prediction scores, combining SNPs to yield composite genotype risk scores has also been tested. In such a simulation study by Janssens et al., risk alleles were weighted according to the type 2 diabetes effect size from the original GWAS; this might not substantially improve the C-statistic for alleles with small effect sizes (odds ratio: 1.10–1.25) (25). However, we found that 680 SNPs with P-values between 1.0E-04 and 1.0E-03 yielded an overall prediction score of 87.7% and AUC of 0.947, while 118 SNPs, with P-values of less than 1.0E-04, yielded an overall prediction score of 67.4% and AUC of 0.735. This shows that a high SNP number is required for higher composite genotype risk scores. However, Janssens et al. used only 40 SNPs. The composite risk score is not equal to the sum of individual SNP scores. Due to the overlapping effect of the risk alleles, we could obtain a higher composite risk score with a higher number of SNPs. However, phenotype risk scores are higher than those of individual SNP scores, i.e. OR is 3.86 for BMI in our study. Thus, small phenotype variables could yield higher scores.

The prediction of an individual's risk of developing type 2 diabetes is the most anticipated clinical use of genetic information. Prediction values of phenotypic and genotypic characters have been investigated in the Malmö Preventive Project, the Botnia Study (8), the Framingham Offspring Study I (9), the Whitehall II study (10), and the GoDARTS Study (26). These studies examined loci ranging in number from 11 to 20 that were associated with type 2 diabetes. The results of these analyses showed no clear improvement in predictive power when adding the genetic risk score to the established risk prediction models by using phenotypic variables such as age, sex, family history, BMI, fasting glucose level, systolic blood pressure, and lipid profile. Basic demographic, clinical, and laboratory predictors have C-statistics (AUC) ranging from 0.66 in the Rotterdam Study (11) to 0.90 in the Framingham Offspring Study I (9). The C-statistic improves from 0.903 to 0.906 with the addition of a 40-SNP score to the clinical model in the Framingham Offspring Study II (7) and from 0.74 to 0.75 in the larger Malmö Preventive Project (8). In other studies, adding genetic information to phenotype-based risk models did not improve discrimination and showed a maximum increase of only 2% over phenotype in ROC curves (6,10,26). AUC values were equal to or lower than 0.60 for genetic variants alone in these studies (9–11,26). Therefore, phenotype scores were found to be superior to the scores achieved thus far by using genotype alone.

Genotype-based risk prediction may work better in younger individuals. In the Framingham Offspring II study, the addition of a 40-SNP score to a full clinical model achieved better net reclassification improvement (NRI) among those younger than 50 years old (7). However, the degree of prediction scores obtained from genotype is still below the widely accepted clinical prevention target. The greater contribution of genotype over the prediction value of phenotype for patients at a younger age is expected since phenotype variables are more overt only at middle age or older. The most desirable risk prediction method is one with a higher prediction value at an early age, even in childhood. Therefore, our findings provide an opportunity for risk prediction of type 2 diabetes with high accuracy at an early stage.

A limitation on the use of phenotypic variables is the reduced range of ages and follow-up durations for type 2 diabetes genetic prediction. In previous studies, participants with baseline ages were generally in middle adulthood, and the follow-up period was around 10 years. However, we need a model that can estimate the risk earlier, which should be validated at a young age with a longer prediction time horizon to help achieve early prevention. As noted above, in the Framingham Offspring Study II, the 40-SNP genotype risk score significantly improved NRI in younger participants but not in older ones. Here, we show that genetic risk prediction alone using 798 SNPs could yield higher risk prediction for type 2 diabetes.

Due to the low predictive value of the genetic susceptibility loci of type 2 diabetes so far, alternative GWAS strategies, such as enrichment of genetic effects for improving predictive power (i.e. selecting more severe cases, early onset of disease, and family history of type 2 diabetes), and original GWAS study designs (such as response to an antidiabetic treatment or type 2 diabetes in the presence of extreme obesity) (15,27) have been proposed. Complementary epigenomic approaches such as DNA methylation studies have also been proposed in addition to GWAS (27). However, our strategy of using more SNPs may provide greater risk prediction for type 2 diabetes; therefore, the need for a sophisticated approach to risk prediction could be reviewed. Our approach might be combined with epigenomic, environmental, or other enrichment methods for further insight into type 2 diabetes etiology.

In the future, follow-up studies with a reasonable time period should be designed to evaluate the development of type 2 diabetes using the genotype-based risk prediction value from our study. We were able to calculate individual risk scores using the constants of the present

study obtained through analysis. Our findings should be validated by comparing the cumulative type 2 diabetes incidence in low- and high-risk groups in a follow-up study. In addition, interethnic differences should be reviewed from the perspective of our results, since some GWAS studies did not mention the sex of the participants (28,29). Furthermore, our prediction strategy could also be tested for treatment success of type 2 diabetes by establishing a pharmacogenetic investigation of a genome-wide approach. In a previous study, it was found that a SNP, rs11212617, at a locus containing the ataxia telangiectasia mutated gene could explain 2.5% of the variance in the metformin response (30). Variance greater than this can probably be explained using the composite SNP score approach. Translation of the findings of the present study will provide a gateway into personalized preventive and therapeutic medicine.

In conclusion, we found that genotype-based risk prediction could yield higher risk prediction values when a sufficient number of SNPs are used. This could enable early risk prediction for type 2 diabetes. The growing importance of the threshold P-value in GWAS analysis should be reviewed, depending on the investigation field. Our findings open up new horizons for translating GWAS findings into improved care for patients with diabetes. The value of genotype-based risk prediction alone or in combination with phenotypic variables should be further investigated in follow-up studies for validation.

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Appendix. Chromosomes, P-values, odds ratios, and MAF values of 798 SNPs.

#	rsid	OR	P value	MAF	CHR	BP	A1	A2	EntrezGene	Gene Symbol	Gene Name
1	rs4654582	0,8513	5,28E-04	0,213	1	4630143	T	A	55966	AJAP1	adherens junctions associated protein 1
2	rs11121467	0,7922	2,34E-04	0,105	1	9620920	A	T			
3	rs2336381	0,7559	9,28E-04	0,055	1	11931611	G	A	5351	PLOD1	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1
4	rs11580525	1,225	5,35E-04	0,114	1	14119518	C	T			
5	rs149562	1,154	8,72E-04	0,259	1	16667788	T	C	114819	CROCCP3	ciliary rootlet coiled-coil, rootletin pseudogene 3
6	rs6660946	0,8611	7,63E-04	0,239	1	18606142	G	A			
7	rs7529705	1,139	8,30E-04	0,380	1	19592679	A	G	832	CAPZB	capping protein (actin filament) muscle Z-line, beta
8	rs10492998	0,8585	8,99E-04	0,219	1	19645434	T	C	832	CAPZB	capping protein (actin filament) muscle Z-line, beta
9	rs1546263	0,8541	8,28E-04	0,207	1	19646020	A	G	832	CAPZB	capping protein (actin filament) muscle Z-line, beta
10	rs6701048	1,237	7,70E-04	0,097	1	29676041	G	C			
11	rs6704040	1,294	7,84E-04	0,065	1	30417261	C	T			
12	rs215770	1,165	3,04E-04	0,268	1	37358560	A	C			
13	rs215773	0,8676	2,84E-04	0,369	1	37368827	T	G			
14	rs215792	0,8748	6,10E-04	0,376	1	37378028	C	T			
15	rs215791	0,8776	8,13E-04	0,375	1	37378878	C	T			
16	rs12131641	0,8424	2,90E-04	0,198	1	37384100	A	G			
17	rs12118788	0,82	3,08E-05	0,198	1	37398350	T	C			
18	rs1587578	0,8518	2,23E-04	0,254	1	37401328	C	A			
19	rs11579242	0,8546	9,45E-04	0,197	1	47987966	G	A			
20	rs11584807	0,8304	1,28E-04	0,187	1	47993041	T	C			
21	rs783323	0,8723	3,10E-04	0,468	1	66713368	A	G			
22	rs699253	0,8535	2,96E-05	0,476	1	66713736	A	G			
23	rs12739235	1,232	3,14E-04	0,119	1	66728087	C	T			
24	rs12142962	1,247	1,53E-04	0,118	1	66730690	A	G			
25	rs7537440	1,142	5,02E-04	0,426	1	66804495	G	T	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
26	rs1373909	1,142	5,08E-04	0,426	1	66813463	G	A	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
27	rs6697088	0,8595	8,66E-05	0,404	1	66817312	C	G	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
28	rs10889634	0,8708	3,05E-04	0,414	1	66838499	G	A	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
29	rs6696927	0,8703	2,89E-04	0,414	1	66842969	T	C	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
30	rs1562217	0,8682	2,24E-04	0,414	1	66846154	T	C	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
31	rs6656912	0,8658	2,15E-04	0,405	1	66856259	T	C	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1

Appendix. (Continued).

32	rs4655648	0,8718	3,51E-04	0,415	1	66886897	C	T	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
33	rs9662943	0,8762	5,82E-04	0,407	1	66893720	C	T	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
34	rs6681460	0,8745	4,57E-04	0,415	1	66895645	A	G	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
35	rs6694782	1,135	8,31E-04	0,457	1	66899350	G	A	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
36	rs6588215	0,8694	2,56E-04	0,414	1	66914537	A	G	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
37	rs4655650	0,8726	4,00E-04	0,415	1	66914874	T	C	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
38	rs7542924	0,8699	2,78E-04	0,414	1	66915643	G	A	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
39	rs4655506	0,8717	3,60E-04	0,422	1	66923399	G	A	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
40	rs10789215	0,8755	5,22E-04	0,413	1	66923773	T	C	84251	SGIP1	SH3-domain GRB2-like (endophilin) interacting protein 1
41	rs344935	0,8661	4,06E-04	0,321	1	67910451	G	A			
42	rs1780731	1,15	9,22E-04	0,274	1	79108612	C	T			
43	rs1434431	1,139	5,85E-04	0,477	1	87960918	A	G			
44	rs2143992	1,141	5,19E-04	0,437	1	94109636	C	T	30836	DNTTIP2	deoxynucleotidyltransferase, terminal, interacting protein 2
45	rs3789439	0,8588	8,37E-04	0,220	1	94352014	C	T	24	ABCA4	ATP-binding cassette, sub-family A (ABC1), member 4
46	rs3789442	0,8538	4,95E-04	0,222	1	94354044	C	G	24	ABCA4	ATP-binding cassette, sub-family A (ABC1), member 4
47	rs2220760	1,138	9,66E-04	0,372	1	94977931	A	G			
48	rs3767273	1,149	2,96E-04	0,417	1	103173621	G	C	1301	COL11A1	collagen, type XI, alpha 1
49	rs12046389	1,147	3,45E-04	0,416	1	103181688	A	C	1301	COL11A1	collagen, type XI, alpha 1
50	rs2616010	1,148	3,74E-04	0,413	1	103181905	C	T	1301	COL11A1	collagen, type XI, alpha 1
51	rs7550118	1,141	8,33E-04	0,357	1	103335690	T	C	1301	COL11A1	collagen, type XI, alpha 1
52	rs1415359	1,139	9,58E-04	0,359	1	103337029	C	T	1301	COL11A1	collagen, type XI, alpha 1
53	rs10493988	1,141	8,36E-04	0,356	1	103338744	G	A	1301	COL11A1	collagen, type XI, alpha 1
54	rs2761441	0,8785	6,23E-04	0,493	1	110538385	G	A	388662	SLC6A17	solute carrier family 6, member 17
55	rs1942216	0,8648	7,95E-04	0,262	1	115721322	A	C			
56	rs1543594	0,8413	2,22E-04	0,204	1	115845877	A	C			
57	rs11579824	0,8034	5,29E-06	0,190	1	145469224	C	T			
58	rs12133943	1,236	4,74E-04	0,106	1	145561705	G	C	607	BCL9	B-cell CLL/lymphoma 9
59	rs1208517	0,8426	9,76E-04	0,155	1	183539106	T	C	10625	IVNS1ABP	influenza virus NS1A binding protein
60	rs7539680	1,232	2,53E-04	0,123	1	186584179	G	C			
61	rs10753046	1,25	8,65E-05	0,124	1	186631148	G	C			
62	rs6425178	1,248	1,18E-05	0,164	1	186632905	C	G			
63	rs3919967	1,252	1,28E-05	0,161	1	186638225	A	C			
64	rs10753049	1,248	1,12E-05	0,165	1	186639485	A	G			

Appendix. (Continued).

65	rs7516670	1,242	1,78E-05	0,164	1	186642303	T	C			
66	rs6667131	1,25	1,04E-05	0,164	1	186649073	T	A			
67	rs1565272	1,234	4,24E-05	0,165	1	186649670	A	G			
68	rs172235	1,171	1,22E-04	0,296	1	186726999	C	A			
69	rs4313401	1,136	7,69E-04	0,499	1	187650996	A	G			
70	rs11800563	0,8811	8,25E-04	0,496	1	187698667	G	C			
71	rs4428892	0,8806	7,86E-04	0,495	1	187719770	T	A			
72	rs10922227	0,882	8,96E-04	0,486	1	187787128	A	G			
73	rs1119030	0,8829	9,94E-04	0,485	1	187787822	A	G			
74	rs4950949	0,8767	8,67E-04	0,372	1	201077185	C	T			
75	rs2250509	0,8247	7,20E-04	0,129	1	201405593	A	G	4608	MYBPH	myosin binding protein H
76	rs340835	1,138	6,34E-04	0,473	1	212230298	A	G	5629	PROX1	prospero homeobox 1
77	rs2820444	0,8653	6,80E-04	0,276	1	217808443	A	G			
78	rs3002142	0,8268	8,38E-04	0,129	1	220854685	C	T			
79	rs2133189	0,8579	2,78E-04	0,283	1	220881065	C	T	375056	MIA3	melanoma inhibitory activity family, member 3
80	rs17163358	0,8592	3,42E-04	0,284	1	220887262	G	A	375056	MIA3	melanoma inhibitory activity family, member 3
81	rs17465637	0,8632	5,02E-04	0,281	1	220890152	A	C	375056	MIA3	melanoma inhibitory activity family, member 3
82	rs1053316	0,8119	4,82E-04	0,117	1	220906461	A	G	375056	MIA3	melanoma inhibitory activity family, member 3
83	rs2378607	0,8567	1,50E-04	0,315	1	220986518	T	G	400823	FAM177B	family with sequence similarity 177, member B
84	rs6429366	0,8731	3,87E-04	0,426	1	240833628	T	C			
85	rs2362255	0,81	3,66E-04	0,126	1	244130482	G	A	64754	SMYD3	SET and MYND domain containing 3
86	rs7520116	0,8719	7,19E-04	0,329	1	244271398	G	C	64754	SMYD3	SET and MYND domain containing 3
87	rs3893111	0,8655	4,40E-04	0,302	2	8692795	G	A			
88	rs1550105	0,8791	7,11E-04	0,444	2	20613584	T	C			
89	rs11897611	0,836	6,05E-04	0,161	2	20638798	C	T			
90	rs4666430	0,8301	2,33E-04	0,173	2	20641940	G	A			
91	rs930760	0,8558	8,79E-05	0,355	2	20669817	C	T			
92	rs4666438	1,156	7,02E-04	0,264	2	20674067	A	G			
93	rs11096680	1,15	9,87E-04	0,270	2	20675712	A	T			
94	rs3796064	1,16	5,39E-04	0,260	2	20701799	A	G	64342	HS1BP3	HCLS1 binding protein 3
95	rs10166174	0,8685	3,97E-04	0,349	2	20702484	A	G	64342	HS1BP3	HCLS1 binding protein 3
96	rs17803553	0,8743	6,86E-04	0,356	2	25678607	T	C	1838	DTNB	dystrobrevin, beta
97	rs12613835	0,874	6,66E-04	0,356	2	25682705	A	G	1838	DTNB	dystrobrevin, beta

Appendix. (Continued).

98	rs7562790	1,146	3,94E-04	0,399	2	36527059	G	T	51232	CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)
99	rs2160367	1,148	3,09E-04	0,429	2	36535123	G	C	51232	CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)
100	rs3821153	1,139	6,86E-04	0,417	2	36606626	G	T	51232	CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)
101	rs2727880	1,141	5,83E-04	0,429	2	52408156	C	T			
102	rs17730780	0,8557	4,53E-04	0,236	2	52416883	G	A			
103	rs6545274	0,8526	3,46E-04	0,233	2	52497718	C	T			
104	rs2552356	0,8732	3,56E-04	0,459	2	52508248	G	A			
105	rs12622811	0,8602	2,44E-04	0,303	2	52641453	T	C			
106	rs6720390	1,139	6,06E-04	0,467	2	52654578	C	T			
107	rs13430296	0,8517	8,30E-05	0,313	2	52672168	G	C			
108	rs17043120	0,8574	1,70E-04	0,313	2	52679905	G	A			
109	rs1843032	1,138	8,27E-04	0,396	2	52694816	A	G			
110	rs1446441	0,828	2,42E-04	0,170	2	53155170	T	C			
111	rs7575107	1,228	1,94E-04	0,133	2	55159490	G	T			
112	rs4672367	0,8309	2,06E-04	0,176	2	60251920	T	C			
113	rs17329726	1,23	2,03E-04	0,129	2	60338590	A	G			
114	rs359274	1,175	9,55E-04	0,178	2	60360385	C	G			
115	rs17662176	0,7373	1,65E-04	0,059	2	64950508	G	C			
116	rs12470994	1,288	3,02E-04	0,082	2	67528010	A	C			
117	rs1159766	1,151	8,91E-04	0,273	2	72317749	T	C	23233	EXOC6B	exocyst complex component 6B
118	rs1159764	1,15	9,47E-04	0,273	2	72317874	A	T	23233	EXOC6B	exocyst complex component 6B
119	rs10221769	1,158	5,05E-04	0,276	2	72332562	T	A	23233	EXOC6B	exocyst complex component 6B
120	rs2118836	1,165	2,46E-04	0,292	2	96526699	C	T			
121	rs11123406	1,147	4,66E-04	0,365	2	111667012	T	C			
122	rs17715688	0,8029	2,28E-04	0,113	2	115089550	G	T	57628	DPP10	dipeptidyl-peptidase 10 (non-functional)
123	rs17715867	0,7716	2,45E-04	0,078	2	115096853	C	A	57628	DPP10	dipeptidyl-peptidase 10 (non-functional)
124	rs6705790	1,175	5,21E-04	0,213	2	121609358	T	A			
125	rs17010780	0,8116	4,87E-04	0,113	2	124531274	G	T	129684	CNTNAP5	contactin associated protein-like 5
126	rs17575791	0,8652	6,66E-04	0,283	2	129802415	T	C			
127	rs4954045	0,8795	9,06E-04	0,390	2	133695340	A	C	344148	NCKAP5	NCK-associated protein 5
128	rs17786300	1,189	9,41E-04	0,149	2	140253872	C	A			
129	rs1355421	0,7852	4,95E-05	0,118	2	160621464	A	G	22925	PLA2R1	phospholipase A2 receptor 1, 180kDa
130	rs1355420	0,7953	1,12E-04	0,119	2	160621517	T	C	22925	PLA2R1	phospholipase A2 receptor 1, 180kDa

Appendix. (Continued).

131	rs4665146	0,8047	5,34E-05	0,147	2	160624329	A	C	22925	PLA2R1	phospholipase A2 receptor 1, 180kDa
132	rs16844742	0,7949	1,94E-05	0,148	2	160639530	T	A			
133	rs7573469	0,7916	1,27E-05	0,149	2	160653973	G	A			
134	rs3111397	0,8201	2,58E-05	0,204	2	160759609	C	T	3694	ITGB6	integrin, beta 6
135	rs12692585	1,163	4,91E-04	0,254	2	160789087	G	A			
136	rs10181181	0,809	4,03E-07	0,290	2	160795657	T	C			
137	rs2925757	0,7906	1,71E-06	0,183	2	160809415	G	A			
138	rs13023477	1,176	8,11E-04	0,193	2	160820133	T	C			
139	rs12692588	0,8511	2,43E-05	0,435	2	160832428	C	T			
140	rs7572970	0,8261	5,97E-06	0,281	2	160844902	A	G	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
141	rs1020731	0,8064	2,45E-07	0,293	2	160852301	G	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
142	rs1020732	0,8552	4,42E-05	0,422	2	160852485	G	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
143	rs12692590	0,8606	9,21E-05	0,419	2	160861443	C	G	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
144	rs12692592	0,8126	5,95E-06	0,221	2	160871627	G	T	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
145	rs9917155	0,8574	5,20E-05	0,454	2	160871805	C	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
146	rs4077463	0,807	3,16E-06	0,218	2	160874480	A	G	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
147	rs7593730	0,8053	2,55E-06	0,218	2	160879700	T	C	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
148	rs4589705	0,806	2,75E-06	0,219	2	160884382	T	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
149	rs4386280	0,8605	7,99E-05	0,449	2	160891041	A	G	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
150	rs4664013	0,8334	6,49E-06	0,331	2	160892410	G	C	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
151	rs10165319	0,8585	1,41E-04	0,337	2	160901051	T	C	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
152	rs4538150	0,8508	2,18E-05	0,451	2	160917573	G	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
153	rs9287795	0,8055	2,66E-06	0,218	2	160918034	C	G	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
154	rs6718526	0,7817	2,74E-07	0,197	2	160922421	T	C	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
155	rs11693602	0,8048	2,29E-06	0,219	2	160932904	C	T	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
156	rs10929982	0,8021	4,55E-06	0,195	2	160944523	C	T	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
157	rs12998587	0,8344	1,19E-05	0,307	2	160950541	T	C	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
158	rs7587102	0,8384	1,99E-05	0,306	2	160967528	T	C	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
159	rs4664323	0,8711	3,11E-04	0,428	2	160967931	C	T	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
160	rs13009374	0,8469	5,84E-05	0,305	2	160973345	C	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
161	rs6742799	0,8377	2,39E-04	0,198	2	161025706	C	A	5937	RBMS1	RNA binding motif, single stranded interacting protein 1
162	rs6752569	1,15	4,89E-04	0,327	2	161182219	C	T			
163	rs13390172	1,169	1,69E-04	0,287	2	161233847	C	T			

Appendix. (Continued).

164	rs12473293	1,18	6,70E-05	0,287	2	161237591	C	A			
165	rs4383351	1,172	1,35E-04	0,286	2	161242414	A	G			
166	rs4368343	1,198	4,39E-06	0,353	2	161242897	C	G			
167	rs16851382	1,21	1,55E-04	0,169	2	166621721	A	G	6323	SCN1A	sodium channel, voltage-gated, type I, alpha subunit
168	rs1402108	0,8632	6,78E-04	0,257	2	176957972	G	T			
169	rs12185628	1,207	4,01E-05	0,219	2	179389216	C	T			
170	rs10190741	0,8765	5,27E-04	0,443	2	179396117	T	C			
171	rs12477346	0,8777	6,60E-04	0,444	2	179445855	A	G	285025	CCDC141	coiled-coil domain containing 141
172	rs10176147	1,138	6,24E-04	0,466	2	184378789	G	C			
173	rs826186	0,8776	7,66E-04	0,397	2	184403897	G	A			
174	rs2369202	1,134	9,11E-04	0,468	2	184694310	T	C			
175	rs12232884	1,135	8,70E-04	0,454	2	184709630	G	C			
176	rs1526212	1,135	8,54E-04	0,460	2	184719102	A	G			
177	rs10497643	1,137	6,98E-04	0,462	2	184761027	T	C			
178	rs13010985	1,15	2,49E-04	0,458	2	184812923	A	G			
179	rs719736	1,137	7,00E-04	0,487	2	184895389	G	A			
180	rs4241279	1,236	3,06E-04	0,117	2	192317911	T	C			
181	rs6739080	1,216	8,61E-04	0,119	2	192322352	T	G			
182	rs4675425	0,8212	6,52E-04	0,124	2	204734173	A	G			
183	rs7583852	0,8505	4,74E-04	0,214	2	204766132	T	G			
184	rs10198084	0,8448	4,67E-05	0,297	2	204855576	A	G			
185	rs6435252	1,229	4,89E-04	0,116	2	205366261	A	G	117583	PARD3B	par-3 partitioning defective 3 homolog B (C. elegans)
186	rs1075041	1,22	7,58E-04	0,119	2	205372981	A	G	117583	PARD3B	par-3 partitioning defective 3 homolog B (C. elegans)
187	rs2663891	1,267	9,40E-04	0,078	2	208281566	A	G			
188	rs16840004	1,298	8,31E-04	0,064	2	208325193	A	G	151195	CCNYL1	cyclin Y-like 1
189	rs7585736	1,17	7,85E-04	0,213	2	214300694	T	G	79582	SPAG16	sperm associated antigen 16
190	rs4673054	0,8649	1,25E-04	0,487	2	223796106	A	T			
191	rs2203733	0,8618	8,41E-05	0,484	2	223801345	A	G			
192	rs10933000	0,8657	1,37E-04	0,488	2	223801654	G	A			
193	rs969494	0,8637	1,07E-04	0,484	2	223803302	G	A			
194	rs970816	0,8605	7,28E-05	0,481	2	223805584	G	A			
195	rs7595029	1,218	7,62E-05	0,168	2	236056702	C	T			
196	rs4663596	1,203	2,29E-04	0,167	2	236065943	A	G			

Appendix. (Continued).

197	rs4685598	1,175	7,98E-04	0,191	3	348693	A	C	10752	CHL1	cell adhesion molecule with homology to L1CAM (close homolog of L1)
198	rs7630509	1,172	8,62E-04	0,195	3	349168	G	A	10752	CHL1	cell adhesion molecule with homology to L1CAM (close homolog of L1)
199	rs7649544	1,243	8,03E-04	0,092	3	353069	C	A	10752	CHL1	cell adhesion molecule with homology to L1CAM (close homolog of L1)
200	rs6442929	1,148	7,55E-04	0,308	3	5072993	T	C			
201	rs6773179	1,148	6,47E-04	0,327	3	5073759	A	T			
202	rs1161171	0,8322	6,51E-05	0,225	3	8417494	C	T	100288428	LOC100288428	uncharacterized LOC100288428
203	rs359025	0,8336	8,15E-05	0,221	3	8420729	T	C	100288428	LOC100288428	uncharacterized LOC100288428
204	rs359024	0,8434	2,13E-04	0,224	3	8421265	G	A	100288428	LOC100288428	uncharacterized LOC100288428
205	rs359033	0,86	9,99E-04	0,227	3	8431789	A	G	100288428	LOC100288428	uncharacterized LOC100288428
206	rs359032	0,8549	5,74E-04	0,232	3	8432379	C	T	100288428	LOC100288428	uncharacterized LOC100288428
207	rs2088620	0,8501	4,58E-04	0,223	3	8435932	G	T	100288428	LOC100288428	uncharacterized LOC100288428
208	rs11712016	1,206	7,15E-04	0,134	3	9174613	G	C	9901	SRGAP3	SLIT-ROBO Rho GTPase activating protein 3
209	rs12185978	0,8598	3,98E-04	0,272	3	11061367	C	G			
210	rs2130505	0,8432	1,43E-05	0,368	3	21727970	G	A	79750	ZNF385D	zinc finger protein 385D
211	rs4858348	0,8554	7,59E-05	0,358	3	21730685	G	A	79750	ZNF385D	zinc finger protein 385D
212	rs4858352	0,8526	4,51E-05	0,374	3	21743250	G	A	79750	ZNF385D	zinc finger protein 385D
213	rs9830825	1,275	3,53E-04	0,083	3	31431027	A	C			
214	rs12485914	1,207	7,85E-04	0,133	3	31437904	C	T			
215	rs11917010	0,8644	7,17E-04	0,259	3	54181107	A	G	55799	CACNA2D3	calcium channel, voltage-dependent, alpha 2/delta subunit 3
216	rs6794229	0,8528	2,15E-04	0,260	3	54189989	T	G	55799	CACNA2D3	calcium channel, voltage-dependent, alpha 2/delta subunit 3
217	rs13061634	0,8717	7,75E-04	0,307	3	56029117	C	T	26059	ERC2	ELKS/RAB6-interacting/CAST family member 2
218	rs1021734	0,8224	7,23E-04	0,129	3	56938384	T	C	50650	ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3
219	rs17288993	0,8128	3,12E-04	0,131	3	56940107	G	A	50650	ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3
220	rs4626067	0,8091	2,09E-04	0,135	3	56968071	T	C	50650	ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3
221	rs10155027	1,254	1,60E-04	0,118	3	60259909	T	G	2272	FHIT	fragile histidine triad
222	rs17400084	1,254	1,46E-04	0,117	3	60261426	T	C	2272	FHIT	fragile histidine triad
223	rs11707184	1,184	2,12E-04	0,215	3	62316084	T	C			
224	rs831080	0,8579	3,13E-04	0,273	3	71515191	C	G	27086	FOXP1	forkhead box P1
225	rs831081	0,8493	1,91E-04	0,250	3	71515298	A	G	27086	FOXP1	forkhead box P1
226	rs6766190	1,24	9,16E-04	0,102	3	73871082	A	T			
227	rs291475	1,261	6,23E-04	0,091	3	73883578	C	G			
228	rs524431	0,8666	5,60E-04	0,296	3	74383584	A	G			

Appendix. (Continued).

229	rs471800	0,8741	9,77E-04	0,312	3	74392334	T	C			
230	rs6551483	0,8779	9,58E-04	0,364	3	87568689	C	T			
231	rs9815149	0,8716	4,77E-04	0,366	3	87569165	G	C			
232	rs9816344	1,141	5,71E-04	0,408	3	115162780	C	T	254887	ZDHHC23	zinc finger, DHHC-type containing 23
233	rs9840925	1,342	7,41E-04	0,054	3	116582546	G	A			
234	rs16823934	1,162	9,09E-04	0,228	3	116818374	A	G			
235	rs17281612	1,208	8,85E-04	0,122	3	120606689	C	T	57514	ARHGAP31	Rho GTPase activating protein 31
236	rs1132202	1,216	5,93E-04	0,122	3	120633181	C	G	55254	TMEM39A	transmembrane protein 39A
237	rs4314124	0,8663	6,53E-04	0,278	3	127270322	A	G	54946	SLC41A3	solute carrier family 41, member 3
238	rs6796610	0,8683	7,97E-04	0,278	3	127280603	A	G	54946	SLC41A3	solute carrier family 41, member 3
239	rs2365012	0,8541	6,97E-05	0,348	3	127299894	T	A	54946	SLC41A3	solute carrier family 41, member 3
240	rs11715474	1,171	6,46E-05	0,350	3	150284605	T	G	6596	HLTF	helicase-like transcription factor
241	rs7646166	1,149	4,62E-04	0,345	3	150307102	A	G			
242	rs6792168	1,15	6,29E-04	0,307	3	150319263	C	T			
243	rs12695943	1,163	9,81E-04	0,225	3	150988107	A	T	389161	ANKUB1	ankyrin repeat and ubiquitin domain containing 1
244	rs877439	0,8819	8,89E-04	0,497	3	169282596	C	T	27333	GOLIM4	golgi integral membrane protein 4
245	rs1522378	0,8768	5,13E-04	0,496	3	169283231	G	A	27333	GOLIM4	golgi integral membrane protein 4
246	rs10490809	0,842	1,64E-04	0,227	3	172699449	G	A			
247	rs2131017	0,8595	7,95E-04	0,242	3	172700255	C	T			
248	rs1565567	0,8511	4,30E-04	0,224	3	172706855	A	T			
249	rs1402002	1,135	8,86E-04	0,451	3	185125488	A	G	10057	ABCC5	ATP-binding cassette, sub-family C (CFTR/MRP), member 5
250	rs939338	1,144	4,01E-04	0,446	3	185186762	G	A	10057	ABCC5	ATP-binding cassette, sub-family C (CFTR/MRP), member 5
251	rs10937330	1,144	3,64E-04	0,479	3	189221460	G	A			
252	rs7613340	0,8474	7,90E-04	0,179	3	189233423	C	T			
253	rs11929598	0,8355	2,93E-04	0,179	3	189235958	T	C			
254	rs10938681	0,7794	8,69E-05	0,099	4	8066769	A	G	84448	ABLIM2	actin binding LIM protein family, member 2
255	rs7662477	1,138	6,44E-04	0,482	4	23847568	A	G			
256	rs11726723	1,174	8,07E-04	0,190	4	26065365	T	G			
257	rs10034033	1,209	1,21E-04	0,176	4	26071049	A	C			
258	rs17219704	1,168	9,18E-04	0,200	4	61735051	A	G			
259	rs13150883	0,8059	4,64E-04	0,108	4	65828632	C	T			
260	rs17750311	0,8294	3,36E-04	0,157	4	65866784	G	A			

Appendix. (Continued).

261	rs6849315	1,173	9,60E-04	0,191	4	83795901	A	T	79966	SCD5	stearoyl-CoA desaturase 5
262	rs7377204	0,8534	2,29E-04	0,261	4	88727430	C	T			
263	rs7377225	0,8562	3,10E-04	0,262	4	88727547	C	T			
264	rs4693846	0,8494	1,52E-04	0,262	4	88728693	A	C			
265	rs10006978	1,258	3,07E-05	0,136	4	96898971	G	A			
266	rs7657124	1,241	3,38E-05	0,155	4	96914610	C	A			
267	rs11931752	1,268	1,64E-05	0,135	4	96938876	A	T			
268	rs11946552	1,24	4,24E-05	0,151	4	96940053	A	C			
269	rs17024571	1,226	1,09E-04	0,147	4	96942220	G	A			
270	rs1836900	1,173	6,12E-04	0,204	4	96958725	G	A			
271	rs10433975	1,175	6,58E-04	0,195	4	96960072	G	A			
272	rs1836899	1,172	8,21E-04	0,195	4	96966126	A	G			
273	rs10019264	1,173	7,48E-04	0,202	4	96966176	C	G			
274	rs17473405	1,237	1,54E-04	0,126	4	96970645	A	T			
275	rs13107501	1,17	9,34E-04	0,194	4	96971822	C	T			
276	rs17024826	1,215	5,54E-04	0,126	4	96983626	C	T			
277	rs17475948	1,284	3,09E-05	0,109	4	97002780	C	G			
278	rs12501586	1,174	8,91E-05	0,307	4	102861035	T	C			
279	rs12505043	1,177	2,15E-04	0,244	4	102874385	T	C			
280	rs17508289	0,7895	1,96E-04	0,104	4	106334482	A	G	54790	TET2	tet methylcytosine dioxygenase 2
281	rs12644625	1,204	9,67E-04	0,130	4	111935962	T	C			
282	rs13136521	0,8591	9,10E-05	0,392	4	144425014	T	C			
283	rs12501200	0,8522	2,20E-04	0,266	4	155170600	C	A			
284	rs7679856	0,8773	7,03E-04	0,401	4	160315988	G	C			
285	rs7683671	0,8794	8,79E-04	0,401	4	160334667	A	G			
286	rs11939106	0,8803	9,63E-04	0,402	4	160335911	T	C			
287	rs10050099	0,8766	8,45E-04	0,358	4	160343857	T	G			
288	rs1434621	1,151	8,80E-04	0,274	4	162869105	G	C	56884	FSTL5	follistatin-like 5
289	rs7660373	1,374	9,21E-06	0,077	4	162915033	T	C	56884	FSTL5	follistatin-like 5
290	rs13117869	1,193	3,19E-05	0,269	4	189923244	G	C			
291	rs4863069	1,202	1,64E-05	0,263	4	189928060	A	C			
292	rs6553232	1,188	2,00E-04	0,206	4	189947109	G	A			
293	rs11942138	1,175	2,58E-04	0,238	4	189969188	G	C			

Appendix. (Continued).

294	rs1017924	1,164	9,47E-04	0,220	5	2029187	A	G			
295	rs10491223	0,8729	4,47E-04	0,395	5	8843528	C	G			
296	rs10491222	0,8724	4,18E-04	0,395	5	8870497	A	G			
297	rs396	0,8796	8,05E-04	0,428	5	9668339	C	G			
298	rs2530913	0,7781	1,32E-04	0,094	5	11638455	T	C	1501	CTNND2	catenin (cadherin-associated protein), delta 2
299	rs4866046	0,8759	8,30E-04	0,357	5	20270802	A	G			
300	rs4866047	0,8746	7,19E-04	0,354	5	20270828	C	A			
301	rs10037115	0,8766	8,77E-04	0,355	5	20272670	G	A			
302	rs8180522	0,8719	5,26E-04	0,355	5	20274979	C	G			
303	rs2974602	0,8805	8,66E-04	0,431	5	20286581	C	T			
304	rs13164886	0,8797	7,06E-04	0,484	5	20302871	T	G			
305	rs2974591	0,8784	6,79E-04	0,437	5	20325791	C	T			
306	rs4429812	0,8601	3,48E-04	0,277	5	27209030	C	T			
307	rs4518345	0,8576	2,68E-04	0,277	5	27221661	A	G			
308	rs4510545	0,8557	2,17E-04	0,277	5	27225107	C	A			
309	rs6880526	0,8558	2,22E-04	0,280	5	27227465	T	C			
310	rs6890310	0,8586	2,95E-04	0,278	5	27229330	A	G			
311	rs2199214	0,8431	8,33E-04	0,166	5	27338180	C	T			
312	rs1428256	1,182	4,18E-04	0,198	5	38309217	T	G	133584	EGFLAM	EGF-like, fibronectin type III and laminin G domains
313	rs1834967	1,228	2,95E-04	0,123	5	38401890	A	G	133584	EGFLAM	EGF-like, fibronectin type III and laminin G domains
314	rs4336383	1,149	5,91E-04	0,323	5	38831091	A	T			
315	rs6886001	0,879	6,63E-04	0,483	5	52222194	C	T	3672	ITGA1	integrin, alpha 1
316	rs6866823	0,8769	5,37E-04	0,484	5	52222328	A	G	3672	ITGA1	integrin, alpha 1
317	rs6871286	0,8781	5,92E-04	0,479	5	52222513	T	C	3672	ITGA1	integrin, alpha 1
318	rs1979398	0,8801	7,33E-04	0,473	5	52230084	A	G	3672	ITGA1	integrin, alpha 1
319	rs16886034	0,7589	3,06E-04	0,067	5	56019613	C	T			
320	rs16886364	0,7709	5,91E-04	0,068	5	56158101	G	A	4214	MAP3K1	mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase
321	rs16886448	0,7709	5,91E-04	0,068	5	56206570	G	C	4214	MAP3K1	mitogen-activated protein kinase kinase kinase 1, E3 ubiquitin protein ligase
322	rs16886496	0,7772	1,20E-04	0,093	5	56253286	C	T			
323	rs7726354	0,7451	3,94E-04	0,056	5	56292240	T	C			
324	rs7725377	0,8078	6,65E-04	0,103	5	56292353	A	G			
325	rs786699	1,315	8,76E-04	0,056	5	64711237	A	C	11174	ADAMTS6	ADAM metallopeptidase with thrombospondin type 1 motif, 6

Appendix. (Continued).

326	rs12514992	1,154	6,33E-04	0,282	5	75554502	G	T	22987	SV2C	synaptic vesicle glycoprotein 2C
327	rs12516836	1,15	8,41E-04	0,278	5	75554524	A	G	22987	SV2C	synaptic vesicle glycoprotein 2C
328	rs4704438	0,861	1,83E-04	0,339	5	76980795	G	A			
329	rs1422406	0,8771	5,85E-04	0,433	5	76981162	C	A			
330	rs9293433	1,134	9,84E-04	0,468	5	84630874	C	G			
331	rs3846620	1,229	3,40E-04	0,120	5	103014552	C	G			
332	rs6892259	1,224	5,65E-04	0,121	5	110113641	C	A	91137	SLC25A46	solute carrier family 25, member 46
333	rs456236	0,8798	8,55E-04	0,413	5	110115057	G	T	91137	SLC25A46	solute carrier family 25, member 46
334	rs7723767	1,166	9,17E-04	0,216	5	110182685	C	T			
335	rs12517265	1,17	6,16E-04	0,224	5	110189680	T	C			
336	rs12655815	1,19	1,58E-04	0,224	5	110196417	A	G			
337	rs1350294	1,174	4,86E-04	0,222	5	110205180	A	C			
338	rs2416248	1,166	8,16E-04	0,224	5	110206705	G	A			
339	rs11745646	1,144	8,64E-04	0,323	5	110521442	G	A			
340	rs9326826	1,156	5,05E-04	0,295	5	110522145	A	G			
341	rs9327027	1,286	7,69E-04	0,067	5	116418496	A	T			
342	rs9327165	1,135	9,62E-04	0,418	5	120168056	C	T			
343	rs4895286	1,145	4,64E-04	0,408	5	120206274	A	G			
344	rs6878559	1,142	4,69E-04	0,445	5	120236091	G	A			
345	rs13165374	1,144	8,02E-04	0,344	5	125177257	T	G			
346	rs31330	0,8478	3,07E-04	0,225	5	132889400	C	G	23105	FSTL4	follistatin-like 4
347	rs2160505	0,872	3,34E-04	0,431	5	157292346	A	C			
348	rs7709212	1,156	3,08E-04	0,335	5	158696755	C	T			
349	rs6861600	1,158	3,38E-04	0,315	5	158752193	G	C			
350	rs6887695	1,158	3,08E-04	0,321	5	158755223	C	G			
351	rs454036	1,142	9,82E-04	0,326	5	172486267	C	G	153222	CREBRF	CREB3 regulatory factor
352	rs255318	1,345	5,60E-05	0,068	5	172548635	A	G			
353	rs10456781	0,8734	4,91E-04	0,396	6	16125021	G	A			
354	rs1150644	1,168	2,13E-04	0,278	6	16922283	A	C			
355	rs686269	1,155	2,84E-04	0,356	6	16922625	G	A			
356	rs9396712	1,157	5,37E-04	0,276	6	16926604	T	C			
357	rs1240833	1,145	6,80E-04	0,349	6	16939387	A	G			
358	rs9348440	1,223	3,45E-04	0,131	6	20749315	T	C	54901	CDKAL1	CDK5 regulatory subunit associated protein 1-like 1

Appendix. (Continued).

359	rs7767391	1,178	5,69E-04	0,198	6	20833219	C	T	54901	CDKAL1	CDK5 regulatory subunit associated protein 1-like 1
360	rs16894194	1,17	2,39E-04	0,276	6	28756062	A	T			
361	rs2516478	1,196	3,64E-04	0,168	6	31606716	A	G			
362	rs2523503	1,191	7,91E-04	0,152	6	31621538	A	C	534	ATP6V1G2	ATPase, H+ transporting, lysosomal 13kDa, V1 subunit G2
363	rs3117108	0,8686	5,92E-04	0,305	6	32450800	C	G			
364	rs9268835	1,166	2,66E-04	0,303	6	32536093	A	G			
365	rs9269202	0,8629	3,91E-04	0,289	6	32557501	T	C			
366	rs12202197	0,8605	1,32E-04	0,363	6	39200945	C	T			
367	rs12195232	0,866	2,60E-04	0,360	6	39201111	T	C			
368	rs1361864	1,14	8,60E-04	0,371	6	48627226	G	A			
369	rs6910476	1,184	9,97E-04	0,164	6	48633649	G	A			
370	rs6458620	1,155	8,94E-04	0,261	6	48678807	C	G			
371	rs3010529	1,157	7,94E-04	0,262	6	48701049	C	T			
372	rs761167	1,136	7,52E-04	0,471	6	52219767	T	C			
373	rs1266825	1,136	7,75E-04	0,466	6	52221625	T	C			
374	rs3765446	1,137	7,63E-04	0,428	6	52249629	T	A	4172	MCM3	minichromosome maintenance complex component 3
375	rs12204627	0,8179	2,42E-05	0,204	6	71778351	A	T			
376	rs9342803	0,841	6,73E-04	0,172	6	71781245	C	T			
377	rs1996679	0,836	6,36E-05	0,241	6	71783440	G	C			
378	rs9446323	0,8393	1,81E-04	0,216	6	71789723	G	A			
379	rs7739908	0,7784	9,65E-04	0,067	6	72090767	G	T			
380	rs16885102	0,8226	2,30E-04	0,157	6	75341319	T	C			
381	rs9343877	1,277	5,26E-04	0,076	6	79922723	T	A			
382	rs6454097	1,277	5,05E-04	0,077	6	79934936	T	G			
383	rs1343232	1,138	7,49E-04	0,415	6	82187051	G	A			
384	rs17438648	1,138	7,37E-04	0,418	6	82216223	A	G			
385	rs11966310	1,138	7,49E-04	0,418	6	82217732	G	A			
386	rs11964002	1,136	9,02E-04	0,418	6	82217840	A	T			
387	rs4642522	0,8758	5,66E-04	0,407	6	82249727	T	G			
388	rs1341230	0,882	9,00E-04	0,482	6	82436294	C	T			
389	rs9373855	1,141	7,74E-04	0,363	6	106922248	T	G			
390	rs488282	1,14	8,44E-04	0,363	6	106923806	A	G			
391	rs10457307	0,7555	1,56E-04	0,071	6	116927364	A	G	100128327	BET3L	BET3 like (S. cerevisiae)

Appendix. (Continued).

392	rs1338980	1,17	4,64E-04	0,232	6	118325563	A	G			
393	rs1998458	1,162	7,43E-04	0,239	6	118367258	G	T	222553	SLC35F1	solute carrier family 35, member F1
394	rs2789010	1,164	6,40E-04	0,239	6	118368173	T	G	222553	SLC35F1	solute carrier family 35, member F1
395	rs1416419	1,161	7,72E-04	0,239	6	118369087	T	A	222553	SLC35F1	solute carrier family 35, member F1
396	rs1572045	0,8553	7,19E-04	0,216	6	137972810	C	T			
397	rs9321916	0,8315	7,90E-04	0,139	6	143878225	A	T			
398	rs6570562	0,8389	4,51E-04	0,181	6	143879508	A	G			
399	rs6908896	1,22	2,20E-04	0,151	6	156869074	C	A			
400	rs317801	0,8598	8,16E-04	0,240	6	159010196	T	C	94120	SYTL3	synaptotagmin-like 3
401	rs6902491	1,207	4,71E-04	0,142	6	166381836	G	T			
402	rs4722483	0,8304	5,78E-04	0,143	7	3159273	C	G			
403	rs17789894	0,8228	4,66E-04	0,131	7	6709622	T	G	7559	ZNF12	zinc finger protein 12
404	rs7456390	1,186	2,31E-04	0,217	7	14784079	G	C	1607	DGKB	diacylglycerol kinase, beta 90kDa
405	rs7782529	0,8132	3,11E-04	0,132	7	27264316	A	G			
406	rs11769156	1,244	8,68E-04	0,091	7	28545359	C	T	9586	CREB5	cAMP responsive element binding protein 5
407	rs10228072	1,148	2,98E-04	0,428	7	29542212	C	T			
408	rs4722930	1,146	3,77E-04	0,427	7	29552436	A	G			
409	rs12700969	1,137	7,82E-04	0,425	7	29552772	A	C			
410	rs4722932	1,166	1,00E-04	0,352	7	29578479	G	A			
411	rs17159921	1,36	3,09E-04	0,051	7	31123725	T	C			
412	rs964126	1,149	8,69E-04	0,284	7	47620828	A	G			
413	rs2113643	1,14	5,56E-04	0,482	7	52104228	G	T			
414	rs7787769	0,8011	1,25E-04	0,126	7	52963068	G	C			
415	rs11763192	0,8105	6,06E-04	0,110	7	53002660	T	C			
416	rs17735671	0,7745	1,03E-05	0,126	7	53034984	C	T			
417	rs1404198	0,8066	1,46E-04	0,130	7	54052372	A	G			
418	rs10225389	0,8372	4,45E-04	0,171	7	62973655	C	A			
419	rs17148752	0,7622	2,83E-04	0,078	7	75092000	C	T	3092	HIP1	huntingtin interacting protein 1
420	rs4416776	0,8519	2,66E-05	0,439	7	82814002	G	A			
421	rs2618989	1,147	8,54E-04	0,299	7	95193842	C	A			
422	rs450854	0,8777	8,10E-04	0,392	7	101485453	T	C	1523	CUX1	cut-like homeobox 1
423	rs12538286	0,8597	3,15E-04	0,285	7	101536040	A	G	1523	CUX1	cut-like homeobox 1
424	rs10270614	0,876	4,83E-04	0,459	7	101624464	A	G	1523	CUX1	cut-like homeobox 1

Appendix. (Continued).

425	rs7341475	1,179	9,79E-04	0,169	7	103192051	A	G	5649	RELN	reelin
426	rs4730052	1,166	8,69E-04	0,213	7	104269557	C	T	375612	LHFPL3	lipoma HMGIC fusion partner-like 3
427	rs4730053	1,171	6,34E-04	0,213	7	104269619	A	G	375612	LHFPL3	lipoma HMGIC fusion partner-like 3
428	rs10245031	0,8761	8,89E-04	0,346	7	117285697	C	T	83992	CTTNBP2	cortactin binding protein 2
429	rs7801931	0,8633	2,49E-04	0,329	7	117294094	G	C	83992	CTTNBP2	cortactin binding protein 2
430	rs10270960	0,8641	2,77E-04	0,328	7	117312875	C	G			
431	rs1357674	1,173	8,70E-04	0,191	7	119236456	G	A			
432	rs11764046	1,171	9,94E-04	0,188	7	119324606	G	A			
433	rs12707008	1,136	8,86E-04	0,404	7	131282522	T	C			
434	rs6467643	0,8632	5,23E-04	0,274	7	135614381	T	G			
435	rs2701016	0,8703	9,73E-04	0,279	7	135622254	A	C			
436	rs2555048	1,141	8,64E-04	0,348	7	135622266	C	T			
437	rs361445	1,208	7,34E-04	0,127	7	141838625	T	C	28601	TRBV6-6	T cell receptor beta variable 6-6
438	rs855733	0,8632	2,38E-04	0,333	7	148993580	A	G			
439	rs1731847	0,8764	5,00E-04	0,467	7	155348283	C	T			
440	rs1968853	1,135	8,65E-04	0,457	8	9083722	C	A			
441	rs2929301	1,146	5,16E-04	0,363	8	9085514	G	A			
442	rs2705042	1,37	2,66E-04	0,053	8	17366632	T	C			
443	rs11989798	0,7405	3,97E-04	0,055	8	22326597	A	C	23516	SLC39A14	solute carrier family 39 (zinc transporter), member 14
444	rs2976405	0,8705	4,33E-04	0,358	8	24911831	A	G			
445	rs12681837	0,8643	9,95E-04	0,249	8	27191888	T	G			
446	rs6997728	0,8641	9,68E-04	0,250	8	27196000	T	A			
447	rs4733453	0,8793	7,26E-04	0,443	8	33770287	G	A			
448	rs4733456	0,8799	7,79E-04	0,443	8	33775901	A	G			
449	rs4389890	0,8804	8,23E-04	0,442	8	33777560	A	G			
450	rs7825337	0,8801	8,20E-04	0,431	8	41626394	C	T			
451	rs12549902	0,8771	6,57E-04	0,405	8	41628416	G	A			
452	rs4317621	0,8807	9,46E-04	0,410	8	41635738	A	G	286	ANK1	ankyrin 1, erythrocytic
453	rs10504242	0,7733	2,66E-04	0,079	8	59148749	G	A	90362	FAM110B	family with sequence similarity 110, member B
454	rs12678728	0,8559	6,74E-04	0,218	8	62909278	G	A			
455	rs4562310	0,7894	3,93E-05	0,127	8	63207496	G	C			
456	rs4268118	0,8079	2,08E-04	0,125	8	63217632	G	A			
457	rs4256587	0,8034	1,06E-04	0,132	8	63218545	T	C			

Appendix. (Continued).

458	rs7832144	0,8034	1,35E-04	0,126	8	63225135	A	G			
459	rs10504344	0,8093	2,11E-04	0,128	8	63229338	G	T			
460	rs16928545	0,7521	4,81E-06	0,105	8	63256978	G	A			
461	rs7833958	0,8204	1,75E-04	0,152	8	63273320	A	G			
462	rs16928602	0,8151	9,57E-05	0,156	8	63309109	T	C			
463	rs10957216	0,8109	1,14E-04	0,143	8	63319367	T	A			
464	rs13278423	0,8768	5,08E-04	0,488	8	87789535	A	C	54714	CNGB3	cyclic nucleotide gated channel beta 3
465	rs2436860	1,252	5,49E-04	0,092	8	103811225	A	G			
466	rs2514756	1,158	8,04E-04	0,247	8	119151124	A	G	2131	EXT1	exostosin 1
467	rs11777070	1,172	7,54E-04	0,200	8	141019541	T	G	83696	TRAPPC9	trafficking protein particle complex 9
468	rs10960363	1,196	5,55E-04	0,162	9	1190703	C	T			
469	rs1319332	1,37	2,16E-04	0,055	9	20182495	G	A			
470	rs10811330	1,228	1,65E-05	0,200	9	20197095	C	T			
471	rs10964477	1,37	9,75E-05	0,060	9	20206063	C	T			
472	rs10465048	1,244	6,32E-06	0,196	9	20208695	A	G			
473	rs4977395	1,474	7,64E-06	0,053	9	20216358	G	A			
474	rs10964493	1,338	2,87E-04	0,061	9	20229840	C	T			
475	rs10964495	1,37	6,32E-05	0,064	9	20235283	C	T			
476	rs16923521	1,438	1,07E-05	0,058	9	20251635	C	T			
477	rs12553948	1,35	1,14E-04	0,067	9	20253186	G	A			
478	rs7041951	1,456	6,41E-06	0,057	9	20265354	G	C			
479	rs4977251	1,371	6,35E-05	0,063	9	20269793	G	A			
480	rs13300741	0,8262	1,41E-04	0,178	9	20953339	C	T	54914	FOCAD	focadhesin
481	rs10966484	0,8278	1,74E-04	0,169	9	24802191	G	A			
482	rs676484	1,141	7,52E-04	0,367	9	25953989	C	A			
483	rs17559639	0,8709	5,63E-04	0,334	9	26011612	A	C			
484	rs10738743	1,146	4,94E-04	0,371	9	26027974	C	T			
485	rs511545	0,8698	3,28E-04	0,404	9	78501010	C	T	158471	PRUNE2	prune homolog 2 (Drosophila)
486	rs506086	0,8444	1,07E-04	0,257	9	78516428	C	G	158471	PRUNE2	prune homolog 2 (Drosophila)
487	rs491798	0,8682	3,00E-04	0,401	9	78519989	T	A	158471	PRUNE2	prune homolog 2 (Drosophila)
488	rs2209882	1,256	5,06E-04	0,090	9	81127236	A	G			
489	rs2013557	1,206	9,56E-04	0,132	9	103615815	T	A			
490	rs6479067	0,8569	3,92E-04	0,257	9	103635386	A	T			

Appendix. (Continued).

491	rs2786716	0,8623	6,66E-04	0,257	9	103636342	C	T			
492	rs1415647	0,8643	8,06E-04	0,256	9	103636455	A	T			
493	rs10739816	0,8619	6,53E-04	0,251	9	103656291	C	T			
494	rs10739592	1,34	2,08E-14	0,485	9	123011433	G	A			
495	rs10760182	1,137	6,75E-04	0,481	9	123452782	A	G	153090	DAB2IP	DAB2 interacting protein
496	rs7468351	1,14	8,33E-04	0,369	9	138114710	T	C	138151	NACC2	NACC family member 2, BEN and BTB (POZ) domain containing
497	rs3802577	0,8656	5,18E-04	0,298	10	13361864	C	T	5264	PHYH	phytanoyl-CoA 2-hydroxylase
498	rs956007	1,176	1,35E-04	0,276	10	23761418	G	T			
499	rs7920535	1,147	8,72E-04	0,309	10	23774744	G	A			
500	rs12246098	1,155	4,55E-04	0,312	10	23786957	G	A			
501	rs11013514	1,174	1,12E-04	0,291	10	23799607	A	G			
502	rs7085999	1,141	9,35E-04	0,347	10	23800758	G	C			
503	rs7900252	1,163	1,62E-04	0,340	10	23802398	G	A			
504	rs6482285	1,143	7,67E-04	0,348	10	23808719	T	C			
505	rs4333914	1,156	3,31E-04	0,328	10	23810664	A	G			
506	rs6482289	1,143	7,67E-04	0,347	10	23816469	T	C			
507	rs12244668	1,145	7,84E-04	0,337	10	23841366	G	A			
508	rs7913401	1,154	3,30E-04	0,341	10	23844221	A	C			
509	rs1856113	1,159	2,23E-04	0,341	10	23844775	T	C			
510	rs983990	1,157	2,63E-04	0,342	10	23846388	G	A			
511	rs11013555	1,149	9,25E-04	0,284	10	23858933	A	G			
512	rs10763790	0,8642	9,06E-04	0,244	10	30831361	C	G			
513	rs11593943	0,8722	4,44E-04	0,377	10	33585087	T	C	8829	NRP1	neuropilin 1
514	rs10430541	0,8777	7,30E-04	0,395	10	56494253	A	G			
515	rs2658641	0,8287	1,29E-04	0,186	10	59394437	G	A			
516	rs2658630	0,8453	3,09E-04	0,208	10	59409250	A	G			
517	rs1930450	0,8418	1,74E-04	0,221	10	59410701	T	G			
518	rs2939583	0,8453	2,19E-04	0,224	10	59412336	T	C			
519	rs2393400	0,846	2,32E-04	0,225	10	59414510	T	G			
520	rs1930455	0,8507	3,87E-04	0,223	10	59414530	A	G			
521	rs1930456	0,8447	2,03E-04	0,224	10	59414551	A	G			
522	rs10740725	0,8784	9,56E-04	0,371	10	59460061	G	A			

Appendix. (Continued).

523	rs11006021	0,8718	4,72E-04	0,377	10	59460712	C	T			
524	rs1759365	0,8511	3,68E-04	0,226	10	59490502	A	G			
525	rs3915932	0,8544	4,70E-05	0,409	10	80611942	C	G	57178	ZMIZ1	zinc finger, MIZ-type containing 1
526	rs810517	0,8533	3,08E-05	0,452	10	80612626	T	C	57178	ZMIZ1	zinc finger, MIZ-type containing 1
527	rs12571751	0,8533	3,05E-05	0,452	10	80612637	G	A	57178	ZMIZ1	zinc finger, MIZ-type containing 1
528	rs703982	0,8567	6,72E-05	0,395	10	80612727	G	A	57178	ZMIZ1	zinc finger, MIZ-type containing 1
529	rs11553840	1,323	7,27E-04	0,054	10	82268160	C	T	81619	TSPAN14	tetraspanin 14
530	rs17415112	0,837	7,52E-04	0,156	10	99194781	A	G	51013	EXOSC1	exosome component 1
531	rs11191841	0,8746	3,97E-04	0,500	10	105629601	C	T			
532	rs7100920	0,8741	3,81E-04	0,488	10	105630968	T	C			
533	rs10883942	0,8699	2,30E-04	0,486	10	105641376	C	T	79991	OBFC1	oligonucleotide/oligosaccharide-binding fold containing 1
534	rs12765878	0,8699	2,30E-04	0,486	10	105659612	C	T	79991	OBFC1	oligonucleotide/oligosaccharide-binding fold containing 1
535	rs1421503	1,164	7,37E-04	0,227	10	107485090	G	A			
536	rs2111995	1,16	9,82E-04	0,226	10	107497352	G	A			
537	rs10787019	1,146	9,79E-04	0,306	10	109050808	T	G			
538	rs2804611	1,245	4,64E-04	0,107	10	113837462	C	T			
539	rs2804614	1,235	7,72E-04	0,107	10	113841831	C	T			
540	rs4074720	1,156	1,30E-04	0,476	10	114738487	T	C	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
541	rs7901695	1,28	8,18E-10	0,328	10	114744078	C	T	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
542	rs4506565	1,278	9,48E-10	0,331	10	114746031	T	A	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
543	rs4132670	1,282	6,53E-10	0,331	10	114757761	A	G	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
544	rs6585201	1,144	3,96E-04	0,459	10	114758773	A	G	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
545	rs10787472	1,155	1,38E-04	0,474	10	114771287	C	A	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
546	rs12243326	1,292	6,12E-10	0,295	10	114778805	C	T	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
547	rs7077039	1,157	1,35E-04	0,467	10	114779067	C	T	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
548	rs11196205	1,17	3,49E-05	0,473	10	114797037	C	G	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
549	rs10885409	1,172	2,71E-05	0,472	10	114798062	C	T	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
550	rs12255372	1,292	4,37E-10	0,302	10	114798892	T	G	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
551	rs11196208	1,173	2,40E-05	0,472	10	114801306	C	T	6934	TCF7L2	transcription factor 7-like 2 (T-cell specific, HMG-box)
552	rs10510004	0,8647	1,97E-04	0,373	10	116214569	A	G	3983	ABLIM1	actin binding LIM protein 1
553	rs2483593	0,7592	4,89E-04	0,062	10	116359696	G	A	3983	ABLIM1	actin binding LIM protein 1
554	rs1091179	0,7741	1,03E-04	0,092	10	116556258	A	G			
555	rs2420928	0,8735	4,36E-04	0,408	10	123143462	G	A			

Appendix. (Continued).

556	rs1322328	0,8817	9,04E-04	0,466	10	123911094	C	G	10579	TACC2	transforming, acidic coiled-coil containing protein 2
557	rs12412485	1,163	6,93E-04	0,234	10	131731590	T	G			
558	rs7075825	0,7641	1,83E-04	0,075	10	133720979	T	C			
559	rs11827296	1,187	3,63E-04	0,186	11	3334236	C	T			
560	rs7104128	1,232	9,03E-04	0,106	11	4697321	T	C			
561	rs935951	0,8276	2,12E-04	0,166	11	5918145	T	G			
562	rs2723663	0,8763	4,90E-04	0,466	11	6440086	C	A	10612	TRIM3	tripartite motif containing 3
563	rs2303493	0,8762	5,63E-04	0,474	11	6455791	A	G	23647	ARFIP2	ADP-ribosylation factor interacting protein 2
564	rs4277103	0,7731	7,73E-05	0,097	11	8345806	C	T			
565	rs1881820	0,8518	1,09E-04	0,292	11	13757134	G	C			
566	rs2351044	1,169	6,83E-05	0,363	11	15535033	A	G			
567	rs7117077	0,8411	4,65E-04	0,182	11	19510993	C	T	89797	NAV2	neuron navigator 2
568	rs329526	1,137	7,56E-04	0,438	11	29458729	T	G			
569	rs2926461	0,8703	7,80E-04	0,303	11	34208169	C	T	25841	ABTB2	ankyrin repeat and BTB (POZ) domain containing 2
570	rs2957523	0,8663	5,25E-04	0,303	11	34208431	G	A	25841	ABTB2	ankyrin repeat and BTB (POZ) domain containing 2
571	rs2926463	0,8694	7,23E-04	0,302	11	34208964	G	T	25841	ABTB2	ankyrin repeat and BTB (POZ) domain containing 2
572	rs2955949	0,863	3,64E-04	0,304	11	34210651	A	T	25841	ABTB2	ankyrin repeat and BTB (POZ) domain containing 2
573	rs7115702	1,175	9,69E-05	0,291	11	61787955	T	A			
574	rs11603383	1,174	9,99E-05	0,291	11	61794159	A	G	4250	SCGB2A2	secretoglobin, family 2A, member 2
575	rs17709552	1,245	1,59E-04	0,117	11	61797095	G	A	4250	SCGB2A2	secretoglobin, family 2A, member 2
576	rs11228506	0,8812	8,60E-04	0,458	11	68645758	A	G			
577	rs644961	0,8824	9,73E-04	0,473	11	78370468	T	C	26011	ODZ4	odz, odd Oz/ten-m homolog 4 (Drosophila)
578	rs10793350	0,8643	1,17E-04	0,483	11	78372163	T	C	26011	ODZ4	odz, odd Oz/ten-m homolog 4 (Drosophila)
579	rs10751301	0,8623	9,09E-05	0,485	11	78372286	G	C	26011	ODZ4	odz, odd Oz/ten-m homolog 4 (Drosophila)
580	rs11237675	0,8708	2,56E-04	0,490	11	78375191	C	T	26011	ODZ4	odz, odd Oz/ten-m homolog 4 (Drosophila)
581	rs17310875	1,207	7,14E-04	0,130	11	79832113	C	G			
582	rs11232429	1,347	3,79E-04	0,052	11	80397567	T	A			
583	rs11235302	1,21	5,02E-04	0,135	11	87132574	A	T			
584	rs17150852	1,263	3,74E-04	0,089	11	87202808	A	G			
585	rs17833579	1,258	5,03E-04	0,087	11	87203798	C	T			
586	rs17150882	1,267	2,10E-04	0,095	11	87219070	C	T			
587	rs9666479	1,202	3,35E-04	0,160	11	87250138	G	A			
588	rs7121252	1,206	2,52E-04	0,163	11	87256116	C	T			

Appendix. (Continued).

589	rs1939168	1,17	7,65E-04	0,212	11	87288340	A	G			
590	rs7101865	1,174	3,13E-04	0,231	11	87577209	A	G			
591	rs11018816	1,225	8,87E-05	0,160	11	87579357	C	T			
592	rs7937882	1,225	8,26E-05	0,157	11	87579997	G	A			
593	rs4122057	0,8374	6,05E-04	0,165	11	87619967	A	G			
594	rs11020093	0,8564	4,36E-04	0,247	11	92267291	T	C	120114	FAT3	FAT tumor suppressor homolog 3 (Drosophila)
595	rs17134278	1,246	6,85E-04	0,094	11	99106275	G	C	53942	CNTN5	contactin 5
596	rs4559717	1,253	7,39E-04	0,087	11	112656309	A	G			
597	rs1600223	0,8376	4,84E-04	0,165	11	126798259	T	C			
598	rs3935794	0,7246	4,41E-05	0,063	11	127895887	G	A	2113	ETS1	v-ets erythroblastosis virus E26 oncogene homolog 1 (avian)
599	rs3935795	0,7216	3,45E-05	0,064	11	127896001	C	T	2113	ETS1	v-ets erythroblastosis virus E26 oncogene homolog 1 (avian)
600	rs3935796	0,7476	2,56E-04	0,061	11	127896137	A	T	2113	ETS1	v-ets erythroblastosis virus E26 oncogene homolog 1 (avian)
601	rs4937342	0,7488	2,31E-04	0,063	11	127903519	G	T	2113	ETS1	v-ets erythroblastosis virus E26 oncogene homolog 1 (avian)
602	rs433443	0,8724	6,98E-04	0,334	11	130876412	A	G	50863	NTM	neurotrimin
603	rs1870199	0,8733	3,73E-04	0,444	12	656499	A	G			
604	rs10849464	0,8563	6,59E-05	0,391	12	659413	A	C			
605	rs2887474	0,8693	2,37E-04	0,471	12	666392	C	T			
606	rs10848958	0,8312	2,51E-04	0,174	12	3901365	T	C			
607	rs10849040	1,147	3,01E-04	0,498	12	4312167	C	T	57103	C12orf5	chromosome 12 open reading frame 5
608	rs17700406	0,864	1,81E-04	0,378	12	4332859	C	T	57103	C12orf5	chromosome 12 open reading frame 5
609	rs10849045	0,862	1,57E-04	0,368	12	4337744	A	G	57103	C12orf5	chromosome 12 open reading frame 5
610	rs7135390	0,8718	3,18E-04	0,444	12	21489968	T	C	79912	PYROXD1	pyridine nucleotide-disulphide oxidoreductase domain 1
611	rs11610942	0,8747	4,42E-04	0,443	12	21492898	G	A	79912	PYROXD1	pyridine nucleotide-disulphide oxidoreductase domain 1
612	rs10841843	1,176	2,20E-04	0,249	12	21583158	T	C	2998	GYS2	glycogen synthase 2 (liver)
613	rs10492118	1,165	9,48E-04	0,215	12	21583225	T	C	2998	GYS2	glycogen synthase 2 (liver)
614	rs6487236	1,17	5,34E-04	0,227	12	21591183	G	A	2998	GYS2	glycogen synthase 2 (liver)
615	rs10841848	1,163	8,61E-04	0,226	12	21600821	A	G	2998	GYS2	glycogen synthase 2 (liver)
616	rs11046116	1,164	8,22E-04	0,226	12	21600886	G	C	2998	GYS2	glycogen synthase 2 (liver)
617	rs10770836	1,16	6,93E-04	0,248	12	21608008	A	G	2998	GYS2	glycogen synthase 2 (liver)
618	rs10841850	1,161	6,69E-04	0,248	12	21608123	G	A	2998	GYS2	glycogen synthase 2 (liver)
619	rs11046122	1,159	7,69E-04	0,250	12	21608288	T	C	2998	GYS2	glycogen synthase 2 (liver)
620	rs10783760	0,8774	9,15E-04	0,358	12	54262230	A	G			
621	rs4759173	0,877	8,81E-04	0,357	12	54287453	A	G			

Appendix. (Continued).

622	rs10747758	0,8779	9,48E-04	0,369	12	54287594	T	C			
623	rs4759186	0,8419	5,66E-04	0,176	12	54350346	A	G			
624	rs11614506	0,8544	7,92E-04	0,211	12	56101942	C	T			
625	rs3916529	0,8284	3,60E-04	0,153	12	62721863	G	A	57522	SRGAP1	SLIT-ROBO Rho GTPase activating protein 1
626	rs7132617	1,136	9,37E-04	0,392	12	63482244	A	G			
627	rs10878211	1,143	5,35E-04	0,396	12	63486189	C	T			
628	rs3851608	1,137	9,35E-04	0,381	12	63495765	G	A			
629	rs998314	1,143	5,49E-04	0,392	12	63506634	G	A	23329	TBC1D30	TBC1 domain family, member 30
630	rs1275556	0,8717	6,98E-04	0,324	12	74496341	A	G			
631	rs998137	0,8749	6,75E-04	0,401	12	77486027	C	G			
632	rs12582634	1,292	9,45E-04	0,066	12	80385922	T	C	8499	PPFIA2	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 2
633	rs12815988	0,7707	1,70E-04	0,083	12	82183441	T	C			
634	rs11115663	0,7634	9,08E-05	0,084	12	82184765	G	A			
635	rs12578418	0,7861	4,98E-04	0,083	12	95081078	A	G			
636	rs7300815	1,301	2,15E-04	0,076	12	100486144	C	A			
637	rs12580632	1,205	9,75E-04	0,131	12	100486792	C	T			
638	rs855287	0,8329	6,57E-04	0,146	12	101470239	A	T			
639	rs753479	0,8316	3,25E-04	0,163	12	101482692	G	A			
640	rs10860877	0,8429	6,74E-04	0,173	12	101483695	A	G			
641	rs4964671	1,145	6,62E-04	0,349	12	107227824	G	C	1240	CMKLR1	chemokine-like receptor 1
642	rs10400410	1,228	9,70E-04	0,100	12	109677882	A	G			
643	rs11067587	0,863	7,45E-04	0,259	12	114338107	C	T			
644	rs12313339	0,7823	9,90E-04	0,070	12	119870876	A	G			
645	rs11057765	0,8408	8,20E-04	0,161	12	123759382	C	T			
646	rs10773182	0,8758	6,21E-04	0,393	12	124686312	G	T	114795	TMEM132B	transmembrane protein 132B
647	rs2058012	0,879	7,02E-04	0,462	12	124693362	G	A	114795	TMEM132B	transmembrane protein 132B
648	rs979589	0,8686	4,55E-04	0,337	12	124693655	T	C	114795	TMEM132B	transmembrane protein 132B
649	rs3803152	0,8741	4,00E-04	0,454	12	124701148	G	A	114795	TMEM132B	transmembrane protein 132B
650	rs3825381	0,861	6,46E-04	0,253	12	124702816	T	C	114795	TMEM132B	transmembrane protein 132B
651	rs10846941	1,142	4,56E-04	0,483	12	124720392	T	C			
652	rs10773187	1,135	7,97E-04	0,484	12	124724088	G	A			
653	rs10846955	1,134	8,82E-04	0,487	12	124762711	T	C			

Appendix. (Continued).

654	rs10846980	1,143	4,13E-04	0,486	12	124857508	T	G			
655	rs7313371	0,8751	9,86E-04	0,319	12	124861036	A	G			
656	rs7954415	0,8642	2,46E-04	0,343	12	124862134	T	C			
657	rs917334	0,8675	2,41E-04	0,395	12	124864111	G	A			
658	rs6489019	0,8632	1,47E-04	0,393	12	124866835	A	G			
659	rs6489020	0,8582	5,91E-05	0,445	12	124866956	C	T			
660	rs6489021	0,8455	1,63E-05	0,401	12	124872053	T	G			
661	rs7978045	1,193	5,76E-04	0,159	12	124873743	T	C			
662	rs11058369	1,188	7,00E-04	0,162	12	124891017	T	A			
663	rs11610391	0,8484	1,61E-05	0,441	12	124894658	T	G			
664	rs11058371	1,197	3,66E-05	0,248	12	124894762	A	G			
665	rs917337	0,8585	8,28E-05	0,393	12	124903032	T	C			
666	rs11058574	0,866	1,44E-04	0,477	12	125256569	T	C			
667	rs10847114	0,8648	1,24E-04	0,486	12	125256831	G	A			
668	rs10773245	0,8667	1,55E-04	0,486	12	125257058	A	C			
669	rs10773247	0,8625	9,24E-05	0,484	12	125260779	C	T			
670	rs10744243	0,8624	9,12E-05	0,484	12	125260860	A	G			
671	rs2346669	0,8677	1,78E-04	0,483	12	125264114	G	A			
672	rs10773257	0,8732	5,11E-04	0,378	12	125292483	G	A			
673	rs2010484	1,168	1,36E-04	0,309	12	126298378	C	G			
674	rs10847919	1,192	5,42E-04	0,164	12	128706939	T	C	121256	TMEM132D	transmembrane protein 132D
675	rs452876	0,881	9,55E-04	0,416	12	129326198	G	T			
676	rs17357143	0,7415	1,37E-04	0,063	13	22504391	C	T			
677	rs549305	1,179	8,55E-04	0,175	13	26037876	T	G	10810	WASF3	WAS protein family, member 3
678	rs1888810	0,8314	9,95E-04	0,142	13	30442238	T	G	122046	TEX26	testis expressed 26
679	rs2026960	0,8286	8,28E-04	0,139	13	30458544	C	T			
680	rs4258502	1,14	5,87E-04	0,456	13	48461701	A	G	22862	FNDC3A	fibronectin type III domain containing 3A
681	rs9568143	1,148	2,88E-04	0,456	13	48468631	A	T	22862	FNDC3A	fibronectin type III domain containing 3A
682	rs4942796	0,8653	4,10E-04	0,311	13	48484019	T	C	22862	FNDC3A	fibronectin type III domain containing 3A
683	rs9316428	0,8733	9,53E-04	0,311	13	48526552	A	G	22862	FNDC3A	fibronectin type III domain containing 3A
684	rs1407827	0,8688	6,17E-04	0,308	13	48608987	C	T	22862	FNDC3A	fibronectin type III domain containing 3A
685	rs1983805	0,8704	7,21E-04	0,310	13	48609971	C	T	22862	FNDC3A	fibronectin type III domain containing 3A
686	rs9591246	0,8627	3,72E-04	0,306	13	48704899	T	C			

Appendix. (Continued).

687	rs1013347	0,8592	2,95E-04	0,284	13	48708882	T	G			
688	rs9571208	1,22	2,03E-04	0,149	13	63876687	C	T			
689	rs7991210	1,188	9,62E-06	0,395	13	99549906	G	A	5095	PCCA	propionyl CoA carboxylase, alpha polypeptide
690	rs916048	1,138	9,35E-04	0,379	14	21860760	A	C			
691	rs3751488	1,16	9,91E-04	0,224	14	22373934	A	G	122704	MRPL52	mitochondrial ribosomal protein L52
692	rs424964	1,147	3,33E-04	0,425	14	30055554	A	G			
693	rs10135562	1,186	5,23E-04	0,182	14	32198399	T	C	9472	AKAP6	A kinase (PRKA) anchor protein 6
694	rs6571647	0,7866	2,51E-04	0,093	14	33836835	G	A			
695	rs1998193	1,14	5,78E-04	0,456	14	38760507	T	G			
696	rs28502509	1,142	4,79E-04	0,457	14	38761768	C	T			
697	rs1387754	1,143	4,85E-04	0,421	14	62341315	C	T	27133	KCNH5	potassium voltage-gated channel, subfamily H (eag-related), member 5
698	rs4899384	0,88	7,61E-04	0,455	14	70695709	T	A			
699	rs10483837	1,205	1,07E-04	0,193	14	71519244	G	A	9628	RGS6	regulator of G-protein signaling 6
700	rs7156200	1,176	2,48E-04	0,241	14	71527435	C	A	9628	RGS6	regulator of G-protein signaling 6
701	rs12884777	1,177	2,35E-04	0,240	14	71530913	T	C	9628	RGS6	regulator of G-protein signaling 6
702	rs12885258	1,197	1,58E-04	0,197	14	71531051	A	G	9628	RGS6	regulator of G-protein signaling 6
703	rs2283422	1,184	1,44E-04	0,239	14	71531955	C	T	9628	RGS6	regulator of G-protein signaling 6
704	rs2283381	0,805	5,34E-07	0,255	14	71978830	G	A	9628	RGS6	regulator of G-protein signaling 6
705	rs10483845	0,846	3,15E-05	0,342	14	71984874	G	C	9628	RGS6	regulator of G-protein signaling 6
706	rs1548687	0,8381	5,46E-05	0,248	14	72028222	A	G	9628	RGS6	regulator of G-protein signaling 6
707	rs17119980	0,8615	2,01E-04	0,333	14	72253994	A	T	8110	DPF3	D4, zinc and double PHD fingers, family 3
708	rs740974	0,8648	2,76E-04	0,338	14	72257827	G	A	8110	DPF3	D4, zinc and double PHD fingers, family 3
709	rs4243642	0,863	2,33E-04	0,335	14	72258454	C	G	8110	DPF3	D4, zinc and double PHD fingers, family 3
710	rs17808467	0,8227	7,61E-04	0,121	14	76239145	A	G			
711	rs11159227	0,8498	8,86E-04	0,186	14	76269385	A	T			
712	rs17109221	1,164	9,72E-04	0,214	14	78979872	T	C	9369	NRXN3	neurexin 3
713	rs7144011	1,165	8,36E-04	0,216	14	79010136	T	G	9369	NRXN3	neurexin 3
714	rs7153625	0,8089	3,27E-04	0,123	14	79119015	A	G	9369	NRXN3	neurexin 3
715	rs7154599	0,815	4,68E-04	0,126	14	79119562	C	G	9369	NRXN3	neurexin 3
716	rs17764096	0,8089	3,01E-04	0,125	14	79120259	T	G	9369	NRXN3	neurexin 3
717	rs190092	0,8533	1,40E-04	0,299	14	79121236	C	A	9369	NRXN3	neurexin 3
718	rs327465	0,8637	1,07E-04	0,494	14	80299793	C	T	145508	CEP128	centrosomal protein 128kDa

Appendix. (Continued).

719	rs2556611	0,8646	1,19E-04	0,495	14	80415919	A	G	145508	CEP128	centrosomal protein 128kDa
720	rs12050342	0,8686	2,07E-04	0,492	14	80438617	T	C	145508	CEP128	centrosomal protein 128kDa
721	rs2888032	0,8678	1,77E-04	0,500	14	80439264	C	T	145508	CEP128	centrosomal protein 128kDa
722	rs11625199	0,8741	3,73E-04	0,498	14	80442498	A	G	145508	CEP128	centrosomal protein 128kDa
723	rs6574608	0,8742	3,77E-04	0,500	14	80444575	A	C	145508	CEP128	centrosomal protein 128kDa
724	rs10444745	0,8628	1,00E-04	0,470	14	87891057	G	T			
725	rs11848957	1,244	7,53E-04	0,096	14	94731600	C	G	79789	CLMN	calmin (calponin-like, transmembrane)
726	rs12907278	1,149	2,60E-04	0,451	15	31760469	A	G	6263	RYR3	ryanodine receptor 3
727	rs12592542	1,141	5,00E-04	0,456	15	31773110	A	G	6263	RYR3	ryanodine receptor 3
728	rs16962542	0,7151	4,52E-05	0,057	15	34189070	A	T			
729	rs7170955	1,194	1,32E-04	0,209	15	44444884	C	A			
730	rs7180600	1,201	5,53E-04	0,151	15	50857433	A	G	3175	ONECUT1	one cut homeobox 1
731	rs10518694	1,225	1,58E-04	0,142	15	50859965	A	C	3175	ONECUT1	one cut homeobox 1
732	rs2456526	1,215	2,77E-04	0,145	15	50876734	C	T			
733	rs10519107	0,8559	3,93E-05	0,481	15	59114168	G	C	6095	RORA	RAR-related orphan receptor A
734	rs6494307	0,8769	6,36E-04	0,413	15	60181982	G	C			
735	rs10083587	0,8756	5,60E-04	0,413	15	60185825	T	C			
736	rs8030240	0,8632	7,29E-04	0,259	15	60186856	T	C			
737	rs1436955	0,8659	8,85E-04	0,263	15	60191674	T	C			
738	rs10083639	0,836	1,78E-04	0,193	15	68368811	A	G			
739	rs11072156	0,8357	1,82E-04	0,191	15	68369472	A	T			
740	rs2059322	1,246	5,21E-04	0,106	15	68792114	C	A	55075	UACA	uveal autoantigen with coiled-coil domains and ankyrin repeats
741	rs10518921	1,242	6,24E-04	0,105	15	68793963	T	C	55075	UACA	uveal autoantigen with coiled-coil domains and ankyrin repeats
742	rs7177970	1,242	6,51E-04	0,104	15	68832308	G	A	55075	UACA	uveal autoantigen with coiled-coil domains and ankyrin repeats
743	rs6495081	1,139	6,53E-04	0,435	15	71903355	G	T			
744	rs2290271	1,152	3,43E-04	0,358	15	83248639	C	A	9154	SLC28A1	solute carrier family 28 (sodium-coupled nucleoside transporter), member 1
745	rs11629542	1,154	1,99E-04	0,472	15	87899758	C	G			
746	rs11636210	0,8803	8,33E-04	0,434	15	89415484	C	T			
747	rs2131659	0,8711	2,84E-04	0,475	15	98925810	T	G			
748	rs11247226	0,8731	3,46E-04	0,468	15	98938486	C	T	55180	LINS	lines homolog (Drosophila)
749	rs8033689	0,8736	4,08E-04	0,434	15	98951820	G	C	55180	LINS	lines homolog (Drosophila)
750	rs7180844	0,8721	3,11E-04	0,473	15	98953582	T	C	55180	LINS	lines homolog (Drosophila)

Appendix. (Continued).

751	rs8055183	1,183	5,50E-04	0,187	16	919237	T	C	64788	LMF1	lipase maturation factor 1
752	rs8043935	1,181	6,16E-04	0,183	16	6306727	G	A			
753	rs12597219	1,183	3,83E-04	0,195	16	6310627	A	C			
754	rs8062975	1,191	1,86E-04	0,200	16	6311714	T	A			
755	rs809684	1,203	3,94E-05	0,227	16	6322435	A	G			
756	rs249301	1,209	1,61E-04	0,165	16	9377408	T	A			
757	rs171125	1,283	3,43E-05	0,110	16	34618468	T	C			
758	rs216944	0,8718	5,42E-04	0,356	16	58798850	A	G			
759	rs8063424	1,176	5,47E-04	0,208	16	78424987	T	C			
760	rs3924889	1,202	2,83E-04	0,172	16	78426000	C	A			
761	rs8062047	1,366	2,18E-04	0,052	16	78457228	G	T			
762	rs11648295	0,8258	6,97E-04	0,134	16	87432022	T	G	2588	GALNS	galactosamine (N-acetyl)-6-sulfate sulfatase
763	rs16964890	0,7752	4,36E-05	0,106	17	24567546	C	T			
764	rs11652197	0,8246	3,46E-04	0,150	17	28478690	C	A	40	ASIC2	acid-sensing (proton-gated) ion channel 2
765	rs228768	1,143	9,15E-04	0,333	17	39547419	G	T	10014	HDAC5	histone deacetylase 5
766	rs1968393	1,146	7,52E-04	0,320	17	49919431	A	G			
767	rs4968816	0,8764	6,27E-04	0,398	17	64200570	G	A			
768	rs11656969	1,198	5,35E-04	0,150	17	69822772	T	C	64446	DNAI2	dynein, axonemal, intermediate chain 2
769	rs8076794	1,142	4,76E-04	0,461	17	74172864	A	C			
770	rs6501238	1,14	5,87E-04	0,460	17	74181334	T	C			
771	rs10512617	1,133	9,67E-04	0,487	17	74205146	C	G	9267	CYTH1	cytohesin 1
772	rs1531797	1,15	2,27E-04	0,488	17	74333763	T	C	57602	USP36	ubiquitin specific peptidase 36
773	rs767300	1,142	9,45E-04	0,328	18	9830230	A	G	11031	RAB31	RAB31, member RAS oncogene family
774	rs471999	1,16	2,01E-04	0,329	18	9834729	G	A	11031	RAB31	RAB31, member RAS oncogene family
775	rs555935	1,153	2,39E-04	0,387	18	9835307	T	C	11031	RAB31	RAB31, member RAS oncogene family
776	rs575420	1,136	8,21E-04	0,421	18	9838371	A	C	11031	RAB31	RAB31, member RAS oncogene family
777	rs688248	1,155	2,85E-04	0,342	18	9838613	C	T	11031	RAB31	RAB31, member RAS oncogene family
778	rs508816	1,151	2,54E-04	0,393	18	9839620	T	C	11031	RAB31	RAB31, member RAS oncogene family
779	rs2299836	1,167	1,90E-04	0,287	18	9840212	A	G	11031	RAB31	RAB31, member RAS oncogene family
780	rs559655	1,202	2,26E-04	0,173	18	10055123	T	C			
781	rs3737361	1,159	3,64E-04	0,295	18	12821324	C	T	5771	PTPN2	protein tyrosine phosphatase, non-receptor type 2
782	rs9947011	0,8569	4,90E-04	0,249	18	18674407	A	G			
783	rs6507323	0,8509	2,93E-04	0,244	18	18680676	G	C			

Appendix. (Continued).

784	rs3911557	0,848	2,06E-04	0,246	18	18726561	T	C			
785	rs4800138	0,8482	2,15E-04	0,245	18	18768295	G	A	5932	RBBP8	retinoblastoma binding protein 8
786	rs9304261	0,8586	8,68E-04	0,225	18	18860594	T	C	5932	RBBP8	retinoblastoma binding protein 8
787	rs6507457	0,8393	9,33E-05	0,250	18	18880434	T	C			
788	rs2056015	1,134	8,99E-04	0,492	18	32164600	G	T	80206	FHOD3	formin homology 2 domain containing 3
789	rs16973756	0,7505	6,68E-04	0,055	18	36617062	G	A			
790	rs7234864	1,174	1,57E-04	0,281	18	55885837	T	C			
791	rs1942867	1,18	8,71E-05	0,285	18	55887250	A	G			
792	rs11664327	1,173	6,36E-05	0,348	18	55890603	C	T			
793	rs8091524	1,19	5,56E-05	0,267	18	55902940	C	T			
794	rs1539952	1,176	1,73E-04	0,266	18	55917492	G	A			
795	rs9966951	1,148	6,16E-04	0,335	18	55926275	A	G			
796	rs6567157	1,159	2,35E-04	0,340	18	55941205	G	T			
797	rs1942880	1,169	1,02E-04	0,339	18	55944189	T	C			
798	rs7235626	1,162	1,92E-04	0,338	18	55949677	T	G			
799	rs17782313	1,161	7,07E-04	0,253	18	56002077	C	T			
800	rs476828	1,168	3,76E-04	0,258	18	56003567	C	T			
801	rs9947403	1,151	4,18E-04	0,349	18	56020730	T	C			
802	rs639407	1,153	3,44E-04	0,352	18	56021159	G	A			
803	rs619662	1,15	3,05E-04	0,398	18	56035531	A	G			
804	rs607104	1,141	8,97E-04	0,355	18	56042573	G	C			
805	rs557416	1,148	5,53E-04	0,347	18	56046039	G	A			
806	rs9955666	1,152	5,20E-04	0,336	18	56063765	A	G			
807	rs1421521	1,139	9,78E-04	0,348	18	60236486	A	G			
808	rs470443	1,158	5,80E-04	0,267	18	72832968	A	G	4155	MBP	myelin basic protein
809	rs4805258	1,169	8,10E-04	0,211	19	32763882	A	G			
810	rs7252689	1,173	6,56E-04	0,202	19	33080647	T	C			
811	rs1017207	1,176	8,08E-04	0,183	19	39057327	A	G			
812	rs7251215	1,173	2,09E-04	0,259	19	39099587	G	A			
813	rs10409299	1,166	9,10E-04	0,208	19	41016164	G	A	4868	NPHS1	nephrosis 1, congenital, Finnish type (nephrin)
814	rs41332947	0,8161	4,90E-04	0,127	19	55391757	C	T			
815	rs2876409	1,141	7,11E-04	0,367	20	15415075	A	G	140733	MACROD2	MACRO domain containing 2
816	rs3746476	0,8168	9,10E-04	0,109	20	36373583	G	A	671	BPI	bactericidal/permeability-increasing protein

Appendix. (Continued).

817	rs6103249	0,8325	7,24E-04	0,147	20	41399350	C	T			
818	rs6073055	0,8728	7,12E-04	0,338	20	41406604	G	A			
819	rs16985285	0,8374	7,84E-04	0,153	20	41448057	T	C			
820	rs6103716	1,157	3,05E-04	0,327	20	42433044	C	A	3172	HNF4A	hepatocyte nuclear factor 4, alpha
821	rs6063438	1,183	3,04E-04	0,204	20	47874575	T	C	23315	SLC9A8	solute carrier family 9, subfamily A (NHE8, cation proton antiporter 8), member 8
822	rs676035	1,186	2,26E-04	0,205	20	47916399	G	A	23315	SLC9A8	solute carrier family 9, subfamily A (NHE8, cation proton antiporter 8), member 8
823	rs487096	1,217	5,20E-04	0,128	20	47932666	G	C	23315	SLC9A8	solute carrier family 9, subfamily A (NHE8, cation proton antiporter 8), member 8
824	rs1883553	1,193	6,38E-05	0,240	20	48007523	T	C			
825	rs6020178	1,168	9,91E-04	0,200	20	48037347	C	T	6615	SNAI1	snail homolog 1 (Drosophila)
826	rs2257	1,158	3,47E-04	0,306	20	51245861	G	C	128553	TSHZ2	teashirt zinc finger homeobox 2
827	rs6098138	1,214	7,76E-04	0,119	20	52701411	T	C	55816	DOK5	docking protein 5
828	rs1468056	1,154	3,96E-04	0,333	20	54399395	C	G	6790	AURKA	aurora kinase A
829	rs6061921	0,8584	6,35E-05	0,432	20	59966907	C	T			
830	rs6089568	0,8517	2,69E-05	0,425	20	59967110	A	G			
831	rs2037994	1,226	8,93E-04	0,105	21	15880541	A	C			
832	rs2823759	1,245	2,57E-04	0,111	21	16667957	C	G	388815	LINC00478	long intergenic non-protein coding RNA 478
833	rs915856	1,24	3,59E-04	0,111	21	16668120	A	G	388815	LINC00478	long intergenic non-protein coding RNA 478
834	rs1667570	1,254	1,42E-04	0,112	21	16668591	G	A	388815	LINC00478	long intergenic non-protein coding RNA 478
835	rs380220	1,25	2,02E-04	0,109	21	16668953	A	G	388815	LINC00478	long intergenic non-protein coding RNA 478
836	rs369347	1,253	1,44E-04	0,115	21	16669662	G	A	388815	LINC00478	long intergenic non-protein coding RNA 478
837	rs158046	1,22	4,29E-04	0,132	21	18316684	C	T	140578	CHODL	chondrolectin
838	rs2826239	0,8685	5,02E-04	0,326	21	20709622	T	G			
839	rs9980427	0,873	6,81E-04	0,346	21	20709933	A	G			
840	rs2826242	0,8687	5,09E-04	0,326	21	20713322	T	C			
841	rs1985053	0,8615	2,27E-04	0,328	21	20713786	G	A			
842	rs2826244	0,8668	3,54E-04	0,340	21	20716906	G	C			
843	rs1029258	0,8229	5,69E-04	0,136	21	26710675	C	A			
844	rs2831054	1,167	5,52E-04	0,239	21	27954865	A	G			
845	rs1888433	1,139	8,63E-04	0,386	21	27954964	T	C			
846	rs2831854	1,162	3,31E-04	0,283	21	28782159	T	C			
847	rs2831863	1,159	2,21E-04	0,347	21	28788692	T	C			

Appendix. (Continued).

848	rs1999318	1,148	9,33E-04	0,284	21	28817820	C	A			
849	rs9975371	1,215	9,45E-04	0,114	21	28817851	T	C			
850	rs11701035	1,246	5,68E-06	0,186	21	37162840	A	G	3141	HLCS	holocarboxylase synthetase (biotin-(proprionyl-CoA-carboxylase (ATP-hydrolysing)) ligase)
851	rs8132538	1,229	2,21E-05	0,183	21	37197902	A	G	3141	HLCS	holocarboxylase synthetase (biotin-(proprionyl-CoA-carboxylase (ATP-hydrolysing)) ligase)
852	rs2835530	1,237	1,20E-05	0,182	21	37199189	C	T	3141	HLCS	holocarboxylase synthetase (biotin-(proprionyl-CoA-carboxylase (ATP-hydrolysing)) ligase)
853	rs2845812	1,204	1,09E-04	0,189	21	37220194	T	C	3141	HLCS	holocarboxylase synthetase (biotin-(proprionyl-CoA-carboxylase (ATP-hydrolysing)) ligase)
854	rs8127236	1,143	8,21E-04	0,353	21	37271007	T	C	3141	HLCS	holocarboxylase synthetase (biotin-(proprionyl-CoA-carboxylase (ATP-hydrolysing)) ligase)
855	rs220161	0,8149	9,16E-04	0,109	21	42422362	C	G	89766	UMODL1	uromodulin-like 1
856	rs9981459	0,823	2,92E-04	0,148	21	42681878	G	C	64699	TMPRSS3	transmembrane protease, serine 3
857	rs2401163	0,8312	4,02E-04	0,154	22	16511078	C	T	23786	BCL2L13	BCL2-like 13 (apoptosis facilitator)
858	rs2587103	0,8412	8,87E-04	0,156	22	16528454	T	C	23786	BCL2L13	BCL2-like 13 (apoptosis facilitator)
859	rs713999	0,8414	1,07E-05	0,376	22	46210776	A	G			
860	rs6008226	1,189	3,71E-04	0,184	22	46243314	C	T			
861	rs11090806	1,29	9,95E-04	0,065	22	46777160	A	C			
862	rs12009434	1,181	2,51E-04	0,324	23	12875922	A	G			
863	rs5979784	1,169	5,82E-04	0,329	23	12876296	C	A			
864	rs17277503	1,182	8,38E-04	0,239	23	56833086	G	A	550643	LOC550643	uncharacterized LOC550643
865	rs5914799	1,189	5,27E-04	0,239	23	56840879	C	T	550643	LOC550643	uncharacterized LOC550643
866	rs5914807	1,192	4,32E-04	0,240	23	56867944	G	T			
867	rs5960811	1,191	4,95E-04	0,239	23	56870079	G	A			
868	rs1930978	1,197	3,48E-04	0,241	23	56927132	T	C			
869	rs11091598	1,187	6,06E-04	0,240	23	56927696	G	T			
870	rs5914852	1,186	9,99E-04	0,214	23	56948766	C	T			
871	rs4379572	1,184	6,85E-04	0,243	23	56968844	G	A			
872	rs4557841	1,193	2,75E-04	0,274	23	57383907	G	T	158584	FAAH2	fatty acid amide hydrolase 2

Appendix. (Continued).

873	rs10855622	0,8459	5,73E-04	0,267	23	85902249	G	C	117154	DACH2	dachshund homolog 2 (Drosophila)
874	rs5942729	1,216	9,40E-04	0,155	23	108181279	A	G			
875	rs5942752	1,22	7,71E-04	0,155	23	108209528	G	A			
876	rs6642958	1,215	9,84E-04	0,154	23	108249271	G	A			
877	rs4825603	1,206	8,05E-04	0,177	23	117727895	C	G			
878	rs2495622	1,215	5,13E-04	0,176	23	117737020	G	T			
879	rs2495626	1,219	4,27E-04	0,174	23	117742946	T	C			
880	rs2256173	1,204	9,46E-04	0,174	23	117773617	C	T	3597	IL13RA1	interleukin 13 receptor, alpha 1
881	rs2997052	1,213	6,24E-04	0,178	23	117800548	G	A	3597	IL13RA1	interleukin 13 receptor, alpha 1
882	rs5965947	0,8593	5,27E-04	0,408	23	144777233	C	T			
883	rs5919623	0,86	5,09E-04	0,411	23	144779048	C	G			
884	rs12862591	0,8637	7,72E-04	0,406	23	144801782	G	T			
885	rs12861185	0,8554	3,44E-04	0,403	23	144801952	G	C			
886	rs5965955	0,8593	4,87E-04	0,406	23	144807588	A	T			