Genome-wide search for exonic variants affecting translational efficiency: a pilot study
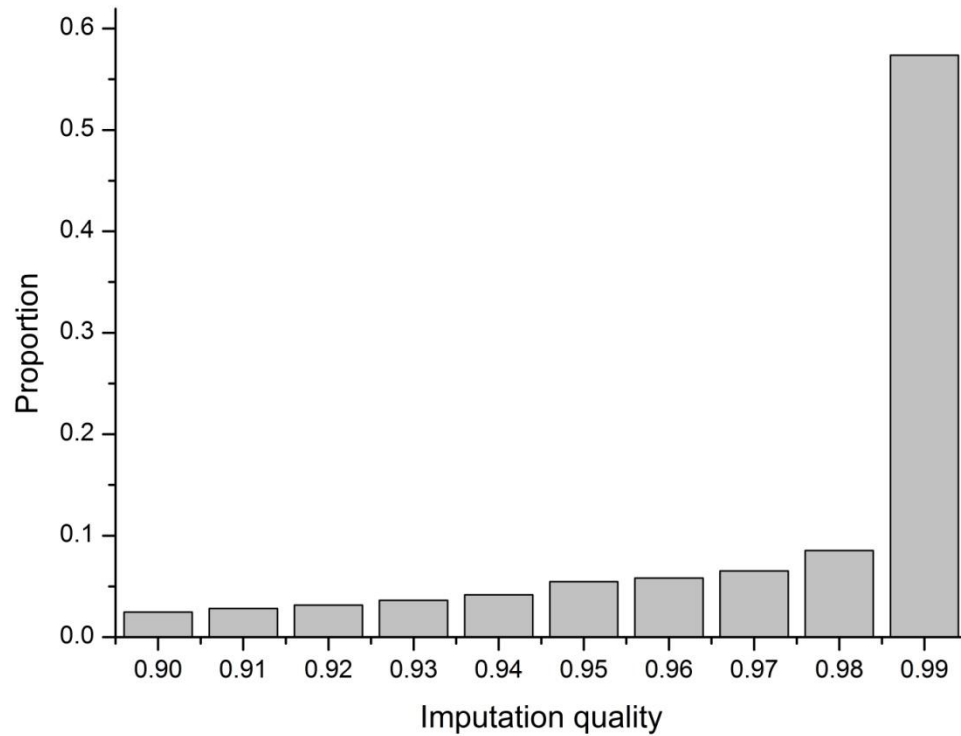
On-line supplementary material

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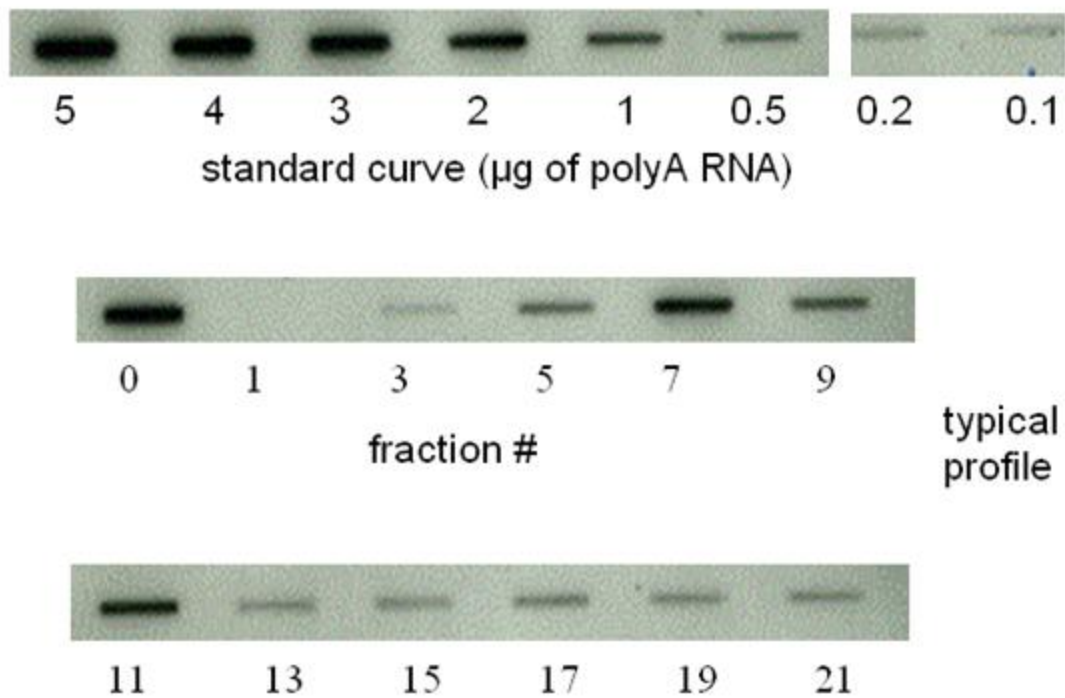
Supplementary Figure S1 The imputation quality scores of 2,598,418 SNPs genotyped by the 1000 Genome Project in 9 samples of this study. The quality of each SNP's imputation was assessed by the average posterior probability for the most likely genotype. The majority (83.7%) of these imputations have good quality with the scores>0.95.
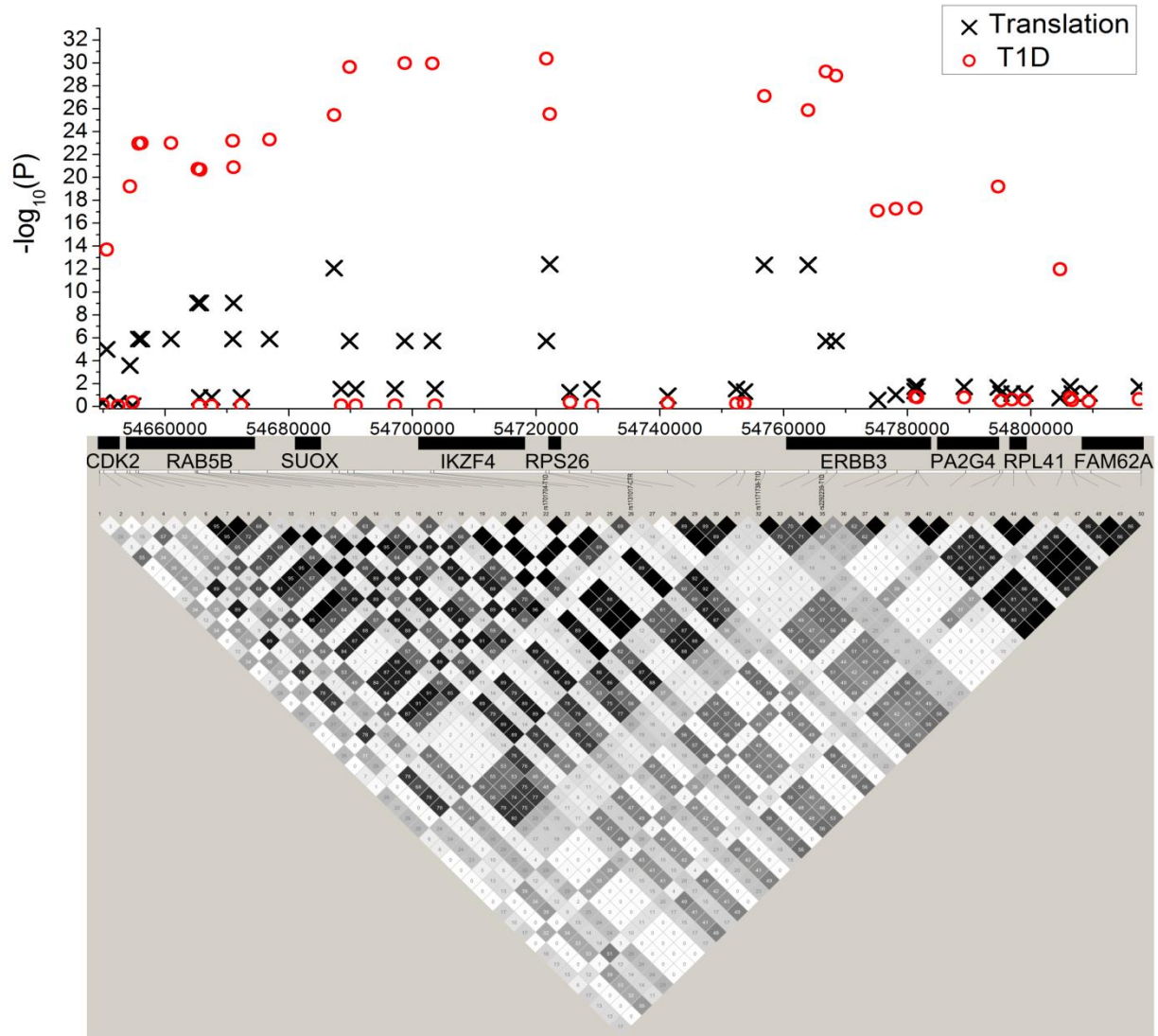
**Supplementary Figure S2** Regional plot of the *RPS26* region at Chr12q13. –log₁₀(P-values) of associations with type 1 diabetes (T1D) susceptibility and ribosomal distribution of mRNAs are shown for SNPs in this region. The P-values of T1D associations are from the meta-analysis of six T1D cohorts reported before [55]. The grey scale in the LD map indicates r² values.
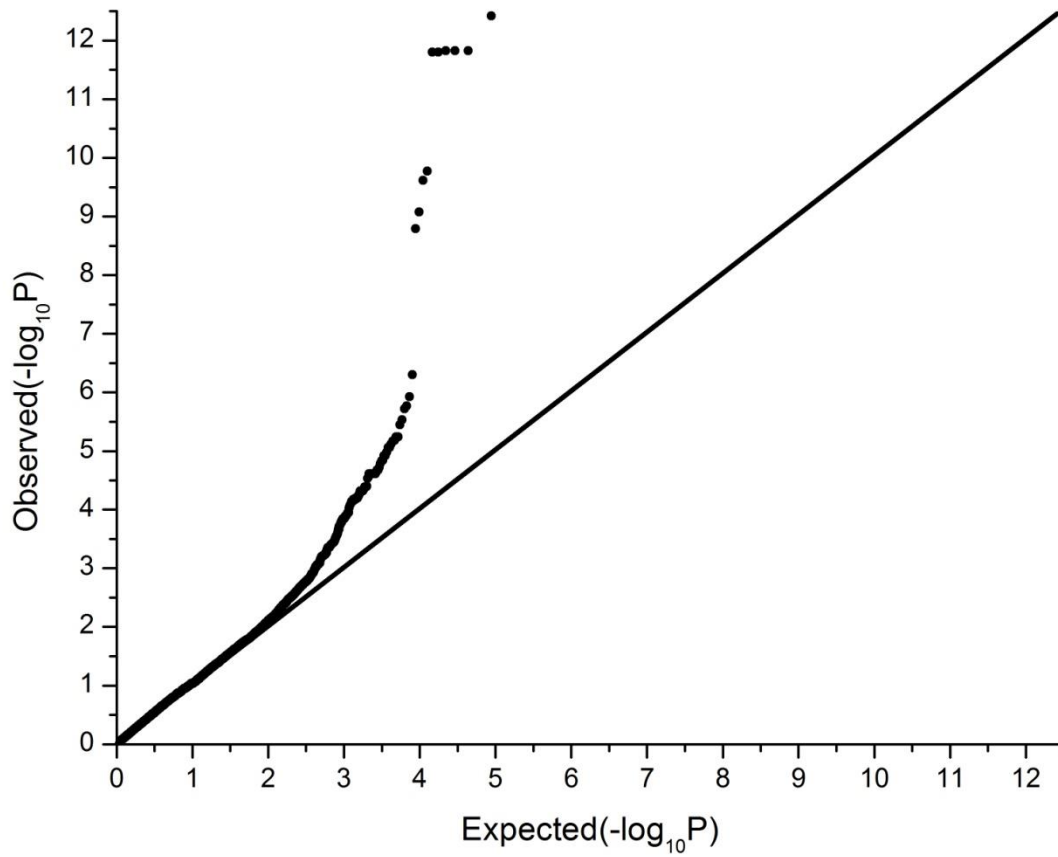
Supplementary Figure S3 QQ-plot of genome-wide tests for associations of exonic SNPs and the ratio of normalized polysomal/nonpolysomal mRNAs.

5 4 3 2 1 0.5 0.2 0.1

standard curve (µg of polyA RNA)

0 1 3 5 7 9

fraction #

typical
profile

11 13 15 17 19 21

**Supplementary Figure S4** The DIG-labeled oligo-dT assay to quantify fraction poly(A) RNA. The first strip shows unfractionated pancreas Poly(A) RNA at the indicated standard concentrations. The lower two strips, from the same membrane, represent a typical profile of LCLs. The numbers represent ultracentrifugal fractions, and larger numbers represent heavier fractions; "0" represents unfractionated RNA.
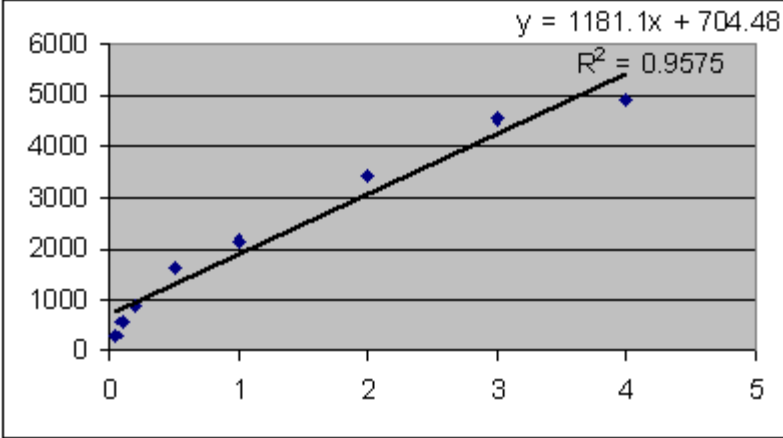
Supplementary Figure S5 The standard curve of the Poly(A) densitometry quantification. X-axis: Poly(A) concentration (ng/µl); Y-axis: OD value.
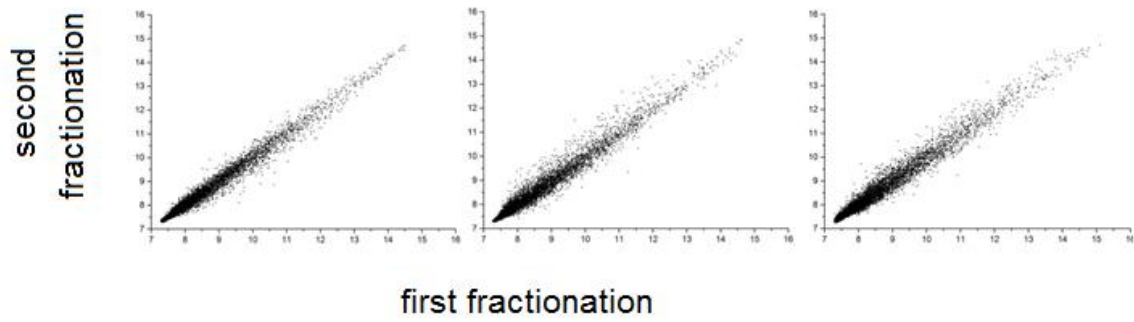
Supplementary Figure S6 Little random noise introduced by the fractionation. The Microarray profiling data from two different ultracentrifugal fractionations of the same LCL culture show relatively little random noise introduced by the fractionation. From left to right, it is light fractions, non-fractioned RNAs, and heavy fractions.
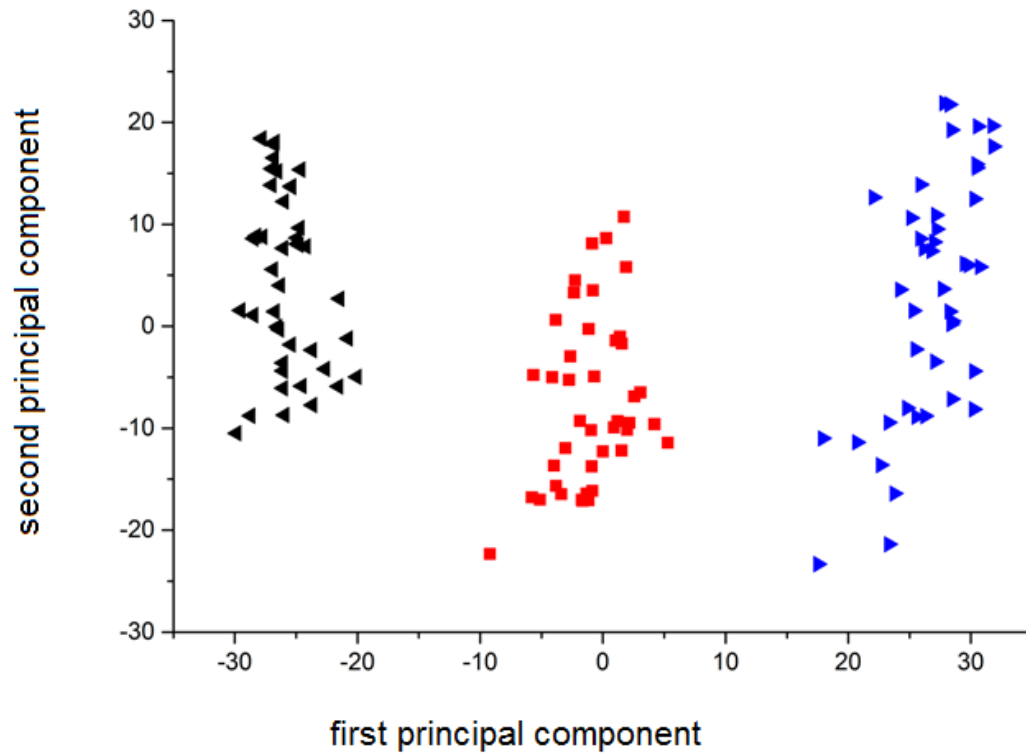
Supplementary Figure S7 Expression profiles in different fractions. After data normalization, the Principal Component Analysis (PCA) showed distinctive genome-wide expression profiles in different fractions. Light fractions, non-fractioned RNA, and heavy fractions, can be clearly distinguished by Component 1 (X-axis). From left to right, it is light fractions, non-fractioned RNAs, and heavy fractions.

Supplementary Table S1 Translational *cis*-regulatory effect of 74 SNPs with Q<0.1

SNP	Function	Chr	Pos*	Gene	MAF	P-value**	Q-value
rs1131017	utr-5	12	54722196	*RPS26*	0.365	3.79E-13	2.08E-08
rs2165490	utr-3	12	91343130	*CLLU1OS*	0.231	1.49E-12	2.08E-08
chr12:91347034	utr-3	12	91347034	*CLLU1OS*	0.250	1.49E-12	2.08E-08
rs12578643	utr-3	12	91348204	*CLLU1OS*	0.231	1.49E-12	2.08E-08
rs12580153	missense	12	91342613	*CLLU1OS*	0.250	1.56E-12	2.08E-08
rs12578105	utr-3	12	91343830	*CLLU1OS*	0.250	1.56E-12	2.08E-08
rs139561	utr-3	22	40525356	*CCDC134*	0.231	1.68E-10	1.92E-06
rs1792174	utr-5	11	73176581	*MRPL48*	0.436	2.41E-10	2.41E-06
rs13876	utr-3	5	99949980	*FAM174A*	0.487	8.43E-10	7.48E-06
rs139562	utr-5	22	40526630	*CCDC134*	0.224	1.62E-09	1.29E-05
rs1334688	utr-5	6	155677316	*TFB1M*	0.449	4.96E-07	3.60E-03
rs3802755	utr-3	11	26639410	*TMEM16C*	0.162	1.18E-06	7.86 E-03
rs162981	utr-5	6	155677277	*TFB1M*	0.434	1.70E-06	0.010
rs11553096	utr-5	7	75515152	*STYXL1*	0.154	1.91E-06	0.011
rs4256900	utr-5	10	127501746	*UROS*	0.421	2.95E-06	0.016
rs1130538	utr-3	6	31344601	*HLA-C*	0.487	3.55E-06	0.018
rs3742289	missense	13	51501195	*ALG11*	0.385	5.75E-06	0.026
rs2897964	utr-3	13	51503676	*ALG11*	0.385	5.75E-06	0.026
rs1049281	utr-3	6	31344546	*HLA-C*	0.474	6.55E-06	0.027
rs28420948	utr-3	6	31344578	*HLA-C*	0.487	6.83E-06	0.027
rs2799680	utr-3	1	199641300	*TNNI1*	0.487	7.62E-06	0.029
rs3742291	coding-synonymous	13	51501776	*ALG11*	0.395	8.73E-06	0.030
rs2277448	utr-5	13	51483549	*ALG11*	0.395	8.73E-06	0.030

rs16947	missense	22	40853887	C22ORF32	0.368	1.04E-05	0.035
rs1807494	utr-3	22	40804084	C22ORF32	0.378	1.19E-05	0.037
rs2269524	utr-5	22	40805649	C22ORF32	0.378	1.19E-05	0.037
rs10423138	coding-synonymous	19	63620114	ZNF584	0.250	1.44E-05	0.041
rs241449	coding-synonymous	6	32904631	TAP2	0.449	1.45E-05	0.041
rs2070610	utr-5	21	29367819	CCT8	0.128	1.64E-05	0.045
rs3747240	utr-3	22	44118888	FAM118A	0.079	1.90E-05	0.048
rs6590520	utr-3	11	130252596	SNX19	0.244	2.10E-05	0.048
rs3740714	utr-5	11	18390465	LDHC	0.244	2.10E-05	0.048
rs177252	coding-synonymous	5	134371698	CATSPER3	0.244	2.33E-05	0.048
rs2857101	utr-3	6	32902654	TAP2	0.244	2.46E-05	0.048
rs241456	utr-3	6	32903943	TAP2	0.244	2.46E-05	0.048
rs241455	utr-3	6	32903997	TAP2	0.244	2.46E-05	0.048
rs241454	utr-3	6	32904122	TAP2	0.244	2.46E-05	0.048
rs241453	utr-3	6	32904204	TAP2	0.244	2.46E-05	0.048
rs17034	utr-3	6	32904499	TAP2	0.167	2.46E-05	0.048
rs241448	nonsense	6	32904663	TAP2	0.434	2.46E-05	0.048
rs241447	missense	6	32904729	TAP2	0.308	2.46E-05	0.048
rs1801311	missense	22	40816669	C22ORF32	0.333	2.79E-05	0.053
rs2272836	coding-synonymous	22	48924677	MOV10L1	0.244	2.93E-05	0.054
rs103612	missense	9	133009913	NUP214	0.333	3.95E-05	0.070
rs1256945	utr-3	1	199642281	TNNI1	0.321	4.09E-05	0.070
rs1256946	utr-3	1	199642374	TNNI1	0.500	4.09E-05	0.070

rs3758144	utr-3	8	18432457	PSD3	0.500	4.13E-05	0.070
rs3751033	utr-5	11	130291555	SNX19	0.237	4.41E-05	0.072
rs3764535	coding-synonymous	19	63620864	ZNF584	0.462	4.80E-05	0.072
rs3764534	coding-synonymous	19	63620948	ZNF584	0.462	4.80E-05	0.072
rs3764533	utr-3	19	63621006	ZNF584	0.462	4.80E-05	0.072
rs1051500	utr-3	19	63636214	ZNF584	0.462	4.80E-05	0.072
rs1465789	missense	19	63637868	ZNF584	0.462	4.80E-05	0.072
rs241441	coding-synonymous	6	32905275	TAP2	0.447	4.88E-05	0.072
rs241451	utr-3	6	32904458	TAP2	0.269	5.48E-05	0.080
rs28381589	utr-3	6	32904433	TAP2	0.211	5.67E-05	0.081
rs9398218	coding-synonymous	6	110252996	FIG4	0.487	5.97E-05	0.081
rs1130838	missense	6	31345103	HLA-C	0.461	6.34E-05	0.081
rs35708511	missense	6	31345141	HLA-C	0.461	6.34E-05	0.081
rs1050180	missense	6	31345812	HLA-C	0.461	6.34E-05	0.081
rs1050716	missense	6	31346209	HLA-C	0.461	6.34E-05	0.081
rs1094	utr-3	6	31344701	HLA-C	0.408	6.67E-05	0.081
rs4716399	coding-synonymous	6	169918572	C6ORF70	0.408	6.69E-05	0.081
rs139299	missense	22	37827400	APOBEC3H	0.408	6.72E-05	0.081
rs139297	missense	22	37827350	APOBEC3H	0.333	6.72E-05	0.081
rs139302	missense	22	37827984	APOBEC3H	0.282	6.72E-05	0.081
rs7767581	utr-5	6	31347834	HLA-C	0.457	7.14E-05	0.083
rs3087804	utr-3	15	81476777	BTBD1	0.276	7.19E-05	0.083
rs13501	utr-3	6	32901501	TAP2	0.500	7.23E-05	0.083

rs3825528	utr-5	13	51500920	*ALG11*	*0.449*	7.26E-05	0.083
rs2071470	utr-5	6	32892731	*TAP2*	*0.289*	7.93E-05	0.089
rs1256947	utr-3	1	199642436	*TNNI1*	*0.487*	8.08E-05	0.090
rs7154785	utr-3	14	23966670	*CBLN3*	*0.171*	8.36E-05	0.091
rs2229642	missense	6	33767450	*ITPR3*	*0.408*	9.01E-05	0.097

* Human genome HG18 build; ** Spearman rank correlation *P* values.

Supplementary Reference:

55.   Bradfield, J.P. et al. A genome-wide meta-analysis of six type 1 diabetes cohorts identifies multiple associated loci. *PLoS Genet.* **7**, e1002293 (2011).