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Genotyping

Genotyping of the Malmö Men and Malmö Training Intervention studies was done simultaneously at Lund University on HumanOmniExpress 12v1 C chips (Illumina, California, USA) and genotype calling was done with the Illumina Genome studio software. A total of 103403 and 81424 SNPs from the Malmö Men and Malmö Training Intervention studies failed to pass the QC. Details on exclusion criteria and a more detailed decomposition of reasons for failure are available in the supplement. Genotyping of the MuTHER samples was completed as part of the larger TwinsUK dataset (N~6000) and was done with a combination of Illumina arrays (HumanHap300, HumanHap610Q, 1M-Duo and 1.2MDuo 1M). Intensity data for each of the three arrays were pooled separately (with 1M-Duo and 1.2MDuo 1M pooled together), and genotypes were called with the Illuminus26 calling algorithm.

Genotyping quality control

The following exclusion criteria were applied to samples from all three cohorts:

(i) sample call rate <98%; (ii) evidence of non-European ancestry as assessed by principal component analysis or multidimensionality scaling comparisons with HapMap populations; (iii) genome-wide heterozygosity outliers detected on a plot of missingness vs. heterozygosity at genome-wide level. In the Malmö cohorts, we also checked for (iv) gender mismatches using standard settings in PLINK; (v) relatedness between individuals using the IBD-test as implemented in PLINK, excluding individuals from pairs with $\pi_{\text{hat}} \geq 0.2$ or outliers based upon average π_{hat} . In the MuTHER dataset, the (v) IBD-test was used to identify samples suggestive of sample identity errors. Exclusion criteria for SNPs were: (i) SNP call rate < 98% (Malmö) or SNP call rate < 97% (SNPs with $\text{MAF} \geq 5\%$) or SNP call rate <99% (SNPs with $1\% \leq \text{MAF} < 5\%$) (MuTHER); (ii) Hardy-Weinberg equilibrium test performed in a set of unrelated samples, p-values < 5.7×10^{-7} (SNPs with $\text{MAF} \geq 5\%$) or p-values < 0.0001 (SNPs with $1\% \leq \text{MAF} < 5\%$) (Malmö) or Hardy-Weinberg equilibrium test p-values < 5.7×10^{-7} (MuTHER); (iii) $\text{MAF} < 1\%$ assessed in a set of unrelated samples.

Imputation

In each study, we imputed individual genotypes to 1000 Genomes data, to provide a common set of SNPs for analysis. Imputation was carried out using IMPUTE2 (https://mathgen.stats.ox.ac.uk/impute/impute_v2) and the June 2011 release of the 1000 Genomes Phase I panel was used as a reference panel (http://mathgen.stats.ox.ac.uk/impute/data_download_1000G_phase1_interim). The MuTHER samples were imputed as part of the TwinsUK dataset (N~6000) and pre-phasing of this data was carried out using IMPUTE2. The two Malmö cohorts were pre-phased using SHAPEIT (<http://www.shapeit.fr>). For all analyses, probabilistic genotypes were used for the subsequent analyses. After imputation, SNPs were filtered using a minor allele frequency (MAF) > 5% and an IMPUTE2 info value of >0.8.

Gene expression

Due to differences in gene expression arrays used across studies, we adopted a gene-centric approach to our analyses, selecting probes in each study that mapped to the 7006 genes common to all three. All probes were mapped to NCBI build 37 of the Genome Browser and only uniquely mapping probes, with no mismatches and either an Ensembl or RefSeq ID, were kept for analysis. Probes encompassing a common SNP ($\text{MAF} > 5\%$) were excluded from all studies. Expression profiling of the MuTHER samples was performed using the Illumina Human HT-12 V3 BeadChips (Illumina Inc.), including more than 48000 probes. 200ng of total RNA was processed according to the protocol supplied by Illumina. All samples were randomized before array hybridization, and technical replicates were always hybridized on different BeadChips. Log₂-transformed expression signals were normalized with quantile normalization of the replicates of each individual, followed by quantile normalization across all

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individuals. Post-quality-control expression profiles were obtained for 42 individuals. The Illumina probe annotations were mapped to build 37 using the R package (`illuminaHumanv3.db`). After applying the probe inclusion criteria above, 9633 probes were left in the analysis. Gene expression analysis in the Malmo Men cohort was assayed using the Affymetrix HG-U133a platform, while the Affymetrix custom array NUGOhs1a520180 was used for the Malmo Intervention cohort (Affymetrix Inc.). All probes were mapped to NCBI build 37 and annotated with R packages `hgu133a.db` and `nugohs1a520180.db`. Log₂-transformed expression signals of both Malmo cohorts were normalized using RMA (Robust Multichip Average) expression measure (16).

Annotation and enrichment analysis

The program SnpEff (1) was used to annotate and predict the effects of both our eQTL SNPs and all *cis* SNPs tested in our study. We assessed the enrichment of low p-values closer to TSSs using the Exact Binomial Test implemented in the R statistical environment. Specifically, we performed an exact test of a null hypothesis about the probability of success in a Bernoulli experiment, in which the number of successes corresponds to the number of eQTL SNPs where the associated gene is the closest. We only tested eQTL SNPs where the eQTL gene and the nearest gene were probed by our meta-analysis (within 250kb of TSS). The Test of Equal or Given Proportions, implemented in R, was used to test the null hypothesis that the proportions (probabilities of success) are the same, or that they are equal certain given values. Specifically, this test was performed to test eQTL SNP enrichment for each gene functional unit and for functional RegulomeDB categories in comparison with the background of all *cis* SNPs tested.

Gene expression analysis of publicly available data sets

Raw expression data for ten public microarray studies were retrieved from ArrayExpress (<http://www.ebi.ac.uk/arrayexpress/>), all based on the Affymetrix HG-U133+2 array platform (Table S5). Data normalization was carried out with Robust Probabilistic Averaging (RPA) (2) with probesets mapped to Ensembl gene identifiers using the R/Bioconductor package `customCDF` v.1.2.1 (3), and quality controlled using the `arrayQualityMetrics` v3.14.0 (4). None of the selected samples failed quality control. Differential expression between subjects with type 2 diabetes (T2D) and normoglycemic (NGT) individuals was estimated by meta-analysis of three datasets with full annotation for these groups: E-GEOD-18732, E-GEOD-19420, and E-GEOD-25462, including 102 T2D and 87 NGT samples. The datasets were individually normalized with RPA and meta-analysed using the `geneMeta` R/Bioconductor package [<http://www.bioconductor.org/packages/release/bioc/html/GeneMeta.html>]. Association to BMI was calculated by retrieving all samples within the seven selected datasets, with annotation for BMI (Table S3), from the HG-U133+2 arrays and normalized as a single dataset using RPA, followed by a linear regression for BMI adjusted for sex.

Integration of genome-wide association data from MAGIC and DIAGRAM

To investigate whether our significant eQTL are enriched for associations to T2D and glycaemic traits, we did a lookup of our significant eQTLs SNPs in GWAS data from the DIAGRAM consortium for T2D (5), and from the MAGIC consortium for HOMA-IR (6), 2 hour glucose, 2 hour glucose adjusted for BMI, fasting insulin, fasting insulin adjusted for BMI, fasting glucose and fasting glucose adjusted for BMI (7). We did a binomial sign test to quantify the extent of the enrichment in each of the GWAS studies, using only independent eQTL SNPs, by calculating the probability of observing the number of GWAS SNPs we found with a p-value < 0.05 amongst our eQTL SNPs. We also noted any eQTL SNP that was associated with any of the DIAGRAM and MAGIC phenotypes with genome-wide significance.

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Supplementary Table 1. Top SNP per gene for all significant (FDR<5%, p-value=1.96E-05) eQTLs identified in the meta-analysis. Information on bimodality of gene expression, distance of eQTL SNPs to transcription start sites (TSS), functional annotation of eQTL SNPs and previously reported eQTLs are also detailed.

SNP (dbSNP137)	Gene	Allele1	Allele2	Weight	Zscore	Pvalue	Direction	Het_I ²	Het_ChiSq	Het_Df	Het_Pval	FDR	Bimodal gene expression	SNP within which gene	gene in our gene list	SNP_pos - TSS	SNP relative transcript location	Regulo meDB score	eQTL seen before
rs2238479	CRYM	a	g	95,5	-11,309	1,18E-29	---	52	8,337	2	0,01548	2,46E-22		CRYM	yes	13 134	intron	6	
rs2296805	PEX6	t	g	95,5	9,065	1,24E-19	+++	86,3	29,248	2	4,46E-07	2,90E-13		GNMT	-	-2 852	intron	1f	yes
rs7810193	SEC61G	t	c	95,5	-8,896	5,78E-19	---	74,3	15,569	2	0,0004162	4,15E-13		-	-	-68 068	intergenic	6	
rs251851	ERAP2	a	t	95,5	8,434	3,35E-17	+++	74,8	15,875	2	0,0003571	6,65E-12		LNPEP	yes	113 375	intron	6	yes
rs138616686	NQO2	a	g	95,5	-8,233	1,83E-16	---	-67,6	2,387	2	0,3032	2,90E-11		NQO2	yes	3 904	intron		yes
rs12483950	DDT	c	g	95,5	8,09	5,96E-16	+++	77,5	17,814	2	0,0001354	9,39E-11		-	-	-17 378	downstream	5	yes
rs10073049	PFDN1	a	c	95,5	-8,089	6,03E-16	---	34,4	6,099	2	0,04739	9,44E-11		CYSTM1	-	-18 515	intron	6	
rs80317390	NUDT2	a	g	95,5	7,988	1,37E-15	+++	0	1,049	2	0,5918	1,25E-10		-	-	49 182	downstream, upstream	5	yes
rs58655904	LDHC	t	c	95,5	7,792	6,60E-15	+++	68,5	12,691	2	0,001755	3,97E-10	yes	-	-	-1 662	downstream, upstream	4	
rs1955657	SERPINA5	a	g	95,5	7,718	1,19E-14	+++	0	0,642	2	0,7252	6,69E-10		SERPINA3	-	24 918	intron	6	
rs7503161	EIF5A	a	c	95,5	-7,418	1,19E-13	---	70	13,347	2	0,001264	5,62E-09		-	-	-2 353	upstream		yes
rs2278022	ATMIN	t	c	95,5	7,357	1,89E-13	+++	55	8,895	2	0,01171	8,74E-09		ATMIN	yes	6 035	missense		
rs2409494	TMEM50B	t	c	95,5	-6,828	8,61E-12	---	71,9	14,23	2	0,000813	2,57E-07		IFNGR2, TMEM50B	yes	3 616	intron		yes
rs3863496	TIMM22	t	c	95,5	6,756	1,42E-11	+++	70,4	13,527	2	0,001155	4,02E-07	yes	TIMM22	yes	2 807	intron		yes
rs2268177	CDC42	a	t	95,5	6,624	3,49E-11	++	93,4	60,627	2	6,84E-14	9,17E-07		CDC42	yes	36 291	intron	5	yes
rs9859086	LRRFIP2	a	c	95,5	6,593	4,30E-11	+++	0	0,548	2	0,7605	1,11E-06		LRRFIP2	yes	52 075	intron		yes
rs4374997	PIWIL2	a	c	95,5	6,544	6,00E-11	+++	0	0,469	2	0,7909	1,44E-06	yes	PIWIL2	yes	36 517	intron	5	yes
rs1055138	FAM149A	c	g	95,5	6,488	8,69E-11	+++	28,8	5,62	2	0,06021	2,05E-06		CYP4V2	-	47 405	missense	4	
rs8076632	SPATA20	c	g	95,5	-6,475	9,46E-11	---	18,1	4,885	2	0,08696	2,22E-06		SPATA20	yes	1 500	missense	1f	yes
rs7008207	EPHX2	a	c	95,5	6,356	2,07E-10	+++	-52,9	2,616	2	0,2704	4,50E-06		EPHX2	yes	42 547	intron	6	
rs11089856	H1FO	a	c	95,5	-6,26	3,85E-10	---	42,4	6,939	2	0,03114	8,11E-06		GCAT	-	4 671	intron	5	
rs178092	SNAP29	a	c	95,5	6,25	4,11E-10	+++	37,7	6,419	2	0,04038	8,51E-06		-	-	45 001	intergenic		yes
rs403908	CARKD	a	g	95,5	-6,101	1,05E-09	---	12	4,547	2	0,103	1,88E-05		CARKD	yes	17 752	intron	5	yes
rs10872251	FABP7	a	g	95,5	6,097	1,08E-09	++	87,3	31,5	2	1,45E-07	1,91E-05	yes	FABP7	yes	3 449	intron	6	
rs10861347	KIAA1033	t	c	95,5	6,091	1,12E-09	+++	78	18,148	2	0,0001146	1,98E-05		ALDH1L2	-	-24 081	intron	3a	

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rs2491020	KIAA1279	a	g	95,5	-6,085	1,17E-09	---	37,2	6,368	2	0,04143	2,05E-05	-	-	30 090	downstream	4	yes	
rs1131017	RPS26	c	g	95,5	-5,999	1,98E-09	---	80,2	20,194	2	4,12E-05	3,28E-05	RPS26	yes	244	5'UTR	4	yes	
rs4443587	KLHDC10	t	g	95,5	5,95	2,67E-09	+++	78,2	18,332	2	0,0001045	4,34E-05	-	-	68 170	downstream	6		
rs1271970	RPP40	a	g	95,5	-5,886	3,95E-09	---	42,9	7,004	2	0,03014	6,22E-05	RPP40	yes	-207	downstream	6	yes	
rs34270592	AMFR	a	c	95,5	5,884	3,99E-09	+++	42,9	7,009	2	0,03006	6,27E-05	AMFR	yes	36 315	intron	6		
rs17137288	TYW1	a	g	95,5	-5,849	4,94E-09	---	46,2	7,437	2	0,02427	7,65E-05	TYW1	yes	120 179	intron	6	yes	
rs11779069	LY96	t	c	95,5	-5,804	6,49E-09	---	44	7,14	2	0,02815	9,88E-05	UBE2W	yes	-134 803	intron	6		
rs8070763	STAT3	t	c	95,5	-5,784	7,29E-09	---	67,9	12,467	2	0,001963	0,00010992	STAT3	yes	71 054	intron			
rs12433361	ARG2	a	t	95,5	5,761	8,38E-09	+++	32,4	5,92	2	0,05182	0,00012319	ARG2	yes	8 488	intron		yes	
rs141761164	PSMG1	t	c	95,5	-5,732	9,90E-09	---	0	1,483	2	0,4764	0,00014325	-	-	-18 253	intergenic			
rs7646106	ARL8B	t	c	95,5	5,694	1,24E-08	+++	0	0,088	2	0,9572	0,00016938	EDEM1	yes	94 042	3'UTR			
rs3762815	PDCD6IP	a	g	95,5	5,646	1,64E-08	+++	70	13,34	2	0,001269	0,00021789	PDCD6IP	yes	23 658	intron	5		
rs17354693	HYDIN	a	g	95,5	5,595	2,21E-08	+++	28,8	5,621	2	0,06019	0,0002602	MARVELD3	-	822 416	intron	5	yes	
rs7487568	CHD4	t	c	95,5	5,593	2,24E-08	+++	0	1,781	2	0,4105	0,00026276	ANO2	-	-686 186	intron			
rs3816864	LPPR2	t	g	95,5	-5,582	2,37E-08	---	-12,9	3,542	2	0,1702	0,00027352	RAB3D	-	-19 541	intron	5	yes	
rs6537035	ZNF330	a	g	95,5	5,581	2,39E-08	+++	51,6	8,262	2	0,01607	0,00027491	RNF150	-	-20 349	intergenic			
rs11131799	AGA	a	g	95,5	-5,56	2,69E-08	---	-8,7	3,678	2	0,1589	0,00028666	yes	AGA	yes	11 450	intron	4	yes
rs113671109	MKRN2	t	c	95,5	5,553	2,81E-08	+++	0	1,01	2	0,6034	0,00029275	yes	MKRN2	yes	22 292	intron	6	yes
rs10902201	TMEM80	a	g	95,5	-5,527	3,25E-08	---	0	0,803	2	0,6693	0,0003311	DEAF1, EPS8L2, TMEM80	yes	8 968	downstream, upstream	5		
rs118129429	PCDH8	a	g	95,5	-5,526	3,29E-08	---	0	1,128	2	0,5688	0,0003311	LECT1	yes	-136 623	intron	6		
rs11237443	GAB2	a	c	95,5	-5,519	3,41E-08	---	0	1,832	2	0,4	0,00034023	GAB2	yes	78 754	intron		yes	
rs4737751	ARMC1	a	g	95,5	5,515	3,49E-08	+++	57	9,298	2	0,009572	0,00034776	MTFR1	yes	85 543	intron			
rs10816774	CTNNA1	a	g	95,5	-5,475	4,36E-08	---	40,2	6,688	2	0,0353	0,00042674	EPB41L4B	yes	232 151	intron	5		
rs4747339	CACNB2	t	c	95,5	-5,453	4,95E-08	---	-15,2	3,473	2	0,1761	0,00045885	CACNB2	yes	161 818	intron			
rs35962983	NR1D2	t	c	95,5	-5,399	6,70E-08	---	0	1,292	2	0,524	0,00059798	NR1D2	yes	24 432	intron			
rs6781329	HRG	a	g	95,5	-5,386	7,20E-08	---	0	1,443	2	0,486	0,0006349	-	-	-203 576	intergenic	6		
rs9428015	CCBL2	a	g	95,5	-5,353	8,65E-08	---	0	1,046	2	0,5928	0,00074335	PKN2	-	-132 115	intron	5	yes	
rs114624166	PRR16	t	g	95,5	-5,316	1,06E-07	---	41,2	6,799	2	0,03339	0,00086608	-	-	-35 365	intergenic	6	yes	

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rs2433611	GATM	a	c	95,5	-5,274	1,34E-07	---	0	0,583	2	0,747	0,00102064	GATM	yes	12 332	intron		
rs62092421	TCF4	t	g	95,5	5,243	1,58E-07	+++	54,6	8,809	2	0,01222	0,00113307	-	-	-23 468	intergenic	5	
rs11668620	TMEM161A	c	g	95,5	-5,242	1,59E-07	---	-98,2	2,018	2	0,3646	0,00114013	SLC25A42	yes	-11 939	intron	5	yes
rs12048758	CNIH4	a	g	95,5	5,235	1,65E-07	+++	0	0,137	2	0,934	0,00117581	WDR26	yes	34 454	intron		
rs111584059	DOPEY2	a	g	95,5	5,229	1,70E-07	+++	-59,3	2,51	2	0,285	0,00120534	DOPEY2	yes	25 465	intron	6	yes
rs150478765	WDR41	a	g	95,5	5,217	1,82E-07	+++	29,3	5,659	2	0,05906	0,00126536	WDR41	yes	70 691	intron		
rs62580498	CDK5RAP2	a	g	95,5	5,192	2,08E-07	+++	56,7	9,237	2	0,00987	0,00141436	CDK5RAP2	yes	8 349	intron	5	yes
rs6689008	NUCKS1	t	c	95,5	-5,188	2,13E-07	---	0	1,969	2	0,3735	0,00144529	yes	SLC45A3	-	-32 773	intron	4
rs9819419	FYCO1	a	g	95,5	-5,182	2,20E-07	---	41,3	6,811	2	0,03319	0,00147624	-	-	177 969	intergenic	5	
rs7289655	GSTT1	a	c	95,5	-5,168	2,37E-07	---	82,2	22,445	2	1,34E-05	0,00158174	-	-	-40 910	intergenic	5	yes
rs9296398	PRPH2	t	c	95,5	5,144	2,69E-07	+++	-29,2	3,095	2	0,2128	0,00177154	PRPH2	yes	9 346	intron		yes
rs6572656	ATP5S	a	c	95,5	5,116	3,13E-07	+++	19,8	4,987	2	0,08263	0,00201754	L2HGDH	-	-3 727	intron	1b	yes
rs246771	KCNIP1	c	g	95,5	-5,113	3,18E-07	---	16,4	4,783	2	0,09148	0,00204533	DOCK2	yes	-658 847	intron	6	
rs2490273	ZNF593	t	g	95,5	5,112	3,19E-07	++	78,3	18,405	2	0,0001008	0,00204985	-	-	-6 629	downstream	5	
rs3120065	OSGEP	t	c	95,5	-5,09	3,58E-07	---	19,5	4,971	2	0,08329	0,00225477	OSGEP	yes	4 506	intron		yes
rs2359614	EIF2B2	a	t	95,5	-5,059	4,22E-07	-+	66,1	11,786	2	0,002758	0,00253322	TMED10	-	160 173	intron	5	yes
rs7657455	MFAP3L	c	g	95,5	5,048	4,46E-07	+++	80,6	20,608	2	3,35E-05	0,00266691	-	-	51 096	intergenic	5	yes
rs17818245	COX4I1	a	g	95,5	5,042	4,60E-07	+++	-0,1	3,995	2	0,1357	0,00272888	yes	-	-	241 929	intergenic	
rs59633892	CDKAL1	t	c	95,5	-5,016	5,28E-07	---	60,3	10,068	2	0,006514	0,00309946	-	-	698 658	downstream		yes
rs10823398	TSPAN15	a	c	95,5	-5,003	5,64E-07	---	0	0,028	2	0,9862	0,00329182	-	-	59 138	downstream		
rs72940355	FECH	a	g	95,5	-4,984	6,22E-07	---	30,9	5,793	2	0,05523	0,00358652	FECH	yes	20 685	intron	6	
17-44619118	NSF	a	g	95,5	4,98	6,35E-07	+++	0	0,575	2	0,7502	0,00364945	LRRC37A2, ARL17A	-	-48 916	intron		
rs35030877	COG7	a	g	95,5	-4,977	6,46E-07	---	-7,5	3,722	2	0,1555	0,00370233	-	-	-4 785	downstream	6	
rs75000818	SGCB	a	g	95,5	4,973	6,59E-07	+++	0	1,685	2	0,4306	0,00377028	-	-	196 337	intergenic		
rs1899288	CPNE3	t	c	95,5	4,967	6,82E-07	+++	71,9	14,226	2	0,0008143	0,00388201	CPNE3	yes	38 671	intron		
rs148654891	FIBP	a	g	95,5	-4,952	7,34E-07	---	-19,1	3,359	2	0,1865	0,00410278	-	-	-75 947	intergenic		
rs10200594	WIPF1	a	g	95,5	-4,95	7,43E-07	---	-72,9	2,313	2	0,3146	0,00410278	-	-	-12 812	upstream	4	
rs8007801	EML1	c	g	95,5	4,942	7,72E-07	+++	-10	3,638	2	0,1622	0,00422405	-	-	393 986	intergenic	5	

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rs78701930	HMBX1	t	c	95,5	4,935	8,00E-07	+++	57,3	9,358	2	0,009289	0,00436969	KIF13B	yes	215 862	intron			
rs2520180	C17orf48	t	c	95,5	4,931	8,17E-07	+++	-12,3	3,561	2	0,1685	0,00443719	SCO1	-	-6 597	intron		yes	
rs12086750	PPIE	c	g	95,5	4,924	8,48E-07	+++	70,5	13,546	2	0,001144	0,0045865	PPIE	yes	5 952	intron	5	yes	
rs11204702	ARNT	a	c	95,5	4,924	8,49E-07	+++	80,3	20,316	2	3,88E-05	0,00459016	GOLPH3L	yes	-118 673	intron			
rs61752479	AMPD1	a	g	95,5	-4,922	8,57E-07	---	64,8	11,369	2	0,003398	0,00460719	AMPD1	yes	15 535	missense			
rs35044129	PDLIM5	a	t	95,5	4,917	8,79E-07	+++	27,8	5,538	2	0,06273	0,00469205	PDLIM5	yes	139 807	intron	6		
rs73181350	PCK1	c	g	95,5	4,913	8,97E-07	++	90,8	43,446	2	3,68E-10	0,00476031	-	-	512 190	intergenic			
11-36166998	TRAF6	a	g	95,5	-4,905	9,34E-07	---	60	10,009	2	0,006708	0,00493152	LDLRAD3	-	-338 318	intron			
rs13267051	CCDC25	a	g	95,5	4,896	9,76E-07	+++	0	1,28	2	0,5273	0,00511079	CCDC25	yes	22 484	intron	5		
rs935074	SPSB1	a	g	95,5	4,876	1,08E-06	+++	0	0,071	2	0,9652	0,00558444	CTNNBIP1	yes	577 027	intron	5		
rs2297811	CYP4B1	t	c	95,5	4,876	1,08E-06	+++	53,5	8,603	2	0,01355	0,00559199	CYP4B1	yes	15 120	intron	6	yes	
rs56007403	LGMN	t	c	95,5	-4,872	1,11E-06	---	0	0,469	2	0,791	0,00568303	yes	SLC24A4	-	-247 484	intron	5	
rs1218556	LENEP	t	g	95,5	-4,861	1,17E-06	---	-1	3,96	2	0,1381	0,00594316	KCNN3	yes	-144 949	intron	5		
rs72670883	ZCCHC11	t	c	95,5	-4,85	1,23E-06	---	0	0,529	2	0,7675	0,006232	SLC1A7	-	709 213	intron			
rs76611793	CPVL	t	c	95,5	-4,836	1,32E-06	---	-5,2	3,802	2	0,1494	0,00661326	CPVL, CHN2	yes	146 872	intron	5		
rs2543519	MPST	a	g	95,5	-4,833	1,35E-06	---	0	1,268	2	0,5305	0,00671862	TMPRSS6	yes	64 568	intron	5		
rs147990233	RPS16	a	t	95,5	4,823	1,41E-06	+++	54,2	8,728	2	0,01273	0,00698077	SUPT5H	yes	28 629	intron		yes	
rs11119673	KCNH1	a	t	95,5	-4,812	1,49E-06	---	-65,7	2,414	2	0,2992	0,00729092	KCNH1	yes	381 442	intron	5		
rs686618	PAMR1	t	c	95,5	-4,811	1,50E-06	---	0	1,812	2	0,4042	0,00730873	-	-	113 019	intergenic			
rs56019197	TMEM110	t	c	95,5	-4,81	1,51E-06	---	0	0,264	2	0,8764	0,0073618	TMEM110	yes	3 982	intron			
rs2032890	ERAP1	a	c	95,5	4,797	1,61E-06	+++	65,3	11,523	2	0,003146	0,00778284	ERAP1	yes	10 965	intron		yes	
rs1033181	MYCT1	a	g	95,5	-4,791	1,66E-06	---	0	1,768	2	0,4131	0,00795101	ESR1	yes	-824 208	intron			
rs2517145	PDGFRL	a	c	95,5	-4,769	1,85E-06	---	0	0,94	2	0,6251	0,00875921	PDGFRL	yes	11 892	intron	6		
rs11057389	ABCB9	t	c	95,5	-4,769	1,85E-06	---	14,9	4,7	2	0,09537	0,00877216	DNAH10	-	968 605	intron			
rs6739468	CRIP1	t	g	95,5	4,761	1,93E-06	+++	0	1,336	2	0,5127	0,00907339	CRIP1	yes	5 056	intron		yes	
rs113265714	ALAS1	a	g	95,5	4,752	2,02E-06	+++	0	1,976	2	0,3724	0,00941876	WDR82	-	77 071	intron			
rs7503584	PNPO	a	g	95,5	-4,751	2,03E-06	---	0	1,26	2	0,5327	0,00945275	CDK5RAP3	-	36 148	intron	1f		
rs2194762	ABI2	t	c	95,5	-4,743	2,11E-06	---	44,3	7,181	2	0,02758	0,00980376	-	-	841 720	intergenic		yes	

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rs11169368	CSRP2	t	c	95,5	4,74	2,14E-06	+++	-1,8	3,928	2	0,1403	0,00993279	-	-	-755 947	intergenic		
rs2114308	MMP20	a	g	95,5	4,731	2,23E-06	+++	0	1,267	2	0,5307	0,01029151	YAP1	yes	-399 232	intron	6	
rs8010851	WARS	t	c	95,5	4,73	2,25E-06	+++	18,9	4,931	2	0,08495	0,0103516	WARS	yes	24 516	intron	6	
rs6443851	MCCC1	a	g	95,5	4,726	2,29E-06	+++	17,1	4,823	2	0,08968	0,01051029	MCCC1	yes	86 044	upstream	6	
rs4268913	TMBIM1	a	g	95,5	-4,719	2,37E-06	---	0	1,809	2	0,4047	0,01082444	PNKD	-	39 959	intron	6	
rs35273276	ZBTB16	t	g	95,5	4,718	2,39E-06	+++	0	0,419	2	0,8109	0,01086709	yes	-	-	936 909	intergenic	
rs10829610	MGMT	a	g	95,5	4,716	2,40E-06	+++	-55,2	2,577	2	0,2756	0,01093736	MGMT	yes	165 615	intron	6	yes
rs200680626	B3GALNT1	a	g	95,5	-4,713	2,44E-06	---	-63,5	2,447	2	0,2942	0,01109586	yes	-	-	848 718	intergenic	
rs12510251	ING2	a	g	95,5	-4,693	2,70E-06	---	-48,6	2,691	2	0,2604	0,01191568	ODZ3	yes	-811 635	intron	6	
rs11265398	S100A9	a	g	95,5	-4,69	2,73E-06	---	89,1	36,632	2	1,11E-08	0,01203476	UBAP2L	yes	905 328	intron	5	
rs7534861	MOSC1	a	g	95,5	-4,689	2,75E-06	---	0	1,138	2	0,566	0,01211015	MARC1	-	25 862	intron	3a	
rs75701904	KLHL2	t	c	95,5	-4,687	2,77E-06	---	-19,5	3,346	2	0,1877	0,01218174	-	-	318 830	intergenic		
rs13275128	MSRA	c	g	95,5	-4,685	2,80E-06	---	0	1,129	2	0,5687	0,01233604	MSRA	yes	170 804	intron	6	yes
rs7725534	MRPL22	t	c	95,5	-4,68	2,87E-06	---	0	0,802	2	0,6698	0,01259078	-	-	403 490	intergenic		
rs10509573	IFIT2	t	c	95,5	-4,674	2,96E-06	---	0	1,034	2	0,5963	0,01284854	-	-	127 516	downstream	6	
rs4383259	ZNF415	a	g	95,5	-4,667	3,06E-06	---	-22,1	3,275	2	0,1945	0,01323687	ZNF347	-	50 206	intron	5	
rs140929099	COL4A2	t	c	95,5	4,66	3,17E-06	+++	-33	3,007	2	0,2224	0,01364047	COL4A1	-	-54 157	intron		
rs3903399	RBBP5	t	c	95,5	4,657	3,20E-06	+++	64	11,101	2	0,003886	0,01376838	CNTN2	yes	-13 727	intron	5	
rs79079466	UNC5B	t	c	95,5	-4,656	3,23E-06	---	0	1,909	2	0,385	0,01384725	CDH23	-	423 042	intron	4	
rs79028889	CNGA1	a	g	95,5	4,65	3,32E-06	+++	0	0,282	2	0,8684	0,01408365	CORIN	yes	-319 732	intron	6	
rs12978924	C19orf57	t	c	95,5	4,645	3,41E-06	+++	0	1,794	2	0,4077	0,01436931	CACNA1A	yes	-454 970	intron		
rs12206195	SMPDL3A	a	c	95,5	-4,641	3,47E-06	---	0	1,75	2	0,4169	0,01452832	-	-	73 794	intergenic	6	
rs10194503	DHX57	c	g	95,5	-4,632	3,63E-06	---	0	0,203	2	0,9034	0,01495591	GALM	-	-104 393	intron	6	
rs79294885	NOP10	a	c	95,5	-4,628	3,69E-06	---	-33,8	2,989	2	0,2244	0,01518109	SLC12A6	yes	-4 046	intron	4	
rs36094466	FOXI1	a	g	95,5	4,628	3,70E-06	+++	0	0,67	2	0,7154	0,01521513	-	-	37 769	intergenic		
rs2216704	PPWD1	a	g	95,5	4,623	3,79E-06	+++	0	0,139	2	0,9329	0,01543906	-	-	-921 047	intergenic	6	yes
rs78291594	PRPSAP2	a	g	95,5	4,62	3,85E-06	+++	0	0,428	2	0,8075	0,01562557	FAM18B1	-	-69 161	intron	5	
rs10751259	UVRAG	t	c	95,5	4,619	3,86E-06	+++	0,2	4,006	2	0,1349	0,01568339	LRRC32	yes	730 661	intron	5	

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rs114026170	PPP2R2D	c	g	95,5	4,616	3,92E-06	+++	66,6	11,968	2	0,002519	0,01585021		PPP2R2D	yes	18 892	intron	5
rs62179167	AGPS	t	c	95,5	-4,616	3,92E-06	---	-80,8	2,213	2	0,3307	0,01585117		OSBPL6	-	902 043	intron	6
rs7534670	USP1	a	g	95,5	-4,613	3,97E-06	---	0	0,969	2	0,616	0,01602956		ALG6	yes	963 636	intron	6
rs12653735	COMMD10	a	c	95,5	-4,605	4,13E-06	---	0	0,648	2	0,7234	0,01646018		COMMD10	yes	301 808	intron	5
rs8062453	DEXI	t	g	95,5	-4,603	4,16E-06	---	0	0,247	2	0,8839	0,01650584	yes	LITAF	yes	651 635	intron	
rs4740353	C9orf78	t	c	95,5	-4,602	4,18E-06	---	-7,6	3,718	2	0,1558	0,01650584		HMCN2	-	658 805	intron	5
rs62223782	DYRK1A	t	c	95,5	4,6	4,24E-06	+++	-94,1	2,061	2	0,3569	0,01655952		HLCS	yes	-573 641	intron	
rs8063558	ABAT	t	c	95,5	-4,596	4,30E-06	---	-15,5	3,463	2	0,177	0,01676633		-	-	-1 012 732	intergenic	6
rs1887353	TPP2	a	g	95,5	-4,594	4,34E-06	---	-25,4	3,19	2	0,2029	0,01687961		-	-	-12 082	intergenic	5
rs56039808	NFKBIB	t	c	95,5	4,592	4,39E-06	+++	0	1,832	2	0,4001	0,01704252	yes	SIPA1L3	yes	-827 407	intron	5
rs184005941	THAP7	a	c	95,5	-4,592	4,39E-06	---	0	0,439	2	0,8031	0,0170478		MAPK1	yes	774 756	intron	
rs1036951	SLC22A3	c	g	95,5	4,591	4,41E-06	+++	0	0,456	2	0,7963	0,01712683		IGF2R	yes	-309 342	intron	yes
rs7334264	MPHOSPH8	c	g	95,5	4,591	4,42E-06	+++	0	1,483	2	0,4765	0,01715148		-	-	641 645	intergenic	
rs2332313	COX11	t	g	95,5	-4,588	4,48E-06	---	0	1,67	2	0,4339	0,01735707		TOM1L1	-	-10 433	intron	5
rs2811555	GLUL	a	g	95,5	-4,587	4,49E-06	---	-83,6	2,178	2	0,3365	0,01738867		NMNAT2	yes	958 681	intron	6
rs9955053	WDR7	a	t	95,5	-4,587	4,51E-06	---	-21,9	3,281	2	0,1939	0,0174325		-	-	382 825	downstream	6
rs74646715	MRS2	a	g	95,5	4,585	4,54E-06	+++	-59,5	2,507	2	0,2855	0,01755546		MRS2	yes	18 587	intron	6
rs2232669	POLR1D	t	c	95,5	-4,579	4,66E-06	---	-62	2,469	2	0,291	0,01796695		POLR1D	yes	-420	intron	4
rs12171327	EXOSC9	a	g	95,5	4,577	4,71E-06	+++	0	1,981	2	0,3715	0,01811298		-	-	-70 791	intergenic	6
rs7851652	LHX3	t	c	95,5	-4,575	4,76E-06	---	-85,4	2,157	2	0,34	0,01826053		-	-	-574 982	downstream	6
rs61946623	FAM48A	a	g	95,5	-4,574	4,78E-06	---	9	4,397	2	0,111	0,01832717		-	-	530 953	intergenic	5
rs9535526	RNASEH2B	t	c	95,5	-4,573	4,82E-06	---	0	0,784	2	0,6756	0,01843265		RNASEH2B	yes	632	intron	1b yes
rs4938447	PHLDB1	a	c	95,5	4,569	4,90E-06	+++	0	1,372	2	0,5037	0,01869764		-	-	-720 862	intergenic	
rs78358857	DLGAP1	t	c	95,5	-4,568	4,92E-06	---	0	1,612	2	0,4467	0,0187572		DLGAP1	yes	571 525	intron	6
rs7782374	CHN2	t	c	95,5	-4,565	5,00E-06	---	-6,7	3,75	2	0,1534	0,01902723		CHN2	yes	-26 428	intron	5
rs6069006	BCAS1	a	g	95,5	4,564	5,03E-06	+++	0	0,313	2	0,8551	0,01912073		-	-	900 116	intergenic	5
rs4254466	PPP1CB	a	g	95,5	-4,558	5,16E-06	---	50,2	8,027	2	0,01807	0,01952426		PPP1CB, SPDYA	yes	34 436	intron	
rs2922932	DLX5	a	g	95,5	-4,555	5,23E-06	---	-14,7	3,488	2	0,1748	0,01973571		-	-	-254 891	intergenic	5

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rs11168700	C12orf41	a	c	95,5	-4,552	5,31E-06	---	-21,8	3,284	2	0,1936	0,01991291	CCNT1	yes	34 204	intron	2b
rs72844739	CD151	c	g	95,5	-4,548	5,41E-06	---	44,8	7,24	2	0,02678	0,02026703	DEAF1	yes	-175 399	intron	5
4-7837218	KIAA0232	a	g	95,5	4,543	5,54E-06	+++	0	1,699	2	0,4275	0,02070535	AFAP1	-	1 052 760	intron	
rs2890662	KLHL5	a	g	95,5	-4,543	5,55E-06	---	0	1,44	2	0,4867	0,02075025	KLHL5	yes	53 929	intron	6
rs7920643	LARP4B	a	t	95,5	-4,538	5,69E-06	---	0	0,749	2	0,6875	0,02114456	-	-	999 011	intergenic	5
rs36073297	OPA3	t	c	95,5	4,538	5,69E-06	+++	0	1,122	2	0,5706	0,02114822	MARK4	yes	-292 775	intron	5
rs143844677	CDC14B	t	c	95,5	-4,535	5,76E-06	---	0	1,275	2	0,5285	0,02131638	-	-	-401 822	intergenic	
rs71455663	FUJ13224	a	t	95,5	4,533	5,82E-06	+++	-73,5	2,306	2	0,3157	0,02148959	DENND5B	-	82 812	intron	6
rs8003968	ESRRB	a	c	95,5	-4,532	5,85E-06	---	0	1,265	2	0,5313	0,02158124	ESRRB	yes	-45 606	intron	6
rs6065703	JPH2	t	c	95,5	-4,527	5,99E-06	---	-24	3,225	2	0,1994	0,02202319	-	-	-3 388	downstream	4
rs9525501	C13orf15	c	g	95,5	4,525	6,05E-06	+++	0	1,059	2	0,5889	0,02221089	-	-	25 148	intergenic	
rs115929263	KIF1A	c	g	95,5	-4,524	6,06E-06	---	0	0,2	2	0,9047	0,02221089	NDUFA10	yes	-797 962	intron	6
rs74676427	MRPL42	a	g	95,5	4,522	6,13E-06	+++	0	0,968	2	0,6164	0,02243002	-	-	625 267	intergenic	5
rs58809197	ELAC2	a	g	95,5	-4,52	6,18E-06	---	0	1,739	2	0,4192	0,02254977	ELAC2	yes	25 332	intron	6
rs10271869	GIMAP4	t	c	95,5	4,517	6,26E-06	+++	0	1,779	2	0,4109	0,02278997	-	-	-211 469	intergenic	4
rs116939934	ZNF550	a	g	95,5	-4,514	6,37E-06	---	-40,3	2,851	2	0,2404	0,02313126	-	-	-263 286	upstream	5
rs581508, rs60228684	OPN3	c	g	95,5	4,513	6,39E-06	+++	-26,8	3,154	2	0,2066	0,02320349	OPN3	yes	44 950	intron	4
rs12711940	RALB	a	t	95,5	4,509	6,51E-06	+++	39,1	6,563	2	0,03757	0,02357759	RALB	yes	25 973	intron	6
rs4351362	FLNC	c	g	95,5	4,505	6,64E-06	+++	30,2	5,732	2	0,05691	0,02388425	-	-	937 884	downstream	6
rs2810715	MIPEP	c	g	95,5	-4,504	6,67E-06	---	62,8	10,743	2	0,004647	0,0239468	-	-	201 789	intron	
rs73164728	MTMR3	a	g	95,5	-4,504	6,68E-06	---	27,1	5,489	2	0,06428	0,02398218	MTMR3, HORMAD2	yes	256 412	intron	6
rs1358085	TMOD3	a	g	95,5	-4,503	6,70E-06	---	0	0,9	2	0,6377	0,02402141	-	-	702 239	upstream	
rs10503718	BIN3	t	c	95,5	-4,503	6,71E-06	---	0	0,058	2	0,9712	0,0240506	PEBP4	-	134 650	intron	4
rs246228	ABCC1	a	c	95,5	-4,502	6,72E-06	->	71,7	14,155	2	0,0008441	0,0240572	ABCC1	yes	92 209	intron	2b
rs12456603	OSBPL1A	c	g	95,5	-4,495	6,96E-06	---	77,3	17,654	2	0,0001467	0,02463214	OSBPL1A	yes	23 409	intron	5
rs9997795	ANK2	a	g	95,5	4,49	7,14E-06	+++	0	0,044	2	0,978	0,02463511	-	-	-351 220	intergenic	
rs60208411	PIK3CD	t	c	95,5	4,479	7,50E-06	+++	0	1,605	2	0,4482	0,02507555	UBE4B	yes	434 591	intron	
rs5050	COG2	t	g	95,5	4,477	7,59E-06	+++	-62,9	2,455	2	0,293	0,02531486	AGT	yes	71 685	5'UTR	1a

SUPPLEMENTARY DATA

rs76826033	FHOD3	a	g	95,5	-4,475	7,64E-06	---	-24	3,226	2	0,1993	0,02544942	yes	FHOD3	yes	114 632	intron		
rs4547172	PFKM	a	g	95,5	-4,474	7,69E-06	---	0	1,272	2	0,5294	0,02554614		-	-	-161 233	intergenic	5	
rs2854181	FTSJ3	t	c	95,5	4,474	7,69E-06	+++	63,5	10,974	2	0,00414	0,02554871		-	-	72 495	downstream		
rs10920310	TIMM17A	c	g	95,5	4,473	7,71E-06	+++	0	0,553	2	0,7585	0,02561107		-	-	73 323	intergenic	5	yes
rs2273630	KHNYN	t	c	95,5	4,47	7,81E-06	+++	-31,1	3,05	2	0,2176	0,02574839		CBLN3, KHNYN	yes	205	5'UTR, upstream	2b	
rs2239325	ABCC6	a	c	95,5	-4,469	7,85E-06	---	-11,4	3,589	2	0,1662	0,02579527		ABCC6	yes	26 710	intron	6	
rs4839353	CSDE1	t	g	95,5	4,464	8,03E-06	+++	-0,2	3,991	2	0,136	0,02627248	yes	-	-	-658 256	intergenic		
rs72669230	MEAF6	a	g	95,5	4,461	8,16E-06	+++	0	1,297	2	0,5227	0,02667234		-	-	975 076	intergenic		
rs66708929	RPL39L	a	c	95,5	4,46	8,20E-06	+++	-72,3	2,322	2	0,3132	0,02675358		DGKG	-	-977 076	downstream	5	
rs6982560	ANXA13	c	g	95,5	-4,458	8,27E-06	---	-33,1	3,004	2	0,2227	0,02687986		-	-	734 981	intergenic		
rs62310596	CLOCK	a	g	95,5	4,456	8,35E-06	+++	0	1,104	2	0,5759	0,02704948		KIAA1211	-	816 257	intron		
rs4736320	LY6D	a	t	95,5	4,455	8,38E-06	+++	-6,2	3,765	2	0,1522	0,02713658		GML, CYP11B2	yes	128 064	intron	5	
rs10948137	RANBP9	t	c	95,5	4,452	8,51E-06	+++	0	0,263	2	0,8769	0,02737097		-	-	-961 440	intergenic	6	
rs12363722	UNC93B1	a	c	95,5	4,444	8,84E-06	+++	0	0,37	2	0,8312	0,02804576		PPP6R3	-	477 717	intron	5	
rs5805912, rs62941261	CLDN10	a	t	95,5	-4,441	8,96E-06	---	0	0,234	2	0,8895	0,0283433		ABCC4	yes	-194 420	intron	6	
rs2690923	CUX1	a	g	95,5	4,436	9,17E-06	+++	0	0,13	2	0,9371	0,02878093	yes	-	-	-24 313	intergenic		
rs28422906	SLC25A22	t	c	95,5	-4,436	9,17E-06	---	0	1,344	2	0,5106	0,02878093		AP2A2	yes	205 161	intron	5	
rs654533	CD3E	t	c	95,5	-4,434	9,25E-06	---	0	0,375	2	0,8292	0,02898132		-	-	412 514	intergenic	5	
rs12702047	GPER	a	g	95,5	4,432	9,35E-06	+++	0	0,682	2	0,7109	0,02926389	yes	C7orf50, GPER	yes	6 278	3'UTR, intron	4	
rs10752954	IVNS1ABP	a	g	95,5	-4,425	9,64E-06	---	43	7,02	2	0,0299	0,02982545		-	-	146 861	intergenic	5	
rs4781128	LITAF	a	g	95,5	4,425	9,65E-06	+++	-64,5	2,431	2	0,2965	0,0298506		LITAF	yes	65 994	intron	2b	
rs7616890	ABHD5	a	g	95,5	-4,421	9,82E-06	---	0	1,149	2	0,5629	0,02992474		ANO10	yes	-124 878	intron		
rs13195767	CDYL	t	c	95,5	4,421	9,85E-06	+++	-6,5	3,757	2	0,1528	0,02994204		-	-	-374 735	intergenic	5	yes
rs4351859	OAS1	a	c	95,5	4,419	9,94E-06	+++	-55,5	2,572	2	0,2764	0,03019668		-	-	707 146	intergenic	6	
rs112042189	OXCT1	t	c	95,5	4,413	1,02E-05	+++	0	0,136	2	0,934	0,03075482		-	-	171 231	upstream		
rs2249888	FN3KRP	a	g	95,5	4,412	1,03E-05	+++	58,9	9,741	2	0,007668	0,03089098		FN3KRP	yes	1 157	intron	1f	yes
rs677991	TULP3	t	c	95,5	-4,404	1,06E-05	---	38,3	6,488	2	0,03901	0,03178429		TSPAN9	-	358 751	intron	5	
rs145785014	FUS	t	c	95,5	4,404	1,06E-05	+++	-6,4	3,761	2	0,1525	0,03180505		-	-	398 896	intergenic		

SUPPLEMENTARY DATA

rs10249186	INSIG1	a	t	95,5	4,401	1,08E-05	+++	0	0,825	2	0,6618	0,03215427	DPP6	yes	-916 802	intron	6
rs9301945	ABCC4	t	c	95,5	4,4	1,08E-05	+++	0	0,415	2	0,8126	0,03230546	GPC6	-	-796 774	intron	6
rs28372678	BAIAP3	a	g	95,5	-4,394	1,11E-05	---	-53,2	2,611	2	0,2711	0,03274606	SPSB3	yes	449 010	upstream	2a
rs139621578	KIAA0922	a	g	95,5	4,391	1,13E-05	+++	27,3	5,499	2	0,06395	0,03305217	-	-	-478 849	intergenic	
rs1391102	ATP2C2	c	g	95,5	-4,389	1,14E-05	---	-85,9	2,151	2	0,3411	0,03328447	CRISPLD2	yes	541 168	downstream	
rs658065	FAM8A1	a	t	95,5	-4,384	1,17E-05	---	-78,6	2,239	2	0,3264	0,03391939	-	-	-808 814	intergenic	6
rs9907526	ITGB4	c	g	95,5	4,381	1,18E-05	+++	0	0,779	2	0,6774	0,03420253	PRPSAP1	yes	597 662	intron	
rs10792434	MEN1	a	g	95,5	4,38	1,19E-05	+++	-27,8	3,13	2	0,2091	0,03432872	AP003774.4	-	-352 575	3'UTR	
rs118122922	POLDIP3	t	g	95,5	-4,378	1,20E-05	---	-6,9	3,741	2	0,1541	0,03445416	MPPED1	-	921 316	intron	5
rs4461	TOM1	a	g	95,5	4,378	1,20E-05	+++	0	0,289	2	0,8656	0,03453109	TOM1	yes	6	intron	4
rs7474813	ADO	t	c	95,5	-4,374	1,22E-05	---	0	0,437	2	0,8038	0,03496645	ZNF365	yes	-175 568	intron	
rs2300371	IL10RB	t	c	95,5	-4,373	1,23E-05	-+	70	13,32	2	0,001281	0,03513308	IFNAR2	-	11 228	intron	6
rs7521247	CD244	a	g	95,5	4,371	1,24E-05	+++	0	0,425	2	0,8087	0,03530857	CD84	yes	-259 389	intron	6
rs882354	CAMK2A	a	g	95,5	-4,37	1,24E-05	---	-59,7	2,505	2	0,2858	0,03541133	SLC6A7	yes	-1 893	downstream	5
rs247902	TAF1C	t	c	95,5	4,369	1,25E-05	+++	47	7,543	2	0,02301	0,03550585	ATP2C2	yes	262 145	intron	6
rs12216486	IGF2R	a	g	95,5	-4,369	1,25E-05	---	-10,4	3,624	2	0,1633	0,0355864	-	-	-60 514	downstream	6
rs4695739	SCRG1	a	c	95,5	4,368	1,25E-05	+++	0	1,428	2	0,4896	0,03566205	-	-	274 873	intergenic	6
rs7210280	EV12A	c	g	95,5	4,368	1,25E-05	+++	56,1	9,105	2	0,01054	0,03568076	SUZ12P	-	-564 657	intron	
rs13053864	CRYBB1	t	c	95,5	-4,36	1,30E-05	---	-59,4	2,51	2	0,2851	0,03669693	-	-	877 102	intergenic	5
rs9481169	LAMA4	t	g	95,5	-4,36	1,30E-05	---	-82,2	2,195	2	0,3337	0,03676676	-	-	-499 271	upstream	5
rs4458132	PDE4C	a	t	95,5	4,358	1,31E-05	+++	0	0,495	2	0,7806	0,03700917	PDE4C	yes	17 590	intron	5
rs431691	BLM	a	g	95,5	4,354	1,34E-05	+++	0	0,829	2	0,6607	0,03759998	-	-	99 177	downstream	5
rs1858790	KCNQ1DN	a	t	95,5	4,351	1,36E-05	+++	0	0,778	2	0,6776	0,03808836	ZNF195	yes	474 308	intron	6
rs2345055	EIF2AK1	a	c	95,5	-4,348	1,37E-05	---	0	1,018	2	0,6011	0,03841638	AIMP2	yes	-1 259	intron	4
rs35755011	HOXB2	t	c	95,5	4,348	1,37E-05	+++	0	0,104	2	0,9492	0,03843405	-	-	-57 563	intergenic	4
rs146608062	SLC30A1	a	g	95,5	-4,348	1,38E-05	---	0	1,637	2	0,4412	0,03850772	-	-	-340 285	intergenic	
rs9318072	C13orf34	t	c	95,5	4,34	1,43E-05	+++	0	1,827	2	0,401	0,03959639	-	-	-309 604	intergenic	
rs2276419	HYOU1	t	c	95,5	-4,338	1,44E-05	---	0	0,763	2	0,6827	0,03973891	UBE4A	yes	-684 536	5'UTR	4

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rs4919639	PSD	c	g	95,5	4,336	1,45E-05	+++	41,6	6,853	2	0,03251	0,04011794	-	-	54 484	upstream	5	
rs4863686	TBC1D9	c	g	95,5	4,336	1,45E-05	+++	-4,4	3,833	2	0,1471	0,04017954	MAML3	yes	-863 769	intron	5	
rs62449081	GGCT	t	c	95,5	-4,32	1,56E-05	---	0	0,806	2	0,6684	0,04224068	yes	FAM188B	-	350 034	intron	5
rs4982255	PSMA6	a	g	95,5	-4,317	1,58E-05	---	0	1,591	2	0,4514	0,04270324	-	-	45 196	intergenic		
rs56982547	SNPH	a	g	95,5	-4,317	1,58E-05	---	0	0,552	2	0,7589	0,04275174	RAD21L1, SNPH	yes	16 742	intron	5	
rs1790469	GRIK4	a	g	95,5	4,317	1,59E-05	+++	31,4	5,832	2	0,05414	0,04282169	-	-	-504 575	intergenic	5	
rs75845312	ANKZF1	t	c	95,5	4,316	1,59E-05	+++	0	0,012	2	0,9939	0,04287016	-	-	815 546	intergenic		
rs35787376	RPL23A	c	g	95,5	-4,313	1,61E-05	---	5,2	4,219	2	0,1213	0,04325673	-	-	-721 322	intergenic		
rs4326952	ELF1	t	c	95,5	-4,311	1,62E-05	---	-31,5	3,043	2	0,2184	0,0434435	-	-	481 791	intergenic		
rs34302476	HBQ1	a	g	95,5	4,31	1,63E-05	+++	0	1,82	2	0,4025	0,04364955	-	-	640 329	intergenic		
rs8078610	EVI2B	t	c	95,5	-4,309	1,64E-05	---	0	0,226	2	0,8932	0,04385082	-	-	285 593	intergenic	6	
rs3818508	CELSR2	t	c	95,5	4,308	1,65E-05	+++	-78,1	2,246	2	0,3254	0,04399117	KIAA1324	-	-52 167	intron	5	
rs3796242	TSC22D2	a	t	95,5	4,308	1,65E-05	+++	0	1,805	2	0,4055	0,04401221	yes	CLRN1	-	563 652	synonymous	5
rs3784330	CIB2	t	c	95,5	4,308	1,65E-05	+++	23	5,195	2	0,07445	0,04401632	CIB2	yes	23 321	intron	4	
rs3008011	RPS6KA2	t	c	95,5	-4,307	1,65E-05	---	-9,5	3,652	2	0,161	0,04406808	PDE10A	yes	-809 093	intron	5	
rs1044522	TMEM134	a	g	95,5	-4,302	1,69E-05	---	0	0,819	2	0,6641	0,04478612	CTSF	yes	-895 986	synonymous	4	
rs11582371	SH3GLB1	t	c	95,5	4,302	1,69E-05	+++	16,1	4,769	2	0,09213	0,04480688	-	-	-180 447	intergenic		
rs339985	RORA	a	t	95,5	4,298	1,72E-05	+++	0	0,478	2	0,7872	0,04545507	RORA	yes	137 621	intron	6	
rs217401	OGDH	a	c	95,5	-4,298	1,73E-05	---	3,4	4,139	2	0,1263	0,04554332	-	-	-54 843	intergenic	6	
rs35334347	NIN	a	g	95,5	-4,296	1,74E-05	---	-90	2,105	2	0,3491	0,04576713	yes	NIN	yes	31 502	intron	
rs11895231	DGKD	t	c	95,5	-4,295	1,74E-05	---	13,2	4,609	2	0,09979	0,0458613	DGKD	yes	-2 250	intron		
rs12731262	NECAP2	t	c	95,5	4,294	1,76E-05	+++	0	1,198	2	0,5493	0,04612456	-	-	-686 224	upstream	6	
rs77604319	RPS6KC1	a	c	95,5	-4,292	1,77E-05	---	0	1,049	2	0,592	0,04648575	-	-	-536 591	intergenic	5	
rs114111458	TRAF5	a	g	95,5	4,288	1,80E-05	+++	-50,6	2,655	2	0,2651	0,04710087	HHAT	-	-901 611	intron	5	
rs2600560	DYNC111	a	g	95,5	-4,286	1,82E-05	---	-11,8	3,579	2	0,167	0,04754005	DYNC111	yes	89 946	intron		
rs12438010	PDE8A	t	g	95,5	4,285	1,82E-05	+++	0	0,528	2	0,7678	0,0475803	-	-	329 662	intergenic	5	
rs72665339	EPHB2	a	g	95,5	-4,285	1,83E-05	---	0	0,297	2	0,862	0,04759446	-	-	-606 410	intergenic	3a	
rs4512352	MATN2	a	g	95,5	-4,285	1,83E-05	---	0	1,937	2	0,3797	0,04760861	MATN2	yes	58 928	intron	6	

SUPPLEMENTARY DATA

rs533494	IL19	t	c	95,5	-4,284	1,83E-05	---	0	1,524	2	0,4667	0,04776932	PIGR	yes	107 570	intron		
rs74444868	ARFGAP3	t	c	95,5	-4,283	1,85E-05	---	0	0,527	2	0,7682	0,04798377	-	-	-7 277	intergenic		
rs61921903	USP15	t	c	95,5	-4,281	1,86E-05	---	32,8	5,949	2	0,05108	0,04826345	-	-	194 750	intergenic		
rs13003555	SP110	a	g	95,5	-4,28	1,87E-05	---	-67,2	2,392	2	0,3024	0,04849208	SP110	yes	-55 795	intron	5	
rs12584413	SACS	t	g	95,5	4,277	1,90E-05	+++	53,2	8,555	2	0,01387	0,04893561	SACS	yes	15 074	intron		
rs11622788	ADAM20	t	c	95,5	4,275	1,91E-05	++	53,7	8,648	2	0,01325	0,04926932	-	-	298 423	intergenic	6	
rs62011588	NR2F2	a	c	95,5	4,274	1,92E-05	+++	0	0,121	2	0,9411	0,04928237	NR2F2-AS1	-	-191 252	intron		
rs13278111	TNFRSF10D	t	c	95,5	4,273	1,93E-05	+++	0	1,322	2	0,5164	0,04928237	-	-	-432 912	intergenic	5	
rs12144062	PHGDH	t	c	95,5	4,271	1,95E-05	+++	0	1,341	2	0,5113	0,04954813	-	-	-130 428	intergenic		
rs2949950	HELZ	t	c	95,5	-4,27	1,96E-05	---	0	0,463	2	0,7934	0,04969809	yes	PITPNC1	yes	386 347	intron	6

SUPPLEMENTARY DATA

Supplementary Table 2. Significant (FDR < 5%, p-value = 1.34E-04) associations identified between gene expression (standardized units) and fasting plasma insulin, HOMA-IR and BMI through meta-analysis.

Gene	Phenotype	P-value	Direction	Het P-value
RCAN2	BMI	2,21E-08	-+-	0,015
SH3GLB2	BMI	3,56E-08	+++	0,508
RBBP6	BMI	8,50E-08	---	0,600
ALDH1A2	HOMA-IR	9,22E-08	++	0,009
DBNDD1	HOMA-IR	2,11E-07	++	0,015
DBNDD1	insulin	3,34E-07	++	0,006
ARHGEF10L	insulin	2,41E-06	+++	0,221
PITPNM1	BMI	3,44E-06	---	0,018
WSB2	BMI	9,29E-06	-+-	0,002
GZMH	insulin	9,89E-06	+++	0,951
BCL7A	HOMA-IR	1,03E-05	---	0,176
BCL7A	insulin	1,15E-05	---	0,186
ENPEP	BMI	1,22E-05	+++	0,440
C17orf101	insulin	1,23E-05	+++	0,229
UGT8	insulin	1,45E-05	---	0,112
FHL2	BMI	1,53E-05	-++	0,010
CA2	BMI	1,55E-05	+++	0,595
MSTN	BMI	1,82E-05	+++	0,088
DHRS7	insulin	1,84E-05	+++	0,762
IMPA2	insulin	2,39E-05	+++	0,063
ARID1A	BMI	2,52E-05	+++	0,560
TRIO	BMI	2,91E-05	---	0,774
RAF1	BMI	3,11E-05	+++	0,490
SPR	BMI	3,36E-05	---	0,011
SPOCK1	HOMA-IR	3,52E-05	---	0,175
TMOD1	BMI	3,92E-05	+++	0,036
SLC30A10	insulin	4,00E-05	---	0,817
ARHGEF10L	HOMA-IR	4,02E-05	+++	0,211
UGT8	HOMA-IR	4,36E-05	---	0,041
ALDH1A2	insulin	4,85E-05	++	0,017
C17orf101	HOMA-IR	5,15E-05	+++	0,300
DAK	insulin	5,83E-05	-++	0,000
BCKDHB	BMI	6,16E-05	---	0,881
EIF4E2	insulin	6,41E-05	+++	0,173
ARHGAP17	BMI	6,51E-05	+++	0,083
ATP6VOC	HOMA-IR	6,66E-05	-++	0,073
GZMH	HOMA-IR	6,82E-05	+++	0,988

SUPPLEMENTARY DATA

PDIA4	BMI	7,14E-05	+++	0,797
G3BP2	insulin	7,87E-05	+++	0,371
AGXT2L1	BMI	8,42E-05	---	0,372
CASQ1	insulin	8,54E-05	+++	0,191
SLC30A10	HOMA-IR	9,04E-05	---	0,764
TMED2	insulin	9,08E-05	+++	0,077
CD46	BMI	9,93E-05	+++	0,781
RNF111	HOMA-IR	1,07E-04	++	0,024
GAS6	insulin	1,20E-04	---	0,367
CTSF	BMI	1,28E-04	-+-	0,001
CALML4	insulin	1,33E-04	+++	0,403
PFKM	insulin	1,34E-04	+++	0,044

Supplementary Table 3. Significant (FDR < 5%, p-value = 7.14E-05) associations identified between gene expression (standardized units) and fasting plasma insulin adjusted for BMI, HOMA-IR adjusted for BMI and BMI through meta-analysis.

Gene	Phenotype	P-value	Direction	Het P-value
RCAN2	BMI	2,21E-08	--	0,015
SH3GLB2	BMI	3,56E-08	+++	0,508
RBBP6	BMI	8,50E-08	---	0,600
UNG	insulin(BMI)	1,08E-06	+++	0,329
CKAP5	insulin(BMI)	1,11E-06	---	0,433
PITPNM1	BMI	3,44E-06	---	0,018
TBC1D1	insulin(BMI)	4,20E-06	+++	0,196
CALML4	insulin(BMI)	9,05E-06	+++	0,192
WSB2	BMI	9,29E-06	-+-	0,002
ENPEP	BMI	1,22E-05	+++	0,440
FHL2	BMI	1,53E-05	++	0,010
CA2	BMI	1,55E-05	+++	0,595
MSTN	BMI	1,82E-05	+++	0,088
ALDH1A2	HOMA-IR(BMI)	1,95E-05	++	0,048
PRRX1	insulin(BMI)	2,32E-05	-+-	0,003
ARID1A	BMI	2,52E-05	+++	0,560
TRIO	BMI	2,91E-05	---	0,774
RAF1	BMI	3,11E-05	+++	0,490
NRXN3	insulin(BMI)	3,25E-05	--	0,008
SPR	BMI	3,36E-05	---	0,011
GAS6	insulin(BMI)	3,63E-05	---	0,724
TMOD1	BMI	3,92E-05	+++	0,036
BCKDHB	BMI	6,16E-05	---	0,881
ING2	HOMA-	6,28E-05	++	0,014

SUPPLEMENTARY DATA

	IR(BMI)			
ARHGAP17	BMI	6,51E-05	+++	0,083
ATP1B1	HOMA- IR(BMI)	6,85E-05	+++	0,534
PDIA4	BMI	7,14E-05	+++	0,797

SUPPLEMENTARY DATA

Supplementary Table 4. Extended analysis in the MM-study of the influence of the PFKM eQTL SNP (rs4547172) on skeletal muscle metabolic phenotypes.

	Non-T2D				T2D				All			
	beta	IQR	p-value	n	beta	IQR	p-value	n	beta	IQR	p-value	n
M-value			0,27		0,22	0.044-0.39	0,015	71	0,15	0.029-0.27	0,016	178
Delta RQ	0,017	0.003-0.031	0,016	102			0,4		0,011	0.00012-0.022	0,048	173
Glycogen			0,56		50,1	4.6-95.6	0,032	63			0,21	
IMTG	15,7	5.20-26.2	0,004	103			0,88		8,69	0.26-17.12	0,043	167
CGOXBW			0,22		0,25	0.022-0.48	0,032	71	0,19	0.025-0.36	0,025	178

Respiratory quotient (RQ), intra muscular triglycerides (IMTG), whole body glucose oxidation rate in the insulin stimulated state during clamp divided by body weight (CGOXBW). Delta RQ = RQclamp – RQbasal. All analysis was adjusted for age and BMI (except for M-value and CGOXBW), Delta RQ was in addition adjusted for RQbasal. M-value was square root transformed.

SUPPLEMENTARY DATA

Supplementary Table 5. Public microarray gene expression data used.

	All			T2D			Non-T2D			T2D vs. Non-T2D
	Mean	SD	n	Mean	SD	n	Mean	SD	n	p-value*
M-value (mg / kg / min)	4.41	2.27	178	3.35	1.88	71	5.12	2.24	107	1.42 x 10 ⁻⁷
Delta RQ (AU)	0.071	0.049	173	0.054	0.047	71	0.082	0.047	102	1.73 x 10 ⁻⁴
Glycogen (mmol / kg)	373	101	166	371	117	63	374	90	103	0.88
IMTG (mmol / kg)	59.3	37.8	167	60.4	39.1	64	58.6	37.2	103	0.76
CGOXBW (mg / kg / min)	1.96	0.74	178	1.75	0.65	71	2.10	0.77	107	1.99 x 10 ⁻³

*analysed using student-t test, unadjusted. SD = standard deviation

Supplementary Table 6. Publicly available expression data sets used

Study	N (T2D)	N (NGT)	N (BMI)
E-GEOD-18832	-	-	21
E-GEOD-22435	-	-	17
E-GEOD-28998	-	-	14
E-GEOD-5109	-	-	6
E-GEOD-6798	-	-	29
E-GEOD-8157	-	-	13
E-MEXP-2559	-	-	35
E-GEOD-18732	66	40	-
E-GEOD-19420	27	10	-
E-GEOD-25462	9	37	50
TOTAL	102	87	185

SUPPLEMENTARY DATA

Supplementary Figure 1. Overview of methods

Data synchronisation MM, MEI and MuTHER	<p style="text-align: center;">Genotype data</p> <p style="text-align: center;">1000 Genomes imputation (June 2011 release of the 1000 Genomes Phase 1 panel)</p> <p style="text-align: center;">Gene expression</p> <p style="text-align: center;">Gene centric approach: 7006 genes common to all 3 studies and mapped to NCBI build 37</p> <p style="text-align: center;">Phenotype Data</p> <p style="text-align: center;">Selected phenotypes: HOMA-IR, fasting plasma insulin and BMI (inversed normalised)</p>
Analysis steps	<p style="text-align: center;">Meta-analysis of <i>cis</i> eQTLs</p> <p style="text-align: center;">Associations of significant eQTL SNPs in GWAS data from MAGIC and DIAGRAM</p> <p style="text-align: center;">Meta-analysis of gene expression - phenotype associations</p> <p style="text-align: center;">Identifying genetic variation influencing clinical phenotypes through gene expression</p> <p style="text-align: center;">Extended phenotype association of <i>PFKM</i> in the Malmo Men study</p> <p style="text-align: center;">Replication of the expression-phenotype associations using publicly available data</p>

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