

Supplemental material

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Supplemental tables

Table S1. Narrow sense heritability of analyzed phenotypes estimated using GCTA.

Trait	h ²	SE	CI 95%
Fasting insulin	0.106	0.093	-0.076 – 0.288
Insulin 30min	0.236	0.109	0.022 – 0.450
Insulin 2h	0.152	0.106	-0.056 – 0.360
Fasting glucagon	0.200	0.090	0.024 – 0.377
Glucagon 2h	0.000	0.095	-0.186 – 0.186
Fasting GLP-1	0.000	0.089	-0.174 – 0.174
GLP-1 2h	0.147	0.102	-0.053 – 0.347
Fasting GIP	0.151	0.094	-0.033 – 0.335
GIP 2h	0.151	0.107	-0.059 – 0.361

Table S2. All independent loci suggestively or significantly associated with insulin and glucagon*

SNP	Chr	Position	EA/NEA	EA	Beta	SE	P	N	Candidate genes	Function
Fasting glucagon										
rs7102710	11	14265613	C/T	0.092	-0.038	0.008	8.2x10 ⁻⁰⁷	6683	SPON1	intron
rs28929474	14	94844947	T/C	0.028	0.067	0.014	1.1x10 ⁻⁰⁶	6682	SERPINA1	E -> K
rs142179968	1	39823159	C/T	0.002	0.215	0.045	2.1x10 ⁻⁰⁶	6683	MACF1	M->T
rs140436257	12	104376624	G/A	0.026	0.067	0.015	3.9x10 ⁻⁰⁶	6682	TDG	M->V
Glucagon 2h										
rs111485612	4	71554974	T/C	0.004	0.159	0.035	6.8x10 ⁻⁰⁶	6242	UTP3	P -> S
rs61740450	15	64021476	G/T	0.031	-0.058	0.013	9.1x10 ⁻⁰⁶	6234	HERC1	K -> T
Fasting insulin										
rs2943641	2	227093745	T/C	0.357	-0.048	0.009	2.4x10 ⁻⁰⁷	7781	NYAP2-IRS1	intergenic
Insulin 30 min										
rs1800437	19	46181392	C/G	0.258	-0.081	0.011	1.4x10 ⁻¹³	7243	GIPR	E -> Q
rs5015480	10	94465559	T/C	0.447	0.048	0.010	4.9x10 ⁻⁰⁷	7236	HHEX-EXOC6	intergenic
rs2248020	11	93259965	A/C	0.204	0.052	0.012	8.7x10 ⁻⁰⁶	7245	SMCO4	intron
Insulin 2h										
rs150152903	12	125451722	A/G	0.001	0.799	0.171	3.1x10 ⁻⁰⁶	7347	DHX37	A -> V

*Only SNPs with MAF>0.1% and a consistent direction of effect were included.

Linear regression of ln-transformed hormone concentrations adjusted for sex and age.

Note: Partially overlapping association data for insulin traits has been reported by the MAGIC consortium (Saxena et al, 2010)

Table S3. All independent loci suggestively and significantly associated with GLP-1 and GIP *

SNP	Chr	Position	EA/NEA	EA	Beta	SE	P	N	Genes	Function
Fasting GLP-1										
rs150495482	2	173881919	T/C	0.001	0.559	0.118	2.4×10^{-6}	4179	RAPGEF4	A->V
rs201320592	6	43487816	A/G	0.002	0.425	0.093	4.4×10^{-6}	4181	POLR1C	G132D
rs1568773	7	1248880	G/A	0.030	-0.113	0.025	5.2×10^{-6}	4180	ZFAND2A-UNCX	intergenic
rs139849083	8	145729719	A/C	0.002	-0.416	0.094	9.1×10^{-6}	4181	GPT	A11E
GLP-1 2h										
rs17683011	22	32445946	G/A	0.079	0.091	0.017	4.2×10^{-8}	3849	SLC5A1	N51S
Fasting GIP										
rs1800437	19	46181392	C/G	0.256	-0.076	0.010	4.1×10^{-15}	7825	GIPR	E->Q
rs17681684	17	9792768	A/G	0.330	0.055	0.009	1.4×10^{-9}	7826	GLP-2R	Asp317Asn
GIP 2h										
rs17683430	22	32487700	A/G	0.074	0.122	0.014	3.0×10^{-18}	7450	SLC5A1	A->T
rs1800437	19	46181392	C/G	0.258	-0.072	0.008	1.6×10^{-17}	7448	GIPR	E->Q
rs635634	9	136155000	T/C	0.195	-0.070	0.009	7.4×10^{-14}	7446	ABO	intergenic
rs150112597	2	177054181	C/G	0.006	-0.280	0.049	1.6×10^{-8}	7443	HOXD1	D218H, G218R
rs927332	6	6331873	T/C	0.550	0.040	0.007	4.1×10^{-8}	7442	F13A1	upstream
rs13421358	2	43247227	C/T	0.471	0.038	0.007	3.0×10^{-7}	7442	LOC105374569	ncRNA
rs201111080	1	176640107	T/G	0.002	-0.503	0.100	5.0×10^{-7}	7449	PAPPA2	
rs78714016	17	6981403	A/G	0.002	-0.436	0.089	9.5×10^{-7}	7446	CLEC10A	R33C
rs3741151	11	73020846	T/G	0.138	0.052	0.011	1.2×10^{-6}	7449	ARHGEF17	R388L
rs73815153	5	180432564	T/G	0.038	0.088	0.019	3.4×10^{-6}	7448	BTNL3	G365W
rs2641348	1	120437884	G/A	0.123	0.051	0.011	8.5×10^{-6}	7449	ADAM30	L359P
rs359312	10	17388143	T/C	0.051	0.076	0.017	8.6×10^{-6}	7449	ST8SIA6	intronic

*Only SNPs with MAF>0.1% and a consistent direction of effect were included.

Linear regression of ln-transformed hormone concentrations adjusted for sex and age.

Table S4. Association with mRNA expression in pancreatic islets from 191 human cadaver donors.

Locus	Gene	beta	p
rs17681684	GLP2R	-0.15	0.16
rs1800437	GIPR	-0.03	0.80
rs150112597	HOXD1	-	-
rs927332	F13A1	-0.04	0.70
rs507666	ABO	0.64	1.0×10^{-7}
rs1783011	SLC5A1	1.00	3.1×10^{-6}

Table S5. Estimated ABO allele frequencies and association results for ABO alleles with fasting and 2-hour GIP in the MDC cohort.

ABO allele	rs8176749	rs8176704	rs687289	Freq. MDC	β fasting GIP	p fasting GIP	β 2h GIP	p 2h GIP
O (Ref)	C	G	G	0.62	-	-	-	-
A1	C	G	A	0.22	-0.036(0.016)	0.027	-0.081(0.016)	3.6x10 ⁻⁷
B	T	G	A	0.08	-0.008(0.024)	0.742	-0.026(0.023)	0.247
A2	C	A	A	0.08	-0.048(0.024)	0.046	-0.041(0.023)	0.079

Linear regression of ln-transformed GIP adjusted for sex and age.

Table S6. Estimated ABO allele frequencies and association results for ABO alleles with fasting and 2-hour GIP in the PPP cohort.

ABO allele	rs687621	rs8176746	rs635634	Freq. PPP	β fasting GIP	p fasting GIP	β 2h GIP	p 2h GIP
O (Ref)	A	G	C	0.62	-	-	-	-
A1	G	G	T	0.18	-0.054(0.017)	0.001	-0.069(0.014)	4.5x10 ⁻⁷
B	G	T	C	0.12	-0.020(0.020)	0.322	-0.022(0.016)	0.171
A2	G	G	C	0.08	-0.036(0.023)	0.116	-0.012(0.019)	0.522

Linear regression of ln-transformed GIP adjusted for sex and age.

Table S7. Interaction between ABO rs635634 and fat intake on BMI.

	Total fat	SFA	MUFA	PUFA	Cholesterol
Beta (SE)	0.049 (0.015)	0.09 (0.02)	0.11 (0.04)	-0.01 (0.06)	0.02 (0.01)
p-value	0.001	0.0002	0.004	0.87	0.02

SFA=Saturated fat; MUFA=Monounsaturated fat; PUFA=Polyunsaturated fat

The intakes were expressed as % of total energy intake (E%). Interaction effects adjusted for age, sex, energy intake.

Table S8. Association between rs635634 genotype and BMI examined in strata of fat tertiles.

Beta (SE) per minor allele				
	Total fat	SFA	MUFA	Cholesterol
Low	-0.23 (0.16)	-0.45 (0.15)	-0.37 (0.16)	-0.22 (0.16)
	P=0.15	P=0.003	P=0.02	P=0.17
Medium	-0.15 (0.17)	0.17 (0.17)	0.13 (0.16)	-0.18 (0.16)
	P=0.38	P=0.32	P=0.42	P=0.26
High	0.28 (0.16)	0.23 (0.17)	0.13 (0.17)	0.29 (0.16)
	P=0.09	P=0.17	P=0.44	P=0.08

Linear regression adjusted for age and sex

Table S9a. SNPs previously associated with T2D analyzed.

T2D Risk SNP	Gene/Nearest Gene	RA	OA	OR	TRAIT	Proxy*	R2	D'
rs17106184	<i>FAF1</i>	G	A	1.1	T2D	rs1278516	1	1
rs2296172	<i>MACF1</i>	G	A	1.1	T2D			
rs10923931	<i>NOTCH2</i>	T	G	1.13	T2D	rs2793831	1	1
rs340874	<i>PROX1</i>	C	T	1.07	T2D/Fasting glucose/HOMA B			
rs243021	<i>BCL11A</i>	A	G	1.08	T2D			
rs243088	<i>BCL11A</i>	T	A	1.07	T2D	rs243083	1	1
rs3792267	<i>CAPN10</i>	G	A	1.17	T2D			
rs2975760	<i>CAPN10</i>	C	T	1.17	T2D	rs3792269	1	1
rs7607980	<i>COBLL1</i>	T	C	1.14	T2D			
rs560887	<i>G6PC2/ABCB11</i>	T	C	1.03	T2D/Fasting glucose/HOMA B			
rs780094	<i>GCKR</i>	C	T	1.06	T2D/Fasting glucose/beta-cell function/triglycerides/fasting insulin			
rs13389219	<i>GRB14</i>	C	T	1.07	T2D			
rs3923113	<i>GRB14</i>	A	C	1.07	T2D	rs10179126	0.97	1
rs2943641	<i>IRS1</i>	C	T	1.19	T2D/Fasting glucose/HOMAB, HOMA IR/AUC ins/AUC ratio/ISI			
rs7578326	<i>KIAA1486/IRS1</i>	A	G	1.11	T2D			
rs7593730	<i>RBMS1/ITGB6</i>	C	T	1.11	T2D			
rs7560163	<i>RND3</i>	G	C	1.33	T2D	NA		
rs7578597	<i>THADA</i>	T	C	1.15	T2D			
rs10200833	<i>THADA</i>	G	C	1.06	T2D	rs6744642	0.85	0.96
rs6723108	<i>TMEM163</i>	T	G	1.31	T2D/Decreased fasting plasma insulin/HOMA-IR			
rs998451	<i>TMEM163</i>	G	A	1.56	T2D/Decreased fasting plasma insulin/HOMA-IR	rs6723108	0.85	1
rs4607103	<i>ADAMTS9-AS2</i>	C	T	1.09	T2D			
rs6795735	<i>ADAMTS9-AS2</i>	C	T	1.09	T2D			
rs11708067	<i>ADCY5</i>	A	G	1.12	T2D/2hr glucose/HOMA B			
rs2877716	<i>ADCY5</i>	C	T	1.12	T2D/2 h insulin adjusted for 2 h glucose/2 h glucose			
rs11071657	<i>FAM148B</i>	A	G	1.03	T2D/Fasting glucose/HOMA B			
rs1470579	<i>IGF2BP2</i>	C	A	1.15	T2D			
rs4402960	<i>IGF2BP2</i>	T	G	1.11	T2D			
rs6808574	<i>LPP</i>	C	T	1.07	T2D			
rs1801282	<i>PPARG</i>	C	G	1.09	T2D			
rs13081389	<i>PPARG</i>	A	G	1.24	T2D			
rs17036160	<i>PPARG</i>	C	T	1.11	T2D	rs13083375	0.9	1
rs1797912	<i>PPARG</i>	A	C	1.06	T2D	rs1177809	0.83	1
rs831571	<i>PSMD6</i>	C	T	1.09	T2D	rs35837	0.96	1
rs7647305	<i>SFRS10</i>	C	T	1.08	BMI/obesity T2D			
rs16861329	<i>ST6GAL1</i>	G	A	1.09	T2D	rs16861317	1	1
rs6780569	<i>UBE2E2</i>	G	A	1.21	T2D			
rs6815464	<i>MAEA</i>	C	G	1.13	T2D	NA		
rs7656416	<i>MAEA</i>	C	T	1.15	T2D	NA		
rs6813195	<i>TMEM154</i>	C	T	1.08	T2D			
rs1801214	<i>WFS1</i>	T	C	1.13	T2D			
rs4689388	<i>WFS1</i>	T	C	1.16	T2D			
rs10010131	<i>WFS1</i>	G	A	1.14	T2D			
rs6446482	<i>WFS1</i>	G	C	1.11	T2D	rs4481292	0.93	1
rs459193	<i>ANKRD55</i>	G	A	1.08	T2D			
rs702634	<i>ARL15</i>	A	G	1.06	T2D			
rs4457053	<i>ZBED3</i>	G	A	1.08	T2D			
rs1048886	<i>C6orf57</i>	G	A	1.54	T2D			
rs10946398	<i>CDKAL1</i>	C	A	1.12	T2D			
rs2206734	<i>CDKAL1</i>	T	C	1.2	T2D			
rs4712523	<i>CDKAL1</i>	G	A	1.27	T2D			
rs7754840	<i>CDKAL1</i>	C	G	1.17	T2D			
rs7756992	<i>CDKAL1</i>	G	A	1.2	T2D			
rs7766070	<i>CDKAL1</i>	A	C	1.23	T2D	rs9368222	1	1
rs2244020	<i>HLA-B</i>	G	A	1.09	T2D	NA		
(rs9266650)								
rs1535500	<i>KCNK16</i>	T	G	1.08	T2D			
rs3130501	<i>POU5F1-TCF19</i>	G	A	1.07	T2D			

rs9505118	<i>SSR1-RREB1</i>	A	G	1.06	T2D			
rs9470794	<i>ZFAND3</i>	C	T	1.12	T2D	rs3800364	1	1
rs17168486	<i>DGKB</i>	T	C	1.15	T2D			
rs2191349	<i>DGKB/TMEM195</i>	T	G	1.06	T2D/Fasting glucose, Homa B			
rs6467136	<i>GCC1-PAX4</i>	G	A	1.11	T2D	rs10281056	0.94	1
rs4607517	<i>GCK</i>	A	G	1.07	T2D/Fasting glucose /HOMA B			
rs849134	<i>JAZF1</i>	A	G	1.13	T2D			
rs864745	<i>JAZF1</i>	T	C	1.1	T2D			
rs12113122	<i>JAZF1</i>	G	C	1.55	T2D			
rs972283	<i>KLF14</i>	G	A	1.07	T2D/Reduced insulin sensitivity			
rs516946	<i>ANK1</i>	C	T	1.09	T2D			
rs515071	<i>ANK1</i>	G	A	1.18	T2D/Reduced beta-cell function	rs516946	1	1
rs13266634	<i>SLC30A8</i>	C	T	1.19	T2D			
rs11558471	<i>SLC30A8</i>	A	G	1.15	T2D/Fasting glucose/HOMA B			
rs3802177	<i>SLC30A8</i>	G	A	1.26	T2D			
rs896854	<i>TP53INP1</i>	T	C	1.06	T2D	rs7845219	0.85	1
rs564398	<i>CDKN2A/2B</i>	T	C	1.12	T2D			
rs10757282	<i>CDKN2A/2B</i>	C	T	1.14	T2D			
rs7018475	<i>CDKN2A/2B</i>	G	T	1.35	T2D			
rs10965250	<i>CDKN2A/2B</i>	G	A	1.2	T2D			
rs2383208	<i>CDKN2A/2B</i>	A	G	1.19	T2D			
rs10811661	<i>CDKN2B</i>	T	C	1.2	T2D	rs2383208	0.96	1
rs7034200	<i>GLIS3</i>	A	C	1.03	T2D/Fasting glucose/HOMA B			
rs7041847	<i>GLIS3</i>	A	G	1.1	T2D	rs7034200	1	1
rs10814916	<i>GLIS3</i>	C	A	1.11	T2D	rs7034200	0.93	0.97
rs17584499	<i>PTPRD</i>	T	C	1.57	T2D			
rs2796441	<i>TLE1</i>	G	A	1.07	T2D			
rs13292136	<i>TLE4 (CHCHD9)</i>	C	T	1.11	T2D			
rs10885122	<i>ADRA2A</i>	G	T	1.04	T2D/Fasting glucose/HOMA B			
rs553668	<i>ADRA2A</i>	A	G	1.42	T2D			
rs12779790	<i>CDC123, CAMK1D</i>	G	A	1.11	T2D	NA		
rs10906115	<i>CDC123/CAMK1D</i>	A	G	1.13	T2D			
rs11257655	<i>CDC123/CAMK1D</i>	C	T	1.15	T2D			
rs10886471	<i>GRK5</i>	C	T	1.12	T2D			
rs5015480	<i>HHEX</i>	C	T	1.13	T2D			
rs1111875	<i>HHEX/IDE</i>	C	T	1.13	T2D	rs10882101	1	1
rs4506565	<i>TCF7L2</i>	T	A	1.34	T2D/Fasting glucose/HOMA B			
rs7901695	<i>TCF7L2</i>	C	T	1.37	T2D			
rs7903146	<i>TCF7L2</i>	T	C	1.35	T2D/ fasting glucose/2 h glucose			
rs1802295	<i>VPS26A</i>	A	G	1.08	T2D			
rs12571751	<i>ZMIZ1</i>	A	G	1.08	T2D			
rs11603334	<i>ARAP1</i>	G	A	1.13	T2D fasting proinsulin levels/fasting glucose			
rs1552224	<i>CENTD2</i>	A	C	1.14	T2D			
rs11605924	<i>CRY2</i>	A	C	1.04	T2D/Fasting glucose/HOMA B			
rs174550	<i>FADS1</i>	T	C	1.04	T2D/Fasting glucose/HOMA B			
rs2334499	<i>HCCA2</i>	T	C	1.35	T2D			
rs3842770	<i>INS-IGF2</i>	A	G	1.18	T2D - African American	NA		
rs5215	<i>KCNJ11</i>	C	T	1.14	T2D			
rs5219	<i>KCNJ11</i>	T	C	1.14	T2D			
rs2237892	<i>KCNQ1</i>	C	T	1.25	T2D/Reduced beta-cell function			
rs2237895	<i>KCNQ1</i>	C	T	1.45	T2D			
rs163184	<i>KCNQ1</i>	G	T	1.22	T2D			
rs231362	<i>KCNQ1</i>	G	A	1.08	T2D			
rs10501320	<i>MADD</i>	G	C	1.01	T2D fasting proinsulin levels/fasting glucose	rs11039165	0.88	1
rs10830963	<i>MTNR1B</i>	G	C	1.09	T2D			
rs1387153	<i>MTNR1B</i>	T	C	1.09	T2D/Reduced beta-cell function			
rs7138803	<i>BCDIN3D/FAIM2</i>	A	G	1.11	BMI/obesity T2D			
rs11063069	<i>CCND2</i>	G	A	1.12	T2D			
rs1153188	<i>DCD</i>	A	T	1.08	T2D			
rs1531343	<i>HMGA2</i>	C	G	1.1	T2D			
rs9668162	<i>HMGA2</i>	G	C	1.26	T2D	rs6581658	1	1
rs7305618	<i>HNF1A</i>	C	T	1.14	T2D			
rs35767	<i>IGF1</i>	G	A	1.04	T2D/Fasting insulin/HOMA IR			
rs10842994	<i>KLHDC5</i>	C	T	1.1	T2D			
rs4275659	<i>MPHOSPH9</i>	C	T	1.06	T2D			

rs7957197	<i>OASL/TCF1/HNF1A</i>	T	A	1.07	T2D				
rs7961581	<i>TSPAN8, LGR5</i>	C	T	1.09	T2D				
rs9552911	<i>SGCG</i>	G	A	1.63	T2D	NA			
rs1359790	<i>SPRY2</i>	G	A	1.15	T2D				
rs2028299	<i>AP3S2</i>	C	A	1.1	T2D				
rs7172432	<i>C2CD4A/B</i>	A	G	1.14	T2D/Reduced beta-cell function				
rs7178572	<i>HMG20A</i>	A	G	1.09	lean T2D	rs1022172	0.96	1	
rs7177055	<i>HMG20A</i>	A	G	1.08	T2D				
rs8042680	<i>PRC1</i>	A	C	1.07	T2D				
rs7403531	<i>RASGRP1</i>	T	C	1.1	T2D				
rs4502156	<i>VPS13C/C2CD4A/B</i>	T	C	1.07	T2D/fasting proinsulin levels				
rs11634397	<i>ZFAND6</i>	G	A	1.06	T2D				
rs7202877	<i>BCAR1</i>	T	G	1.12	T2D				
rs8050136	<i>FTO</i>	A	C	1.17	T2D/Increased BMI, reduced insulin sensitivity				
rs9939609	<i>FTO</i>	A	T	1.25	T2D (obese)				
rs11642841	<i>FTO</i>	A	C	1.13	T2D				
rs4430796	<i>HNF1B</i>	G	A	1.19	T2D/Reduced beta-cell function				
rs7501939	<i>HNF1B</i>	T	C	1.09	T2D				
rs391300	<i>SRR</i>	G	A	1.28	T2D				
rs4523957	<i>SRR</i>	T		1.27	T2D	rs216219	0.93	1	
rs8090011	<i>LAMA1</i>	G	C	1.13	lean T2D	rs7240767	1	1	
rs12970134	<i>MC4R</i>	A	G	1.08	T2D/BMI/waist circumference/insulin resistance				
rs17782313	<i>MC4R</i>	C	T	1.06	BMI/T2D				
rs3794991	<i>GATAD2A/CILP2</i>	T	C	1.12	T2D	rs10401969	1	1	
rs8108269	<i>GIPR</i>	G	T	1.05	T2D				
rs10423928	<i>GIPR</i>	A	T		2 h glucose/Insulinogenic index/AUCins/gluc/2-h insulin, adjusted for 2 h glucose/T2D	rs11672660	1	1	
rs3786897	<i>PEPD</i>	A	G	1.1	T2D	NA			
rs10401969	<i>SUGP1/CILP2</i>	C	T	1.13	T2D				
rs6017317	<i>FITM2-R3HDML-HNF4A</i>	G	T	1.09	T2D	rs6031507	0.85	0.95	
rs4812829	<i>HNF4A</i>	A	G	1.09	T2D	NA			
rs5945326	<i>DUSP9</i>	A	G	1.27	T2D	NA			
rs12010175	<i>FAM58A</i>	G	A	1.21	T2D				

*For SNPs not present on the OmniExpressExome array a proxy SNP was used

Table S9b. SNPs previously associated with T2D-related traits analyzed.

T2D Risk SNP	Gene/Nearest Gene	RA	OA	Beta	TRAIT	Proxy*	R2	D'
rs2785980	LYPLAL1	T	C	0.017	fasting insulin			
rs9727115	SNX7	G	A	0.013	fasting proinsulin levels adj. for fasting glucose			
rs1371614	DPYSL5	T	C	0.022	Fasting glucose			
rs2943634	IRS1	C	A	0.025	fasting insulin, CAD			
rs4675095	IRS1	A	T	-0.006/-0.002	fasting glucose/HOMA-IR	NA		
rs11920090	SLC2A2	T	A	0.02	Fasting glucose/HOMA B/HBA1C			
rs17046216	MSMO1	A	T	0.18/0.19	Fasting Insulin/insulin resistance	rs17488814	0.93	1
rs4691380	PDGFC	C	T	0.021	fasting insulin			
rs6235	PCSK1	G	C	0.039/-0.014	fasting proinsulin levels/Fasting glucose			
rs13179048	PCSK1	C	A	0.018	Fasting glucose			
rs4646949	TAF11	T	G	0.02	fasting insulin			
rs6943153	GRB10	C	T	0.015	FG, FI			
rs4841132	PPP1R3B	A	G	0.03	Fasting glucose			
rs7077836	TCERG1L	T	C	0.28/0.34	Fasting Insulin/ insulin resistance	rs7069620	1	1
rs10838687	MADD	T	G	0.025	fasting proinsulin levels			
rs7944584	MADD	A	T	0.021	Fasting proinsulin/Fasting glucose/Homa B			
rs1483121	OR4S1	G	A	0.015	Fasting glucose			
rs2074356	HECTD4/C12orf51				1-h plasma glucose			
rs2293941	PDX1 - AS1	A	G	0.016	Fasting glucose			
rs1549318	LARP6	T	C	0.019	fasting proinsulin levels			
rs17271305	VPS13C	G	A	0.07	2hr glucose/2-h insulin, adjusted for 2-h glucose			
rs4790333	SGSM2	T	C	0.015	fasting proinsulin levels			
rs6048205	FOXA2/LINC00261	A	G	0.029	Fasting glucose	rs2277763	1	1

*For SNPs not present on the OmniExpressExome array a proxy SNP was used

Table S10. Associations of known T2D loci with serum GIP concentrations.

T2D Risk SNP	Gene/Nearest Gene	EA	Fasting GIP			2-hour GIP				
			Beta	SE	P	N	Beta	SE	P	N
rs17106184*	<i>FAF1</i>	A	0.011	0.019	0.580	3120	-0.011	0.019	0.550	2764
rs2785980	<i>LYPLAL1</i>	C	-0.014	0.013	0.265	3106	-0.006	0.012	0.606	2752
rs2296172	<i>MACF1</i>	G	0.010	0.010	0.319	7828	-0.007	0.009	0.426	7450
rs10923931*	<i>NOTCH2</i>	C	0.010	0.021	0.644	3116	0.014	0.020	0.496	2761
rs340874	<i>PROX1</i>	T	-0.014	0.008	0.103	7828	-0.016	0.007	0.034	7450
rs9727115	<i>SNX7</i>	A	-0.009	0.009	0.298	7825	-0.007	0.008	0.363	7447
rs243021	<i>BCL11A</i>	A	-0.010	0.009	0.232	7827	-0.006	0.007	0.448	7449
rs243088*	<i>BCL11A</i>	G	-0.017	0.012	0.165	3121	0.003	0.012	0.822	2765
rs3792267	<i>CAPN10</i>	A	-0.016	0.013	0.208	3121	0.003	0.013	0.807	2765
rs2975760*	<i>CAPN10</i>	G	0.003	0.016	0.844	3122	-0.001	0.016	0.959	2766
rs7607980	<i>COBLL1</i>	C	-0.027	0.013	0.033	7828	-0.018	0.011	0.114	7450
rs1371614	<i>DPYSL5</i>	T	-0.001	0.014	0.920	3121	0.008	0.013	0.537	2765
rs560887	<i>G6PC2/ABCB11</i>	T	0.007	0.009	0.455	7826	-0.006	0.008	0.453	7448
rs780094	<i>GCKR</i>	T	0.005	0.009	0.554	7828	-0.018	0.008	0.021	7450
rs13389219	<i>GRB14</i>	T	-0.014	0.009	0.110	7816	-0.013	0.008	0.092	7438
rs3923113*	<i>GRB14</i>	G	-0.018	0.009	0.042	7798	-0.016	0.008	0.041	7423
rs2943634	<i>IRS1</i>	A	-0.010	0.009	0.247	7826	0.013	0.008	0.089	7448
rs2943641	<i>IRS1</i>	T	-0.012	0.009	0.173	7824	0.014	0.008	0.075	7446
rs7578326	<i>KIAA1486/IRS1</i>	G	-0.006	0.009	0.479	7828	0.007	0.008	0.385	7450
rs7593730	<i>RBMS1/ITGB6</i>	T	-0.023	0.011	0.028	7827	-0.005	0.009	0.600	7450
rs7578597	<i>THADA</i>	C	-0.017	0.016	0.279	7822	-0.002	0.014	0.878	7446
rs10200833*	<i>THADA</i>	T	0.024	0.014	0.072	3120	0.010	0.013	0.439	2764
rs6723108	<i>TMEM163</i>	T	0.006	0.012	0.597	3122	-0.001	0.011	0.941	2766
rs998451*	<i>TMEM163</i>	T	0.006	0.012	0.597	3122	-0.001	0.011	0.941	2766
rs4607103	<i>ADAMTS9-AS2</i>	T	0.007	0.010	0.512	7821	-0.003	0.009	0.777	7443
rs6795735	<i>ADAMTS9-AS2</i>	T	0.010	0.009	0.236	7828	0.004	0.008	0.615	7450
rs11708067	<i>ADCY5</i>	G	0.009	0.011	0.371	7828	0.002	0.009	0.847	7450
rs2877716	<i>ADCY5</i>	T	0.005	0.010	0.610	7813	-0.008	0.009	0.384	7439
rs11071657	<i>FAM148B</i>	G	0.001	0.009	0.895	7827	0.011	0.008	0.157	7449
rs1470579	<i>IGF2BP2</i>	C	-0.004	0.009	0.662	7828	-0.012	0.008	0.152	7450
rs4402960	<i>IGF2BP2</i>	T	-0.005	0.009	0.573	7827	-0.012	0.008	0.152	7449
rs6808574	<i>LPP</i>	T	0.016	0.012	0.190	3122	0.005	0.012	0.672	2766
rs1801282	<i>PPARG</i>	G	0.009	0.012	0.449	7817	0.017	0.010	0.103	7441
rs13081389	<i>PPARG</i>	G	0.002	0.016	0.919	7800	0.014	0.014	0.309	7425
rs17036160*	<i>PPARG</i>	T	0.002	0.017	0.898	3117	0.021	0.016	0.208	2761
rs1797912*	<i>PPARG</i>	G	0.009	0.013	0.472	3120	0.000	0.012	0.977	2766
rs831571*	<i>PSMD6</i>	C	0.003	0.016	0.862	3121	0.001	0.015	0.923	2765
rs7647305	<i>SFRS10</i>	T	0.000	0.011	0.983	7825	-0.007	0.010	0.494	7446
rs11920090	<i>SLC2A2</i>	A	-0.005	0.012	0.686	7813	0.006	0.011	0.591	7437
rs16861329*	<i>ST6GAL1</i>	A	0.009	0.019	0.627	3122	-0.002	0.017	0.930	2766
rs6780569	<i>UBE2E2</i>	A	-0.004	0.019	0.837	3118	-0.022	0.018	0.233	2764
rs17046216*	<i>MSMO1</i>	G	-0.025	0.013	0.055	3118	0.003	0.012	0.788	2762
rs4691380	<i>PDGFC</i>	T	0.008	0.009	0.412	7825	0.007	0.008	0.400	7447
rs6813195	<i>TMEM154</i>	T	0.011	0.009	0.225	7828	0.000	0.008	0.965	7450
rs1801214	<i>WFS1</i>	C	-0.011	0.008	0.211	7825	-0.018	0.007	0.014	7447
rs4689388	<i>WFS1</i>	G	-0.011	0.008	0.197	7828	-0.020	0.007	0.008	7450
rs10010131	<i>WFS1</i>	A	-0.005	0.012	0.689	3026	-0.018	0.012	0.128	2690
rs6446482*	<i>WFS1</i>	C	-0.009	0.012	0.445	3122	-0.020	0.012	0.083	2766
rs459193	<i>ANKRD55</i>	A	-0.013	0.009	0.151	7825	0.002	0.008	0.763	7447
rs702634	<i>ARL15</i>	G	-0.007	0.013	0.592	3122	-0.004	0.012	0.775	2766
rs6235	<i>PCSK1</i>	G	0.007	0.009	0.473	7826	0.005	0.008	0.515	7449
rs13179048	<i>PCSK1</i>	A	0.002	0.009	0.817	7821	0.002	0.008	0.805	7443
rs4457053	<i>ZBED3</i>	G	-0.011	0.014	0.421	3119	-0.005	0.013	0.697	2763
rs1048886	<i>C6orf57</i>	G	0.006	0.016	0.710	3117	0.017	0.015	0.259	2763
rs10946398	<i>CDKAL1</i>	C	-0.013	0.009	0.142	7827	-0.008	0.008	0.329	7449
rs2206734	<i>CDKAL1</i>	T	-0.007	0.011	0.562	7828	-0.016	0.010	0.100	7450
rs4712523	<i>CDKAL1</i>	G	-0.012	0.009	0.163	7828	-0.007	0.008	0.342	7449
rs7754840	<i>CDKAL1</i>	C	-0.015	0.009	0.095	7817	-0.008	0.008	0.286	7441
rs7756992	<i>CDKAL1</i>	G	-0.007	0.009	0.448	7827	-0.007	0.008	0.358	7449
rs7766070*	<i>CDKAL1</i>	A	-0.008	0.014	0.534	3122	-0.009	0.013	0.469	2766
rs1535500	<i>KCNK16</i>	T	0.022	0.012	0.074	3017	0.006	0.012	0.589	2678
rs3130501	<i>POU5F1-TCF19</i>	A	-0.017	0.010	0.080	7828	-0.012	0.008	0.148	7450
rs9505118	<i>SSR1-RREB1</i>	G	-0.012	0.009	0.163	7828	0.005	0.008	0.477	7450

rs4646949	TAF11	G	0.011	0.010	0.266	7826	-0.004	0.009	0.668	7448
rs9470794*	ZFAND3	G	-0.008	0.024	0.723	3122	-0.049	0.023	0.032	2766
rs17168486	DGKB	T	0.029	0.016	0.063	3116	0.022	0.015	0.141	2762
rs2191349	DGKB/TMEM195	G	-0.002	0.008	0.788	7827	0.008	0.007	0.275	7449
rs6467136*	GCC1-PAX4	C	0.006	0.012	0.634	3121	0.024	0.012	0.040	2766
rs4607517	GCK	A	-0.009	0.012	0.479	7827	0.004	0.011	0.720	7449
rs6943153	GRB10	T	0.003	0.009	0.741	7825	0.009	0.008	0.245	7447
rs849134	JAZF1	G	-0.010	0.008	0.225	7827	0.003	0.007	0.642	7449
rs864745	JAZF1	C	-0.013	0.008	0.134	7821	0.003	0.007	0.715	7443
rs972283	KLF14	A	-0.001	0.008	0.888	7828	0.006	0.007	0.444	7450
rs516946	ANK1	T	0.022	0.010	0.032	7828	0.015	0.009	0.106	7450
rs515071*	ANK1	T	0.022	0.010	0.032	7828	0.015	0.009	0.106	7450
rs4841132	PPP1R3B	A	0.004	0.013	0.782	7828	0.034	0.011	0.002	7450
rs13266634	SLC30A8	T	0.000	0.009	0.968	7828	-0.007	0.008	0.372	7450
rs11558471	SLC30A8	G	0.002	0.009	0.854	7828	-0.005	0.008	0.473	7450
rs3802177	SLC30A8	A	0.000	0.009	0.997	7826	-0.007	0.008	0.352	7448
rs896854*	TP53INP1	C	0.006	0.012	0.640	3119	-0.016	0.012	0.168	2763
rs564398	CDKN2A/2B	C	-0.021	0.008	0.011	7818	-0.007	0.007	0.351	7440
rs10757282	CDKN2A/2B	C	-0.013	0.012	0.305	3122	-0.004	0.012	0.721	2766
rs7018475	CDKN2A/2B	G	-0.011	0.014	0.429	3115	-0.011	0.013	0.418	2759
rs10965250	CDKN2A/2B	A	-0.008	0.017	0.643	3122	-0.003	0.016	0.856	2766
rs2383208	CDKN2A/2B	G	-0.004	0.017	0.826	3122	-0.006	0.016	0.727	2766
rs10811661*	CDKN2B	G	-0.004	0.017	0.826	3122	-0.006	0.016	0.727	2766
rs7034200	GLIS3	A	0.007	0.008	0.420	7818	0.015	0.007	0.046	7440
rs7041847*	GLIS3	A	0.007	0.008	0.420	7818	0.015	0.007	0.046	7440
rs10814916*	GLIS3	A	0.007	0.008	0.420	7818	0.015	0.007	0.046	7440
rs17584499	PTPRD	T	0.000	0.010	0.963	7827	0.001	0.009	0.951	7449
rs2796441	TLE1	A	0.003	0.008	0.692	7828	-0.003	0.007	0.643	7450
rs13292136	TLE4 (CHCHD9)	T	-0.051	0.021	0.017	3113	-0.053	0.021	0.010	2759
rs10885122	ADRA2A	T	0.008	0.013	0.531	7828	0.034	0.011	0.003	7450
rs553668	ADRA2A	A	0.027	0.017	0.109	3122	0.001	0.016	0.965	2766
rs10906115	CDC123/CAMK1D	G	-0.001	0.009	0.934	7828	-0.010	0.008	0.175	7450
rs11257655	CDC123/CAMK1D	T	0.011	0.015	0.440	3121	-0.015	0.014	0.301	2766
rs10886471	GRK5	T	0.014	0.012	0.246	3120	0.021	0.012	0.081	2764
rs5015480	HHEX	T	-0.004	0.008	0.631	7817	-0.001	0.007	0.932	7441
rs1111875*	HHEX/IDE	C	-0.002	0.012	0.845	3115	-0.014	0.012	0.245	2760
rs7077836*	TCERG1L	T	0.004	0.016	0.787	3121	-0.003	0.016	0.858	2765
rs4506565	TCF7L2	T	-0.005	0.010	0.621	7804	0.009	0.009	0.279	7428
rs7901695	TCF7L2	C	-0.006	0.010	0.559	7826	0.009	0.009	0.320	7448
rs7903146	TCF7L2	T	0.002	0.010	0.854	7827	0.003	0.009	0.760	7449
rs1802295	VPS26A	T	0.009	0.013	0.482	3122	0.007	0.012	0.554	2766
rs12571751	ZMIZ1	G	0.003	0.008	0.692	7828	0.011	0.007	0.136	7450
rs11603334	ARAP1	A	-0.005	0.011	0.660	7828	0.025	0.009	0.008	7450
rs1552224	CENTD2	C	-0.004	0.011	0.678	7827	0.025	0.009	0.008	7449
rs11605924	CRY2	A	0.004	0.012	0.723	3122	0.009	0.012	0.451	2766
rs174550	FADS1	C	0.028	0.009	0.001	7827	0.014	0.008	0.062	7449
rs2334499	HCCA2	T	-0.020	0.012	0.109	3121	0.018	0.012	0.121	2765
rs5215	KCNJ11	C	0.010	0.008	0.239	7826	-0.003	0.007	0.723	7449
rs5219	KCNJ11	T	0.010	0.008	0.248	7828	-0.002	0.007	0.779	7450
rs2237892	KCNQ1	T	0.003	0.017	0.841	7828	0.014	0.015	0.357	7450
rs2237895	KCNQ1	C	0.011	0.008	0.197	7828	0.000	0.007	0.961	7450
rs163184	KCNQ1	G	0.020	0.012	0.105	3121	0.012	0.012	0.319	2765
rs231362	KCNQ1	G	-0.017	0.012	0.175	3122	-0.011	0.012	0.352	2766
rs10838687	MADD	G	-0.012	0.010	0.227	7827	0.002	0.008	0.824	7450
rs7944584	MADD	T	-0.007	0.010	0.464	7825	-0.010	0.009	0.241	7447
rs10501320*	MADD	G	-0.011	0.014	0.430	3122	-0.011	0.013	0.415	2766
rs10830963	MTNR1B	G	0.016	0.009	0.076	7826	0.012	0.008	0.121	7448
rs1387153	MTNR1B	T	0.002	0.009	0.802	7827	0.012	0.008	0.131	7449
rs1483121	OR4S1	A	-0.016	0.018	0.365	3119	-0.029	0.017	0.087	2764
rs7138803	BCDIN3D/FAIM2	A	-0.005	0.009	0.589	7828	0.010	0.008	0.206	7450
rs11063069	CCND2	G	-0.009	0.010	0.410	7828	0.009	0.009	0.327	7450
rs1153188	DCD	T	-0.008	0.010	0.386	7816	0.003	0.008	0.689	7439
rs1531343	HMGA2	C	-0.009	0.016	0.575	7824	-0.002	0.014	0.914	7447
rs9668162*	HMGA2	G	-0.023	0.032	0.478	3122	0.024	0.031	0.436	2766
rs7305618	HNF1A	T	-0.024	0.010	0.017	7827	-0.001	0.009	0.950	7449
rs35767	IGF1	A	0.001	0.011	0.907	7828	-0.014	0.009	0.137	7450
rs10842994	KLHDC5	T	0.009	0.011	0.375	7827	0.009	0.009	0.316	7449

rs4275659	MPHOSPH9	T	0.007	0.009	0.436	7828	-0.008	0.008	0.306	7450
rs7957197	OASL/TCF1/HNF1A	A	-0.021	0.010	0.033	7813	-0.006	0.009	0.520	7435
rs7961581	TSPAN8. LGR5	C	-0.010	0.010	0.312	7819	-0.011	0.009	0.208	7442
rs2293941	PDX1 - AS1	A	0.012	0.015	0.419	3122	0.030	0.014	0.033	2766
rs1359790	SPRY2	A	-0.005	0.009	0.609	7826	-0.002	0.008	0.843	7448
rs2028299	AP3S2	C	-0.015	0.013	0.254	3120	0.007	0.013	0.605	2764
rs7172432	C2CD4A/B	G	0.002	0.008	0.807	7826	-0.004	0.007	0.617	7448
rs7178572*	HMG20A	A	0.012	0.013	0.370	3122	0.006	0.013	0.637	2766
rs7177055	HMG20A	G	0.008	0.014	0.556	3121	0.004	0.013	0.770	2765
rs1549318	LARP6	C	0.003	0.009	0.758	7827	0.002	0.007	0.753	7447
rs8042680	PRC1	A	-0.004	0.009	0.654	7828	0.003	0.008	0.673	7450
rs7403531	RASGRP1	T	-0.006	0.015	0.667	3122	0.001	0.014	0.920	2766
rs17271305	VPS13C	G	-0.001	0.013	0.914	3120	-0.009	0.012	0.461	2765
rs4502156	VPS13C/C2CD4A/B	C	-0.003	0.008	0.700	7828	-0.004	0.007	0.629	7450
rs11634397	ZFAND6	A	-0.001	0.009	0.889	7827	-0.005	0.008	0.528	7449
rs7202877	BCAR1	G	0.001	0.013	0.943	7825	-0.012	0.011	0.291	7447
rs8050136	FTO	A	-0.010	0.009	0.263	7826	-0.009	0.008	0.240	7449
rs9939609	FTO	A	-0.011	0.009	0.215	7811	-0.009	0.008	0.210	7436
rs11642841	FTO	A	-0.015	0.012	0.225	3122	-0.018	0.012	0.122	2766
rs4430796	HNF1B	G	0.003	0.008	0.751	7797	-0.006	0.007	0.412	7417
rs7501939	HNF1B	T	-0.003	0.009	0.708	7826	-0.009	0.008	0.244	7449
rs4790333	SGSM2	T	0.004	0.008	0.665	7828	0.010	0.007	0.167	7450
rs391300	SRR	T	-0.004	0.009	0.651	7826	-0.001	0.008	0.921	7447
rs4523957*	SRR	T	0.011	0.013	0.370	3120	0.003	0.012	0.826	2764
rs8090011*	LAMA1	C	0.005	0.013	0.693	3121	-0.017	0.012	0.162	2765
rs12970134	MC4R	A	0.001	0.010	0.913	7828	-0.001	0.009	0.945	7449
rs17782313	MC4R	C	0.010	0.010	0.347	7827	0.008	0.009	0.341	7449
rs3794991*	GATAD2A/CILP2	C	0.027	0.015	0.072	7828	0.034	0.013	0.009	7450
rs8108269	GIPR	G	-0.034	0.009	2.0x10 ⁻⁴	7826	-0.024	0.008	0.003	7448
rs10423928*	GIPR	T	-0.073	0.015	5.2x10 ⁻⁷	3122	-0.073	0.014	2.8x10 ⁻⁷	2766
rs10401969	SUGP1/CILP2	C	0.027	0.015	0.072	7828	0.034	0.013	0.009	7450
rs6017317*	FITM2-R3HDML-HNF4A	C	0.011	0.016	0.492	3122	-0.002	0.015	0.914	2766
rs6048205*	FOXA2/LINC00261	T	-0.028	0.029	0.331	3122	0.009	0.028	0.748	2766
rs12010175	FAM58A	A	-0.021	0.031	0.488	3122	-0.029	0.030	0.330	2766

*Data shown is for proxy SNP (see supplementary table 7)

Linear regression of ln-transformed GIP concentration adjusted for sex and age.

Table S11. Associations of known T2D loci with serum GLP-1 concentrations.

T2D Risk SNP	Gene/Nearest Gene	Fasting GLP-1					2-hour GLP-1			
		EA	Beta	SE	P	N	Beta	SE	P	N
rs17106184*	FAF1	A	0.004	0.017	0.834	3179	-0.035	0.018	0.046	2874
rs2785980	LYPLAL1	C	0.010	0.011	0.342	3164	-0.006	0.012	0.579	2860
rs2296172	MACF1	G	0.008	0.010	0.418	4181	-0.022	0.011	0.046	3849
rs10923931*	NOTCH2	C	0.003	0.018	0.874	3175	0.004	0.019	0.839	2871
rs340874	PROX1	T	-0.004	0.009	0.653	4181	-0.001	0.009	0.889	3849
rs9727115	SNX7	A	0.001	0.009	0.880	4179	0.008	0.009	0.401	3847
rs243021	BCL11A	A	-0.006	0.009	0.507	4180	0.002	0.009	0.821	3848
rs243088*	BCL11A	G	-0.006	0.011	0.575	3180	0.008	0.011	0.503	2875
rs3792267	CAPN10	A	0.006	0.011	0.592	3180	0.002	0.012	0.859	2875
rs2975760*	CAPN10	G	0.014	0.014	0.324	3181	-0.008	0.015	0.561	2876
rs7607980	COBLL1	C	-0.013	0.013	0.314	4181	0.006	0.014	0.679	3849
rs1371614	DPYSL5	T	0.0003	0.012	0.979	3180	-0.017	0.012	0.158	2875
rs560887	G6PC2/ABCB11	T	0.009	0.009	0.348	4179	0.008	0.010	0.392	3847
rs780094	GCKR	T	0.008	0.009	0.385	4181	0.001	0.009	0.928	3849
rs13389219	GRB14	T	-0.002	0.009	0.774	4169	0.011	0.009	0.210	3838
rs3923113*	GRB14	G	-0.004	0.009	0.681	4150	0.009	0.009	0.306	3820
rs2943634	IRS1	A	-0.028	0.009	0.002	4179	0.002	0.009	0.817	3847
rs2943641	IRS1	T	-0.030	0.009	0.001	4178	0.005	0.009	0.560	3845
rs7578326	KIAA1486/IRS1	G	-0.026	0.009	0.003	4181	0.0005	0.009	0.959	3849
rs7593730	RBMS1/ITGB6	T	-0.002	0.011	0.838	4180	-0.012	0.011	0.273	3849
rs7578597	THADA	C	0.017	0.015	0.255	4175	0.019	0.016	0.225	3845
rs10200833*	THADA	T	-0.003	0.012	0.790	3179	0.009	0.012	0.446	2874
rs6723108	TMEM163	T	-0.012	0.010	0.245	3181	0.008	0.011	0.431	2876
rs998451*	TMEM163	T	-0.012	0.010	0.245	3181	0.008	0.011	0.431	2876
rs4607103	ADAMTS9-AS2	T	0.006	0.010	0.581	4175	0.007	0.011	0.538	3843
rs6795735	ADAMTS9-AS2	T	0.004	0.009	0.682	4181	0.002	0.009	0.790	3849
rs11708067	ADCY5	G	0.010	0.010	0.328	4181	0.011	0.011	0.317	3849
rs2877716	ADCY5	T	0.013	0.010	0.219	4165	0.010	0.011	0.351	3838
rs11071657	FAM148B	G	0.005	0.009	0.605	4181	-0.014	0.009	0.131	3848
rs1470579	IGF2BP2	C	0.009	0.010	0.319	4181	0.018	0.010	0.070	3849
rs4402960	IGF2BP2	T	0.011	0.010	0.256	4180	0.019	0.010	0.056	3848
rs6808574	LPP	T	-0.004	0.011	0.712	3181	0.017	0.011	0.125	2876
rs1801282	PPARG	G	0.005	0.012	0.678	4170	-0.003	0.013	0.804	3838
rs13081389	PPARG	G	0.007	0.016	0.657	4154	-0.012	0.017	0.486	3824
rs17036160*	PPARG	T	-0.002	0.015	0.881	3176	0.007	0.015	0.657	2871
rs1797912*	PPARG	G	-0.011	0.011	0.321	3179	-0.006	0.011	0.621	2876
rs831571*	PSMD6	C	-0.024	0.014	0.078	3180	-0.002	0.014	0.907	2875
rs7647305	SFRS10	T	-0.013	0.011	0.239	4177	0.009	0.012	0.433	3845
rs11920090	SLC2A2	A	-0.007	0.013	0.597	4168	0.008	0.013	0.545	3836
rs16861329*	ST6GAL1	A	-0.020	0.016	0.206	3181	-0.021	0.017	0.201	2876
rs6780569	UBE2E2	A	-0.002	0.017	0.908	3177	-0.013	0.017	0.468	2874
rs17046216*	MSMO1	G	-0.015	0.011	0.163	3177	0.027	0.012	0.019	2872
rs4691380	PDGFC	T	0.004	0.009	0.708	4180	0.006	0.010	0.554	3848
rs6813195	TMEM154	T	0.002	0.009	0.822	4181	-0.007	0.010	0.445	3849
rs1801214	WFS1	C	-0.011	0.009	0.208	4178	-0.004	0.009	0.653	3846
rs4689388	WFS1	G	-0.012	0.009	0.173	4181	-0.002	0.009	0.823	3849
rs10010131	WFS1	A	-0.005	0.011	0.664	3090	0.007	0.011	0.509	2792
rs6446482*	WFS1	C	-0.008	0.010	0.441	3181	0.005	0.011	0.621	2876
rs459193	ANKRD55	A	-0.008	0.010	0.382	4179	-0.002	0.010	0.857	3847
rs702634	ARL15	G	0.014	0.011	0.203	3181	-0.005	0.012	0.656	2876
rs6235	PCSK1	G	0.007	0.010	0.450	4179	-0.006	0.010	0.527	3849
rs13179048	PCSK1	A	0.010	0.009	0.260	4175	0.001	0.010	0.949	3844
rs4457053	ZBED3	G	0.00008	0.012	0.995	3178	0.021	0.013	0.089	2873
rs1048886	C6orf57	G	0.027	0.013	0.042	3176	0.033	0.014	0.018	2872
rs10946398	CDKAL1	C	0.008	0.009	0.394	4180	-0.007	0.010	0.449	3848
rs2206734	CDKAL1	T	0.016	0.011	0.166	4181	0.001	0.012	0.907	3849
rs4712523	CDKAL1	G	0.008	0.009	0.372	4180	-0.007	0.010	0.485	3848
rs7754840	CDKAL1	C	0.008	0.009	0.409	4169	-0.006	0.010	0.521	3840
rs7756992	CDKAL1	G	0.013	0.009	0.180	4180	0.002	0.010	0.855	3848
rs7766070*	CDKAL1	A	0.018	0.012	0.110	3181	0.001	0.012	0.964	2876
rs1535500	CNK16	T	-0.009	0.011	0.415	3077	-0.003	0.011	0.789	2783
rs3130501	POU5F1-TCF19	A	-0.012	0.010	0.236	4181	0.019	0.010	0.072	3849
rs9505118	SSR1-RREB1	G	0.004	0.009	0.615	4181	-0.004	0.009	0.660	3849

rs4646949	TAF11	G	-0.004	0.010	0.688	4179	0.010	0.011	0.336	3847
rs9470794*	ZFAND3	G	0.015	0.020	0.465	3181	0.016	0.021	0.442	2876
rs17168486	DGKB	T	-0.013	0.013	0.350	3175	-0.001	0.014	0.919	2872
rs2191349	DGKB/TMEM195	G	-0.005	0.008	0.533	4180	-0.003	0.009	0.748	3848
rs6467136*	GCC1-PAX4	C	0.006	0.010	0.588	3180	-0.011	0.011	0.295	2876
rs4607517	GCK	A	0.014	0.012	0.235	4181	0.040	0.013	0.002	3849
rs6943153	GRB10	T	-0.005	0.009	0.578	4180	0.0003	0.009	0.973	3848
rs849134	JAZF1	G	-0.009	0.009	0.294	4180	0.004	0.009	0.673	3848
rs864745	JAZF1	C	-0.011	0.008	0.216	4175	0.007	0.009	0.443	3843
rs972283	KLF14	A	-0.001	0.009	0.933	4181	-0.004	0.009	0.632	3849
rs516946	ANK1	T	-0.006	0.010	0.540	4181	0.003	0.011	0.790	3849
rs515071*	ANK1	T	-0.006	0.010	0.540	4181	0.003	0.011	0.790	3849
rs4841132	PPP1R3B	A	-0.033	0.014	0.016	4181	-0.016	0.014	0.269	3849
rs13266634	SLC30A8	T	0.010	0.009	0.256	4181	0.012	0.009	0.204	3849
rs11558471	SLC30A8	G	0.011	0.009	0.226	4181	0.013	0.009	0.155	3849
rs3802177	SLC30A8	A	0.010	0.009	0.254	4179	0.012	0.009	0.194	3847
rs896854*	TP53INP1	C	-0.002	0.010	0.863	3179	0.003	0.011	0.785	2874
rs564398	CDKN2A/2B	C	-0.010	0.009	0.265	4169	-0.023	0.009	0.011	3839
rs10757282	CDKN2A/2B	C	0.009	0.011	0.410	3181	0.010	0.011	0.389	2876
rs7018475	CDKN2A/2B	G	0.007	0.012	0.526	3175	0.011	0.012	0.380	2870
rs10965250	CDKN2A/2B	A	0.014	0.014	0.345	3181	0.005	0.015	0.757	2876
rs2383208	CDKN2A/2B	G	0.010	0.014	0.463	3181	-0.001	0.015	0.949	2876
rs10811661*	CDKN2B	G	0.010	0.014	0.463	3181	-0.001	0.015	0.949	2876
rs7034200	GLIS3	A	-0.005	0.009	0.559	4173	-0.001	0.009	0.880	3841
rs7041847*	GLIS3	A	-0.005	0.009	0.559	4173	-0.001	0.009	0.880	3841
rs10814916*	GLIS3	A	-0.005	0.009	0.559	4173	-0.001	0.009	0.880	3841
rs17584499	PTPRD	T	-0.001	0.010	0.897	4180	-0.004	0.011	0.682	3848
rs2796441	TLE1	A	-0.017	0.009	0.043	4181	-0.013	0.009	0.152	3849
rs13292136	TLE4 (CHCHD9)	T	-0.017	0.018	0.360	3172	-0.013	0.019	0.488	2867
rs10885122	ADRA2A	T	0.013	0.013	0.341	4181	-0.003	0.014	0.824	3849
rs553668	ADRA2A	A	-0.019	0.015	0.201	3181	-0.009	0.015	0.566	2876
rs10906115	CDC123/CAMK1D	G	-0.008	0.009	0.339	4181	-0.005	0.009	0.621	3849
rs11257655	CDC123/CAMK1D	T	0.002	0.013	0.851	3180	-0.001	0.013	0.959	2876
rs10886471	GRK5	T	0.005	0.010	0.638	3179	-0.007	0.011	0.550	2874
rs5015480	HHEX	T	-0.007	0.009	0.436	4172	0.0004	0.009	0.965	3842
rs1111875*	HHEX/IDE	C	-0.004	0.011	0.725	3172	0.001	0.011	0.956	2870
rs7077836*	TCERG1L	T	-0.006	0.014	0.657	3180	-0.003	0.015	0.842	2875
rs4506565	TCF7L2	T	0.015	0.010	0.128	4155	0.013	0.010	0.209	3827
rs7901695	TCF7L2	C	0.013	0.010	0.189	4179	0.009	0.010	0.385	3847
rs7903146	TCF7L2	T	0.018	0.010	0.070	4181	0.015	0.011	0.161	3848
rs1802295	VPS26A	T	-0.003	0.011	0.749	3181	-0.019	0.011	0.097	2876
rs12571751	ZMIZ1	G	0.006	0.009	0.513	4181	-0.009	0.009	0.308	3849
rs11603334	ARAP1	A	0.017	0.011	0.134	4181	0.006	0.012	0.585	3849
rs1552224	CENTD2	C	0.016	0.011	0.152	4180	0.006	0.012	0.589	3848
rs11605924	CRY2	A	-0.014	0.011	0.184	3181	-0.008	0.011	0.496	2876
rs174550	FADS1	C	0.010	0.009	0.247	4180	-0.004	0.009	0.704	3848
rs2334499	HCCA2	T	0.017	0.010	0.095	3180	0.014	0.011	0.206	2875
rs5215	KCNJ11	C	-0.007	0.009	0.428	4179	-0.010	0.009	0.267	3847
rs5219	KCNJ11	T	-0.007	0.009	0.412	4181	-0.010	0.009	0.254	3849
rs2237892	KCNQ1	T	0.017	0.017	0.315	4181	-0.027	0.018	0.138	3849
rs2237895	KCNQ1	C	0.015	0.009	0.083	4181	0.005	0.009	0.606	3849
rs163184	KCNQ1	G	-0.001	0.010	0.897	3180	0.022	0.011	0.045	2875
rs231362	KCNQ1	G	-0.002	0.010	0.819	3181	0.004	0.011	0.730	2876
rs10838687	MADD	G	0.011	0.010	0.290	4180	0.004	0.011	0.673	3848
rs7944584	MADD	T	-0.013	0.010	0.209	4178	0.001	0.011	0.896	3846
rs10501320*	MADD	G	-0.009	0.012	0.433	3181	-0.004	0.013	0.767	2876
rs10830963	MTNR1B	G	-0.014	0.009	0.130	4178	-0.024	0.010	0.013	3847
rs1387153	MTNR1B	T	-0.016	0.009	0.084	4180	-0.022	0.010	0.026	3848
rs1483121	OR4S1	A	0.027	0.015	0.069	3178	0.011	0.016	0.505	2874
rs7138803	BCDIN3D/FAIM2	A	-0.005	0.009	0.594	4181	-0.009	0.009	0.299	3849
rs11063069	CCND2	G	-0.008	0.011	0.440	4181	0.008	0.011	0.457	3849
rs1153188	DCD	T	0.008	0.010	0.390	4167	0.002	0.010	0.832	3836
rs2074356	HECTD4/C12orf51	A	NA	NA	NA	NA	NA	NA	NA	NA
rs1531343	HMGA2	C	-0.019	0.016	0.250	4177	-0.008	0.017	0.623	3846
rs9668162*	HMGA2	G	0.007	0.028	0.793	3181	0.035	0.030	0.240	2876
rs7305618	HNF1A	T	0.004	0.010	0.668	4180	-0.005	0.011	0.643	3848
rs35767	IGF1	A	0.019	0.011	0.084	4181	0.030	0.012	0.010	3849

rs10842994	KLHDC5	T	0.009	0.011	0.418	4180	-0.005	0.011	0.670	3848
rs4275659	MPHOSPH9	T	-0.027	0.010	0.005	4181	-0.017	0.010	0.098	3849
rs7957197	OASL/TCF1/HNF1A	A	0.002	0.010	0.885	4166	-0.006	0.011	0.603	3837
rs7961581	TSPAN8. LGR5	C	-0.021	0.010	0.032	4172	-0.002	0.010	0.835	3842
rs2293941	PDX1 - AS1	A	0.007	0.013	0.575	3181	0.014	0.013	0.276	2876
rs1359790	SPRY2	A	0.004	0.010	0.663	4179	0.005	0.010	0.634	3847
rs2028299	AP3S2	C	0.005	0.011	0.656	3179	-0.008	0.012	0.526	2874
rs7172432	C2CD4A/B	G	-0.010	0.009	0.249	4179	-0.013	0.009	0.149	3847
rs7178572*	HMG20A	A	-0.012	0.012	0.307	3181	-0.007	0.012	0.552	2876
rs7177055	HMG20A	G	-0.017	0.012	0.155	3180	-0.009	0.012	0.474	2875
rs1549318	LARP6	C	-0.004	0.009	0.676	4178	-0.010	0.009	0.246	3846
rs8042680	PRC1	A	0.009	0.009	0.328	4181	0.008	0.010	0.398	3849
rs7403531	RASGRP1	T	0.003	0.013	0.829	3181	-0.002	0.013	0.867	2876
rs17271305	VPS13C	G	0.006	0.011	0.569	3179	-0.002	0.011	0.842	2875
rs4502156	VPS13C/C2CD4A/B	C	-0.010	0.009	0.256	4181	-0.010	0.009	0.281	3849
rs11634397	ZFAND6	A	-0.013	0.009	0.159	4180	0.007	0.010	0.469	3848
rs7202877	BCAR1	G	-0.007	0.013	0.568	4180	0.001	0.014	0.969	3848
rs8050136	FTO	A	0.003	0.009	0.734	4179	-0.003	0.009	0.717	3848
rs9939609	FTO	A	0.003	0.009	0.723	4165	-0.004	0.009	0.694	3836
rs11642841	FTO	A	0.004	0.011	0.683	3181	0.006	0.011	0.574	2876
rs4430796	HNF1B	G	0.0004	0.009	0.959	4172	0.009	0.009	0.329	3841
rs7501939	HNF1B	T	-0.001	0.009	0.934	4179	0.004	0.009	0.633	3848
rs4790333	SGSM2	T	0.005	0.008	0.561	4181	0.005	0.009	0.579	3849
rs391300	SRR	T	-0.001	0.009	0.876	4178	-0.007	0.009	0.415	3846
rs4523957*	SRR	T	-0.001	0.011	0.914	3179	-0.011	0.011	0.331	2874
rs8090011*	LAMA1	C	0.015	0.011	0.176	3180	0.006	0.011	0.585	2875
rs12970134	MC4R	A	-0.005	0.010	0.638	4180	-0.003	0.010	0.758	3848
rs17782313	MC4R	C	-0.009	0.010	0.363	4180	-0.005	0.011	0.639	3848
rs3794991*	GATAD2A/CILP2	C	-0.012	0.015	0.394	4181	-0.001	0.015	0.944	3849
rs8108269	GIPR	G	0.019	0.009	0.038	4179	0.008	0.010	0.414	3847
rs10423928*	GIPR	T	0.031	0.013	0.012	3181	0.024	0.013	0.073	2876
rs10401969	SUGP1/CILP2	C	-0.012	0.015	0.394	4181	-0.001	0.015	0.944	3849
rs6017317*	FITM2-R3HDML- HNF4A	C	0.004	0.014	0.788	3181	0.015	0.014	0.296	2876
rs6048205*	FOXA2/LINC00261	T	0.020	0.025	0.420	3181	0.027	0.026	0.306	2876
rs12010175	FAM58A	A	0.023	0.026	0.379	3181	0.020	0.027	0.457	2876

*Data shown is for proxy SNP (see Supplementary table 8)

Linear regression of ln-transformed GLP-1 concentrations adjusted for sex and age.

Table S12. Association of known T2D loci with serum glucagon concentration.

T2D Risk SNP	Gene/Nearest Gene	EA	Fasting Glucagon				2-hour glucagon			
			Beta	SE	P	N	Beta	SE	P	N
rs17106184*	<i>FAF1</i>	A	0.002	0.011	0.821	3290	0.007	0.011	0.552	2925
rs2785980	<i>LYPLAL1</i>	C	-0.016	0.007	0.019	3275	-0.015	0.007	0.046	2911
rs2296172	<i>MACF1</i>	G	0.002	0.006	0.771	6683	-0.001	0.006	0.844	6242
rs10923931*	<i>NOTCH2</i>	C	0.013	0.011	0.238	3286	-0.005	0.012	0.662	2922
rs340874	<i>PROX1</i>	T	0.000	0.005	0.956	6683	0.004	0.005	0.387	6242
rs9727115	<i>SNX7</i>	A	-0.003	0.005	0.560	6681	0.004	0.005	0.464	6240
rs243021	<i>BCL11A</i>	A	0.006	0.005	0.195	6682	0.011	0.005	0.015	6241
rs243088*	<i>BCL11A</i>	G	0.002	0.007	0.810	3291	0.007	0.007	0.332	2926
rs3792267	<i>CAPN10</i>	A	-0.003	0.007	0.691	3291	0.005	0.007	0.471	2926
rs2975760*	<i>CAPN10</i>	G	0.006	0.009	0.480	3292	0.001	0.009	0.910	2927
rs7607980	<i>COBLL1</i>	C	-0.011	0.007	0.101	6683	-0.003	0.007	0.632	6242
rs1371614	<i>DPYSL5</i>	T	-0.014	0.007	0.054	3291	-0.015	0.008	0.052	2926
rs560887	<i>G6PC2/ABCB11</i>	T	0.000	0.005	0.946	6682	0.000	0.005	0.985	6241
rs780094	<i>GCKR</i>	T	0.011	0.005	0.016	6683	0.010	0.005	0.040	6242
rs13389219	<i>GRB14</i>	T	-0.010	0.005	0.034	6670	-0.001	0.005	0.769	6229
rs3923113*	<i>GRB14</i>	G	-0.008	0.005	0.079	6652	0.000	0.005	0.947	6213
rs2943634	<i>IRS1</i>	A	-0.015	0.005	0.002	6681	-0.010	0.005	0.048	6240
rs2943641	<i>IRS1</i>	T	-0.013	0.005	0.006	6679	-0.009	0.005	0.062	6238
rs7578326	<i>KIAA1486/IRS1</i>	G	-0.012	0.005	0.009	6683	-0.007	0.005	0.150	6242
rs7593730	<i>RBMS1/ITGB6</i>	T	-0.003	0.006	0.649	6682	-0.004	0.006	0.468	6242
rs7578597	<i>THADA</i>	C	-0.009	0.008	0.267	6677	-0.012	0.009	0.182	6238
rs10200833*	<i>THADA</i>	T	0.002	0.007	0.787	3290	0.010	0.008	0.201	2925
rs6723108	<i>TMEM163</i>	T	-0.003	0.006	0.626	3292	-0.006	0.007	0.340	2927
rs998451*	<i>TMEM163</i>	T	-0.003	0.006	0.626	3292	-0.006	0.007	0.340	2927
rs4607103	<i>ADAMTS9-AS2</i>	T	0.001	0.005	0.785	6677	-0.003	0.006	0.607	6236
rs6795735	<i>ADAMTS9-AS2</i>	T	0.001	0.005	0.777	6683	-0.003	0.005	0.509	6242
rs11708067	<i>ADCY5</i>	G	0.013	0.006	0.019	6683	0.014	0.006	0.013	6242
rs2877716	<i>ADCY5</i>	T	0.013	0.006	0.022	6667	0.011	0.006	0.055	6231
rs1470579	<i>IGF2BP2</i>	C	0.002	0.005	0.646	6683	0.000	0.005	0.933	6242
rs4402960	<i>IGF2BP2</i>	T	0.002	0.005	0.713	6682	0.000	0.005	0.969	6241
rs6808574	<i>LPP</i>	T	0.002	0.007	0.726	3292	0.006	0.007	0.369	2927
rs1801282	<i>PPARG</i>	G	-0.001	0.006	0.849	6672	-0.002	0.006	0.711	6231
rs13081389	<i>PPARG</i>	G	0.004	0.008	0.670	6655	-0.003	0.009	0.689	6216
rs17036160*	<i>PPARG</i>	T	0.002	0.009	0.828	3287	0.002	0.010	0.840	2922
rs1797912*	<i>PPARG</i>	G	-0.018	0.007	0.011	3290	-0.018	0.007	0.012	2927
rs831571*	<i>PSMD6</i>	C	-0.011	0.008	0.191	3291	-0.005	0.009	0.596	2926
rs7647305	<i>SFRS10</i>	T	0.002	0.006	0.726	6679	0.004	0.006	0.465	6238
rs11920090	<i>SLC2A2</i>	A	0.005	0.007	0.418	6668	-0.003	0.007	0.673	6228
rs16861329*	<i>ST6GAL1</i>	A	-0.017	0.010	0.081	3292	-0.013	0.010	0.209	2927
rs6780569	<i>UBE2E2</i>	A	0.010	0.010	0.349	3288	0.003	0.011	0.787	2925
rs17046216*	<i>MSMO1</i>	G	0.000	0.007	0.978	3288	0.014	0.007	0.049	2923
rs4691380	<i>PDGFC</i>	T	0.001	0.005	0.910	6681	0.003	0.005	0.527	6240
rs6813195	<i>TMEM154</i>	T	-0.001	0.005	0.804	6683	-0.005	0.005	0.274	6242
rs1801214	<i>WFS1</i>	C	-0.007	0.005	0.132	6680	-0.002	0.005	0.602	6239
rs4689388	<i>WFS1</i>	G	-0.007	0.005	0.117	6683	-0.003	0.005	0.477	6242
rs10010131	<i>WFS1</i>	A	-0.005	0.007	0.421	3195	0.001	0.007	0.836	2841
rs6446482*	<i>WFS1</i>	C	-0.007	0.007	0.313	3292	0.001	0.007	0.860	2927
rs459193	<i>ANKRD55</i>	A	-0.005	0.005	0.311	6681	0.000	0.005	0.925	6240
rs702634	<i>ARL15</i>	G	-0.006	0.007	0.415	3292	-0.009	0.007	0.220	2927
rs6235	<i>PCSK1</i>	G	0.009	0.005	0.074	6681	0.008	0.005	0.139	6242
rs13179048	<i>PCSK1</i>	A	0.005	0.005	0.264	6676	0.008	0.005	0.129	6236
rs4457053	<i>ZBED3</i>	G	-0.004	0.008	0.629	3289	-0.002	0.008	0.835	2924
rs1048886	<i>C6orf57</i>	G	0.008	0.008	0.317	3287	0.010	0.009	0.248	2923
rs10946398	<i>CDKAL1</i>	C	0.007	0.005	0.159	6682	0.003	0.005	0.588	6241
rs2206734	<i>CDKAL1</i>	T	0.009	0.006	0.123	6683	0.005	0.006	0.455	6242
rs4712523	<i>CDKAL1</i>	G	0.007	0.005	0.144	6682	0.003	0.005	0.550	6241
rs7754840	<i>CDKAL1</i>	C	0.006	0.005	0.197	6671	0.002	0.005	0.640	6233
rs7756992	<i>CDKAL1</i>	G	0.006	0.005	0.261	6682	0.004	0.005	0.470	6241
rs7766070*	<i>CDKAL1</i>	A	0.002	0.007	0.787	3292	-0.002	0.008	0.800	2927
rs1535500	<i>KCNK16</i>	T	0.011	0.007	0.097	3181	0.008	0.007	0.250	2831
rs3130501	<i>POU5F1-TCF19</i>	A	0.000	0.005	0.943	6683	0.005	0.005	0.313	6242
rs9505118	<i>SSR1-RREB1</i>	G	0.000	0.005	0.924	6683	0.004	0.005	0.358	6242

rs4646949	TAF11	G	0.004	0.005	0.439	6681	0.005	0.006	0.342	6240
rs9470794*	ZFAND3	G	0.000	0.013	1.000	3292	-0.007	0.013	0.618	2927
rs17168486	DGKB	T	0.000	0.008	0.953	3286	0.003	0.009	0.702	2923
rs2191349	DGKB/TMEM195	G	0.006	0.004	0.176	6682	0.000	0.005	0.998	6241
rs6467136*	GCC1-PAX4	C	-0.001	0.007	0.847	3291	-0.008	0.007	0.254	2927
rs4607517	GCK	A	-0.008	0.007	0.247	6683	0.000	0.007	0.999	6242
rs6943153	GRB10	T	0.003	0.005	0.577	6682	-0.002	0.005	0.639	6241
rs849134	JAZF1	G	0.002	0.005	0.617	6682	-0.001	0.005	0.758	6241
rs864745	JAZF1	C	0.002	0.005	0.724	6676	-0.001	0.005	0.868	6235
rs972283	KLF14	A	0.006	0.005	0.180	6683	0.009	0.005	0.063	6242
rs516946	ANK1	T	-0.005	0.006	0.338	6683	-0.002	0.006	0.746	6242
rs515071*	ANK1	T	-0.005	0.006	0.338	6683	-0.002	0.006	0.746	6242
rs4841132	PPP1R3B	A	-0.020	0.007	0.006	6683	-0.013	0.007	0.082	6242
rs13266634	SLC30A8	T	0.000	0.005	0.952	6683	-0.004	0.005	0.462	6242
rs11558471	SLC30A8	G	0.000	0.005	0.937	6683	-0.003	0.005	0.502	6242
rs3802177	SLC30A8	A	0.001	0.005	0.885	6681	-0.003	0.005	0.487	6240
rs896854*	TP53INP1	C	-0.016	0.006	0.011	3289	-0.013	0.007	0.053	2924
rs564398	CDKN2A/2B	C	-0.005	0.005	0.275	6671	-0.003	0.005	0.493	6232
rs10757282	CDKN2A/2B	C	-0.005	0.007	0.482	3292	-0.012	0.007	0.086	2927
rs7018475	CDKN2A/2B	G	-0.001	0.007	0.894	3285	-0.011	0.008	0.174	2920
rs10965250	CDKN2A/2B	A	-0.013	0.009	0.134	3292	-0.005	0.009	0.576	2927
rs2383208	CDKN2A/2B	G	-0.011	0.009	0.230	3292	-0.005	0.009	0.579	2927
rs10811661*	CDKN2B	G	-0.011	0.009	0.230	3292	-0.005	0.009	0.579	2927
rs7034200	GLIS3	A	-0.010	0.005	0.023	6675	-0.005	0.005	0.272	6234
rs7041847	GLIS3	A	-0.010	0.005	0.023	6675	-0.005	0.005	0.272	6234
rs10814916*	GLIS3	A	-0.010	0.005	0.023	6675	-0.005	0.005	0.272	6234
rs17584499	PTPRD	T	0.014	0.006	0.011	6682	0.010	0.006	0.085	6241
rs2796441	TLE1	A	0.001	0.005	0.845	6683	0.001	0.005	0.811	6242
rs13292136	TLE4 (CHCHD9)	T	-0.013	0.012	0.259	3283	-0.034	0.012	0.006	2918
rs10885122	ADRA2A	T	-0.010	0.007	0.165	6683	0.000	0.007	0.953	6242
rs553668	ADRA2A	A	0.006	0.009	0.531	3292	0.000	0.009	0.965	2927
rs10906115	CDC123/CAMK1D	G	-0.002	0.005	0.646	6683	0.000	0.005	0.939	6242
rs11257655	CDC123/CAMK1D	T	0.003	0.008	0.734	3291	-0.015	0.008	0.075	2927
rs10886471	GRK5	T	0.012	0.007	0.058	3290	0.004	0.007	0.519	2925
rs5015480	HHEX	T	-0.005	0.005	0.291	6672	0.002	0.005	0.604	6233
rs1111875*	HHEX/IDE	C	-0.001	0.007	0.876	3283	0.006	0.007	0.354	2921
rs7077836*	TCERG1L	T	-0.010	0.009	0.234	3291	-0.010	0.009	0.300	2926
rs4506565	TCF7L2	T	0.004	0.005	0.395	6657	0.004	0.005	0.433	6220
rs7901695	TCF7L2	C	0.003	0.005	0.552	6681	0.002	0.005	0.685	6240
rs7903146	TCF7L2	T	0.006	0.005	0.279	6682	0.003	0.006	0.592	6241
rs1802295	VPS26A	T	0.009	0.007	0.166	3292	0.004	0.007	0.552	2927
rs12571751	ZMIZ1	G	0.004	0.005	0.387	6683	0.008	0.005	0.069	6242
rs11603334	ARAP1	A	0.005	0.006	0.409	6683	0.004	0.006	0.490	6242
rs1552224	CENTD2	C	0.005	0.006	0.412	6682	0.004	0.006	0.490	6241
rs11605924	CRY2	A	0.007	0.007	0.266	3292	0.009	0.007	0.218	2927
rs174550	FADS1	C	0.013	0.005	0.005	6682	0.005	0.005	0.316	6241
rs2334499	HCCA2	T	0.010	0.007	0.132	3291	0.005	0.007	0.446	2926
rs5215	KCNJ11	C	0.000	0.005	0.926	6681	0.002	0.005	0.635	6240
rs5219	KCNJ11	T	0.001	0.005	0.882	6683	0.003	0.005	0.587	6242
rs2237892	KCNQ1	T	-0.014	0.009	0.118	6683	-0.007	0.009	0.448	6242
rs2237895	KCNQ1	C	0.007	0.005	0.136	6683	0.008	0.005	0.074	6242
rs163184	KCNQ1	G	-0.001	0.007	0.877	3291	0.013	0.007	0.065	2926
rs231362	KCNQ1	G	-0.011	0.007	0.084	3292	-0.018	0.007	0.010	2927
rs10838687	MADD	G	-0.001	0.005	0.902	6682	0.000	0.005	0.937	6241
rs7944584	MADD	T	-0.005	0.005	0.394	6680	0.007	0.006	0.238	6239
rs10501320*	MADD	G	-0.005	0.008	0.550	3292	-0.001	0.008	0.949	2927
rs10830963	MTNR1B	G	-0.001	0.005	0.911	6680	-0.002	0.005	0.713	6240
rs1387153	MTNR1B	T	-0.001	0.005	0.842	6682	-0.001	0.005	0.903	6241
rs1483121	OR4S1	A	-0.003	0.009	0.739	3289	-0.003	0.010	0.798	2925
rs7138803	BCDIN3D/FAIM2	A	0.003	0.005	0.476	6683	0.002	0.005	0.675	6242
rs11063069	CCND2	G	0.003	0.006	0.556	6683	0.003	0.006	0.599	6242
rs1153188	DCD	T	-0.002	0.005	0.744	6669	0.005	0.005	0.347	6229
rs2074356	HECTD4/C12orf51	A	NA	NA	NA	NA	NA	NA	NA	NA
rs1531343	HMGA2	C	0.014	0.009	0.103	6679	0.010	0.009	0.274	6239
rs9668162*	HMGA2	G	0.009	0.017	0.617	3292	0.028	0.018	0.124	2927
rs7305618	HNF1A	T	-0.001	0.005	0.787	6682	0.001	0.005	0.808	6241
rs35767	IGF1	A	0.015	0.006	0.012	6683	0.008	0.006	0.184	6242

rs10842994	KLHDC5	T	0.007	0.006	0.221	6682	0.007	0.006	0.227	6241
rs4275659	MPHOSPH9	T	-0.008	0.005	0.108	6683	-0.004	0.005	0.492	6242
rs7957197	OASL/TCF1/HNF1A	A	0.004	0.005	0.466	6668	0.005	0.005	0.373	6229
rs7961581	TSPAN8. LGR5	C	-0.010	0.005	0.055	6673	-0.010	0.005	0.066	6234
rs2293941	PDX1 - AS1	A	0.013	0.008	0.101	3292	0.019	0.008	0.020	2927
rs1359790	SPRY2	A	-0.006	0.005	0.270	6681	-0.008	0.005	0.103	6240
rs2028299	AP3S2	C	-0.011	0.007	0.139	3290	-0.008	0.008	0.284	2925
rs7172432	C2CD4A/B	G	0.004	0.005	0.348	6681	0.000	0.005	0.958	6240
rs11071657	FAM148B	G	0.009	0.005	0.057	6682	0.008	0.005	0.100	6241
rs7178572*	HMG20A	A	0.002	0.007	0.799	3292	-0.002	0.008	0.770	2927
rs7177055	HMG20A	G	0.003	0.007	0.694	3291	0.000	0.008	0.960	2926
rs1549318	LARP6	C	0.003	0.005	0.454	6680	0.007	0.005	0.133	6239
rs8042680	PRC1	A	-0.002	0.005	0.761	6683	-0.004	0.005	0.445	6242
rs7403531	RASGRP1	T	-0.011	0.008	0.159	3292	-0.016	0.008	0.062	2927
rs17271305	VPS13C	G	0.003	0.007	0.686	3290	0.006	0.007	0.415	2926
rs4502156	VPS13C/C2CD4A/B	C	0.004	0.005	0.344	6683	0.001	0.005	0.835	6242
rs11634397	ZFAND6	A	-0.004	0.005	0.373	6682	-0.007	0.005	0.137	6241
rs7202877	BCAR1	G	-0.005	0.007	0.488	6681	0.007	0.007	0.331	6240
rs8050136	FTO	A	0.009	0.005	0.050	6681	0.004	0.005	0.357	6241
rs9939609	FTO	A	0.009	0.005	0.054	6666	0.004	0.005	0.352	6228
rs11642841	FTO	A	0.008	0.007	0.208	3292	0.004	0.007	0.584	2927
rs4430796	HNF1B	G	0.003	0.005	0.568	6665	0.001	0.005	0.840	6224
rs7501939	HNF1B	T	-0.001	0.005	0.866	6681	0.000	0.005	0.969	6241
rs4790333	SGSM2	T	0.001	0.005	0.869	6683	0.002	0.005	0.724	6242
rs391300	SRR	T	-0.005	0.005	0.304	6680	-0.001	0.005	0.781	6239
rs4523957*	SRR	T	-0.002	0.007	0.736	3290	0.005	0.007	0.510	2925
rs8090011*	LAMA1	C	-0.006	0.007	0.344	3291	-0.003	0.007	0.634	2926
rs12970134	MC4R	A	-0.004	0.005	0.417	6682	-0.002	0.005	0.768	6241
rs17782313	MC4R	C	-0.009	0.005	0.101	6682	-0.005	0.006	0.412	6241
rs3794991*	GATAD2A/CILP2	C	0.007	0.008	0.349	6683	0.010	0.008	0.206	6242
rs8108269	GIPR	G	0.001	0.005	0.773	6681	-0.004	0.005	0.398	6240
rs10423928*	GIPR	T	0.002	0.008	0.797	3292	-0.001	0.008	0.873	2927
rs10401969	SUGP1/CILP2	C	0.007	0.008	0.349	6683	0.010	0.008	0.206	6242
rs6017317*	FITM2-R3HDML-HNF4A	C	-0.005	0.009	0.526	3292	0.003	0.009	0.728	2927
rs6048205*	FOXA2/LINC00261	T	0.011	0.016	0.477	3292	0.000	0.016	0.984	2927
rs12010175	FAM58A	A	-0.007	0.016	0.653	3292	-0.010	0.017	0.548	2927

*Data shown is for proxy SNP (see Supplementary table 8)

Linear regression of ln-transformed glucagon concentration adjusted for sex and age

Table S13. Cohort characteristics in MDC.

Trait	MDC Reinvestigation	
	N	Mean (SD)
N (M/F)	1350/1994	
T2D N (%)	527 (15.8)	
Age (years)	3344	72.45 (5.58)
BMI (kg/m ²)	3309	26.88 (4.43)
Systolic BP (mmHg)	3310	143.44 (18.84)
Diastolic BP (mmHg)	3308	83.03 (10.28)
P-Glucose 0' (mmol/l) †	2757	5.77 (0.62)
P-Glucose 120' (mmol/l) †	2757	6.83 (1.92)
S-Insulin 0' (mU/l)	3078	9.0 (5.22)
S-Insulin 30' (mU/l) †	2644	49.72 (31.92)
S-Insulin 120' (mU/l) †	2770	54.21 (54.59)
Total cholesterol (mmol/l)	3310	5.2 (1.07)
HDL cholesterol (mmol/l)	3307	1.43 (0.43)
Triglycerides (mmol/l)	3307	1.09 (0.54)
S-GIP 0' (pg/ml)	3122	46.93 (25.52)
S-GIP 120' (pg/ml)	2766	239.46 (111.43)
P-Glucagon 0' (pg/ml)	3292	79.58 (22.61)
P-Glucagon 120' (pg/ml)	2927	71.84 (19.22)
P-GLP1 0' (pM)	3181	8.28 (3.48)
P-GLP1 120' (pM)	2876	17.71 (9.29)

† Only non-diabetic individuals included

Table S14. Cohort characteristics in PPP

Trait	PPP Basal Visit		PPP Prospective Visit	
	N	Mean (SD)	N	Mean (SD)
N (M/F)	2300/2605	-	1593/1809	-
T2D N (%)	307 (6.3)	-	284 (8.3)	-
Age (years)	4905	49.59 (15.75)	3402	56.59 (14.61)
BMI (kg/m ²)	4903	26.5 (4.46)	3390	26.88 (4.38)
Systolic BP (mmHg)	4903	133.66 (19.36)	3385	137.31 (19.83)
Diastolic BP (mmHg)	4903	80.58 (10.13)	3386	76.7 (9.9)
P-Glucose 0' (mmol/l)	4566†	5.27 (0.56)	3087	5.31 (0.6)
P-Glucose 30' (mmol/l)	4555†	8.27 (1.61)	3080	8.32 (1.59)
P-Glucose 120' (mmol/l)	4566†	5.23 (1.57)	3082	5.36 (1.61)
S-Insulin 0' (mU/l)	4711	6.8 (5.18)	3223	7.82 (6.59)
S-Insulin 30' (mU/l)	4606†	59.48 (38.86)	3208	67.78 (48.6)
S-Insulin 120' (mU/l)	4584†	34.75 (38.89)	3218	39.46 (44.86)
Total cholesterol (mmol/l)	4889	5.3 (1.05)	3398	5.39 (1.07)
HDL cholesterol (mmol/l)	4889	1.41 (0.4)	3398	1.4 (0.43)
Triglycerides (mmol/l)	4890	1.31 (0.78)	3399	1.32 (0.72)
S-GIP 0' (pg/ml)	4706	38.64 (29.15)	-	-
S-GIP120' (pg/ml)	4684	193.73 (99.97)	-	-
P-Glucagon 0' (pg/ml)	-	-	3391	94.54 (26.5)
P-Glucagon 120' (pg/ml)	-	-	3315	84.29 (22.99)
P-GLP1 0' (pmol/l)	-	-	1000	12.73 (4.55)
P-GLP1 120' (pmol/l)	-	-	973	18.95 (7.19)

† Only non-diabetic individuals included

Supplemental figures

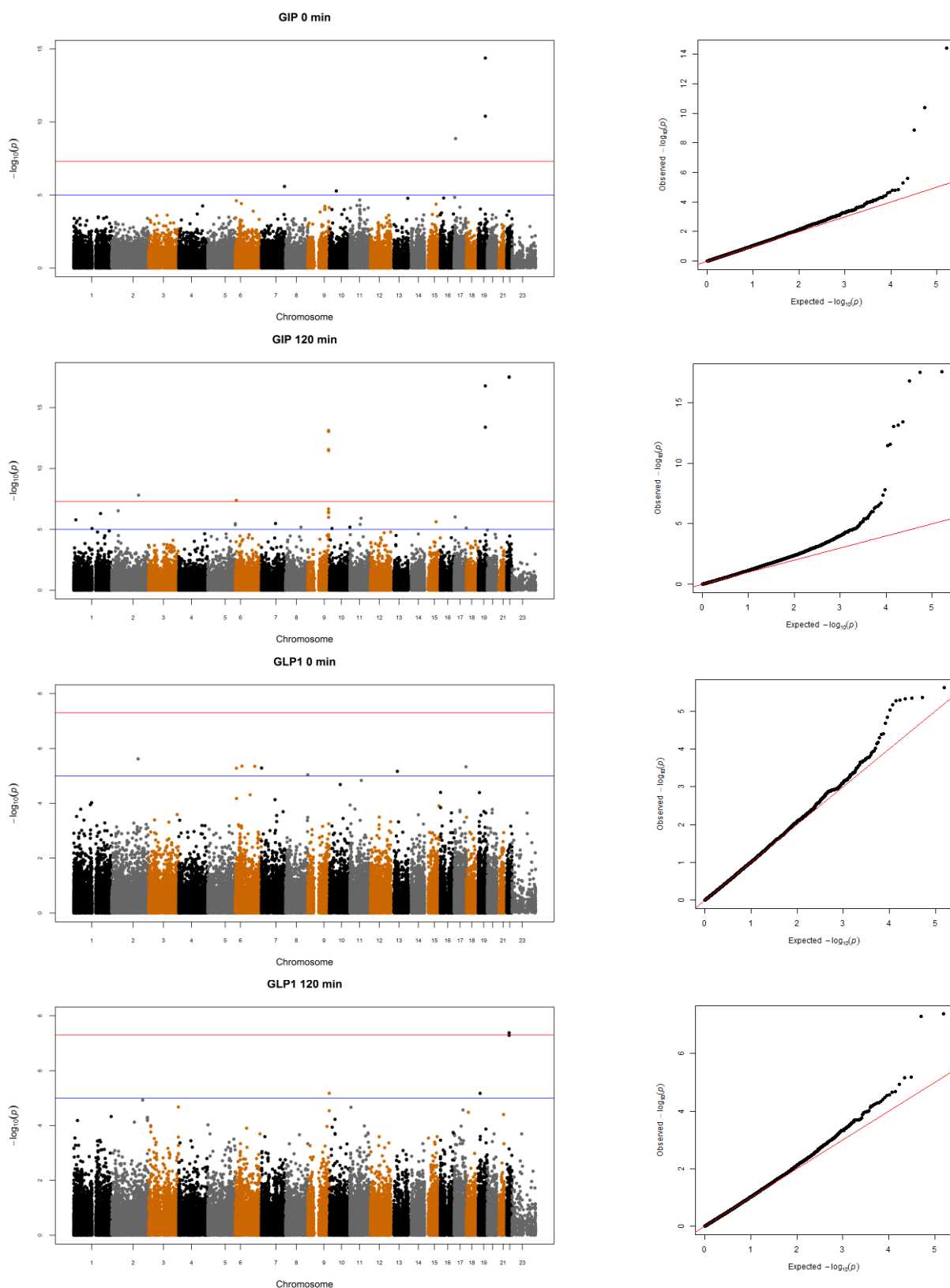


Figure S1. Manhattan and QQ-plots for meta-analysis of GIP (glucose-dependent insulintropic peptide) and GLP-1 (glucagon-like peptide-1) in the MDC and Botnia-PPP cohorts. Association of SNPs with hormone levels was analyzed using linear regression models adjusted for sex and age. Fixed-effects meta-analysis was performed using estimates of the allelic effect size and standard error.

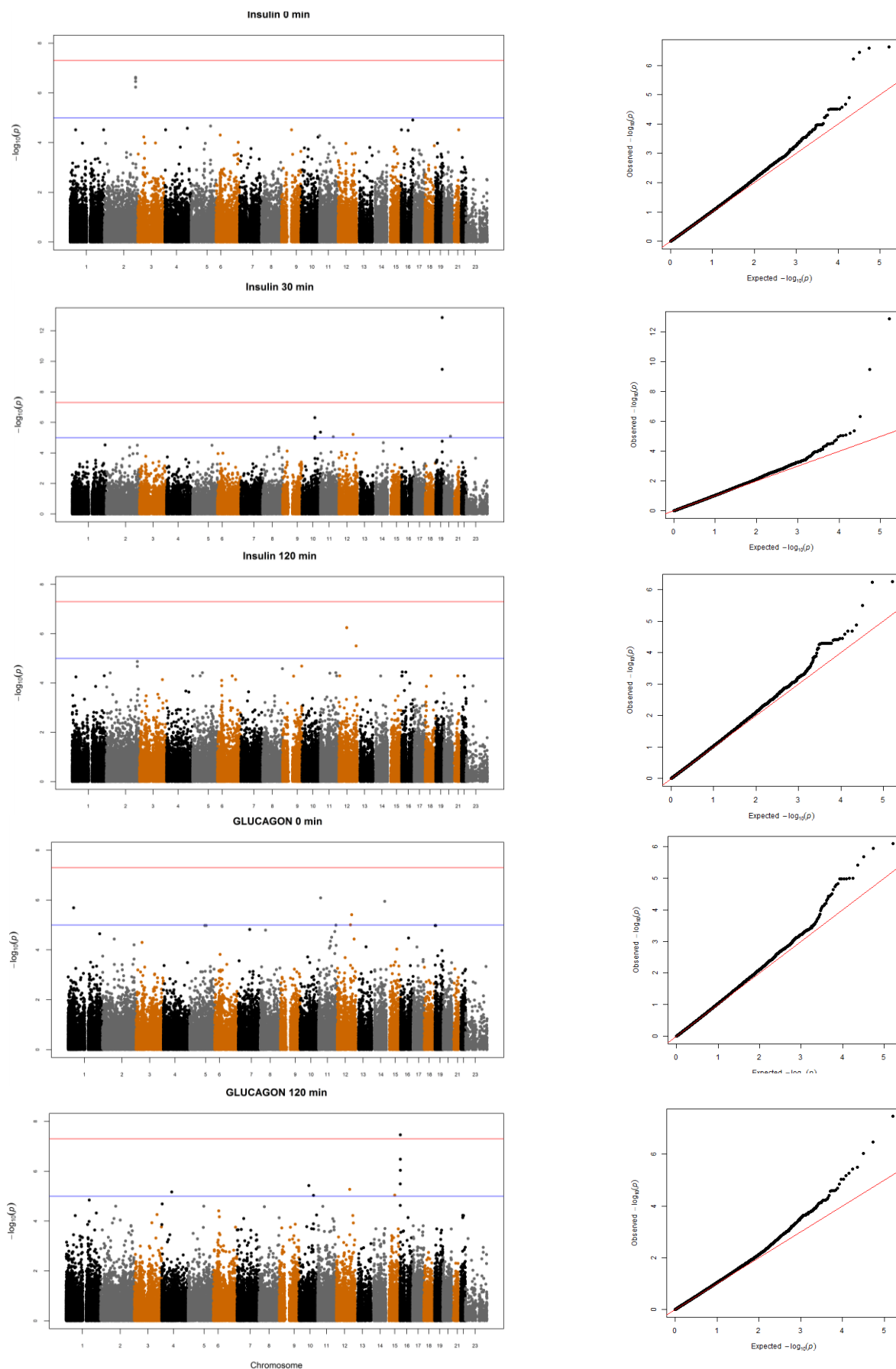
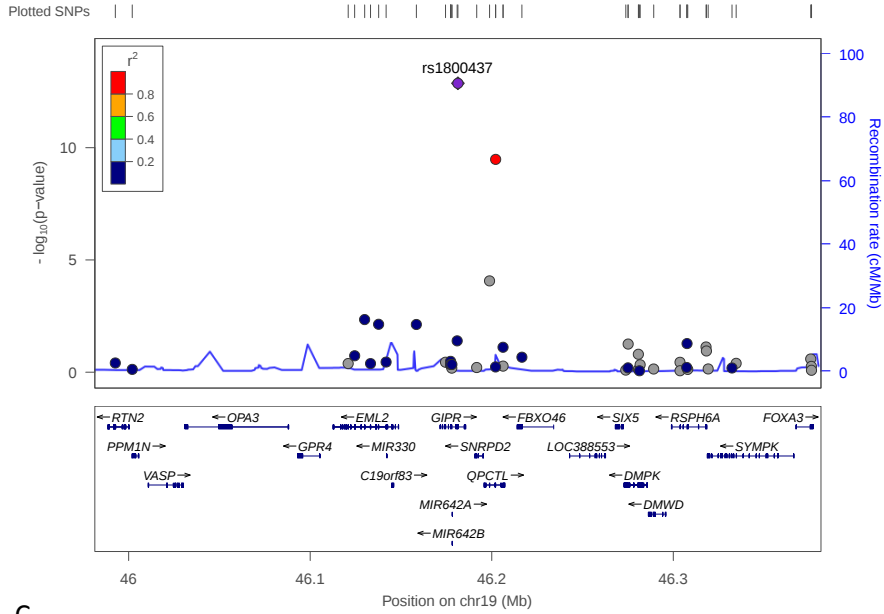
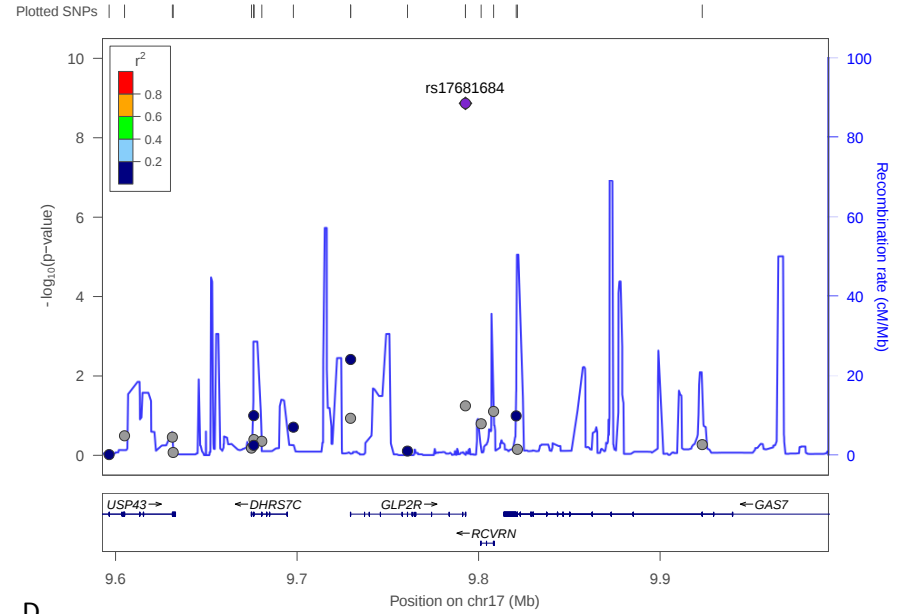


Figure S2. Manhattan and QQ-plots for meta-analysis of insulin and glucagon in the MDC and Botnia-PPP cohorts. Association of SNPs with hormone levels was analyzed using linear regression models adjusted for sex and age. Fixed-effects meta-analysis was performed using estimates of the allelic effect size and standard error.

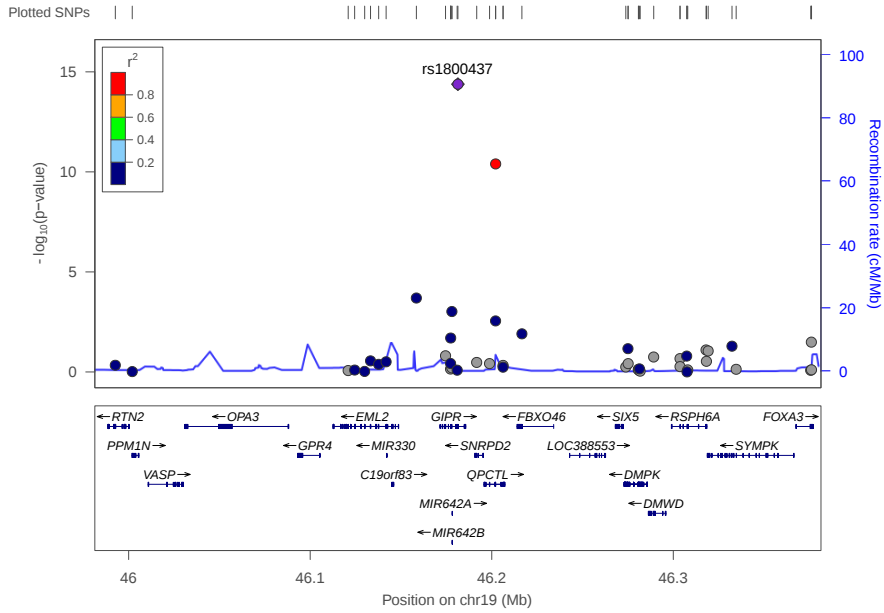
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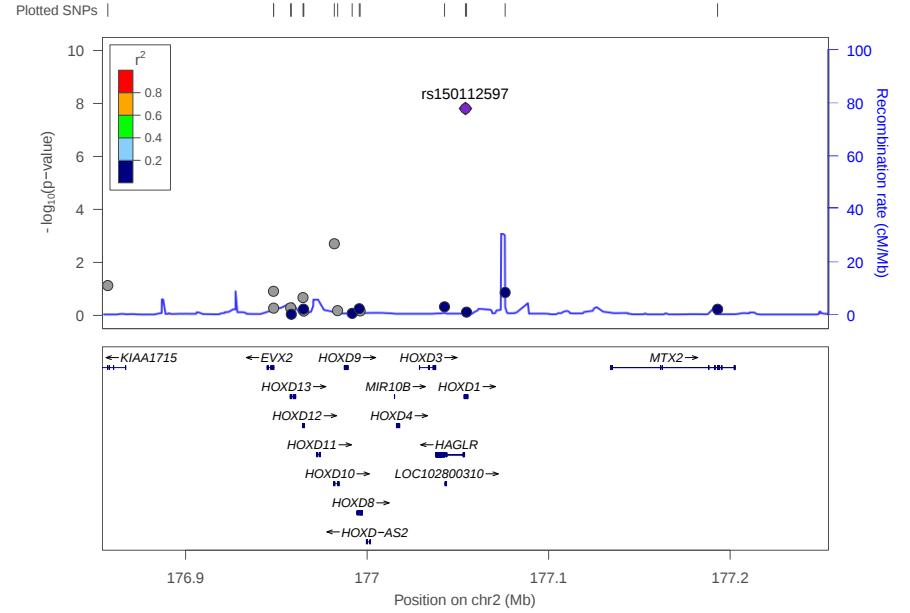
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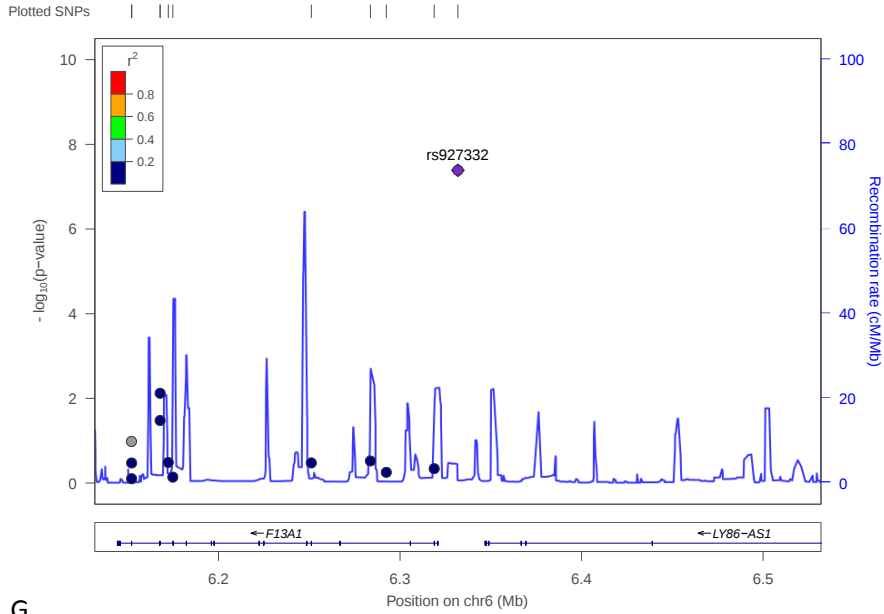
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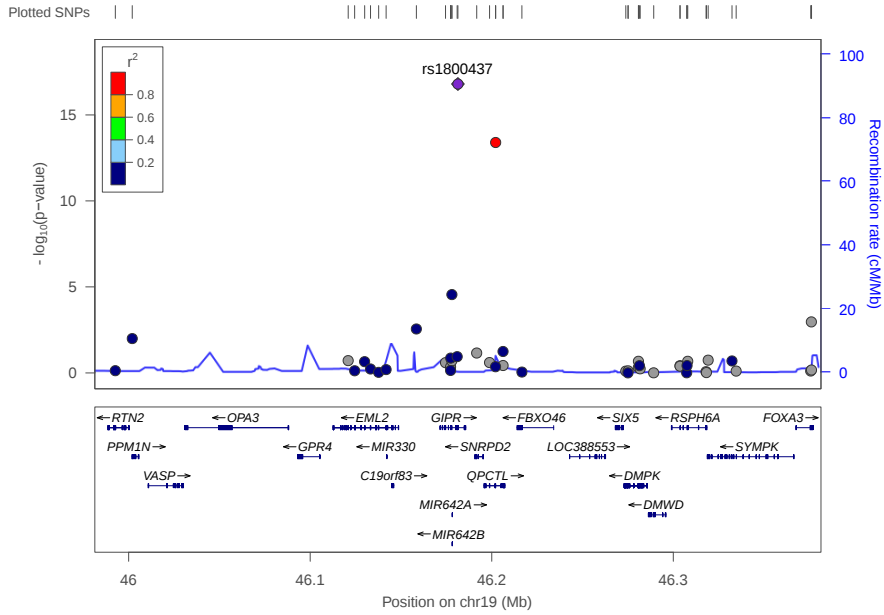
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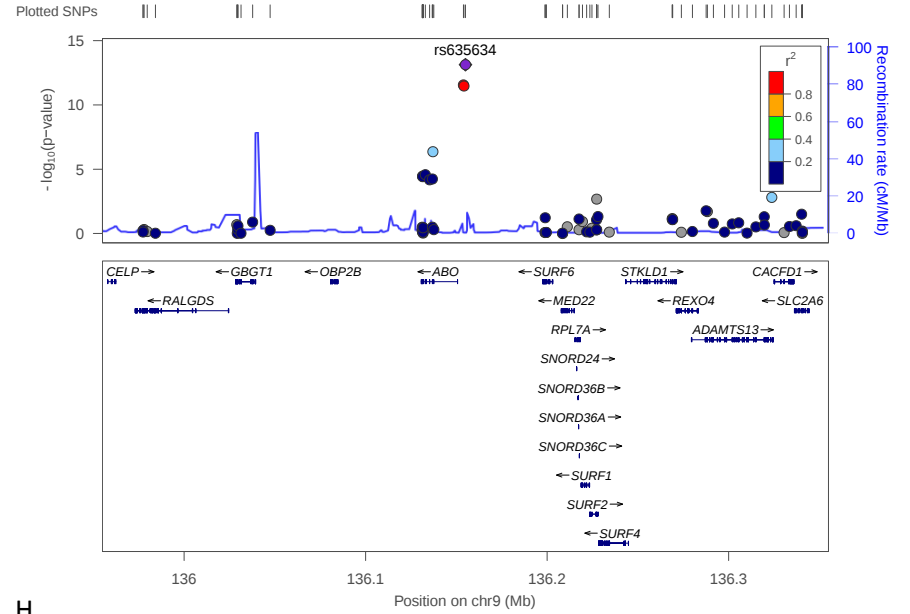
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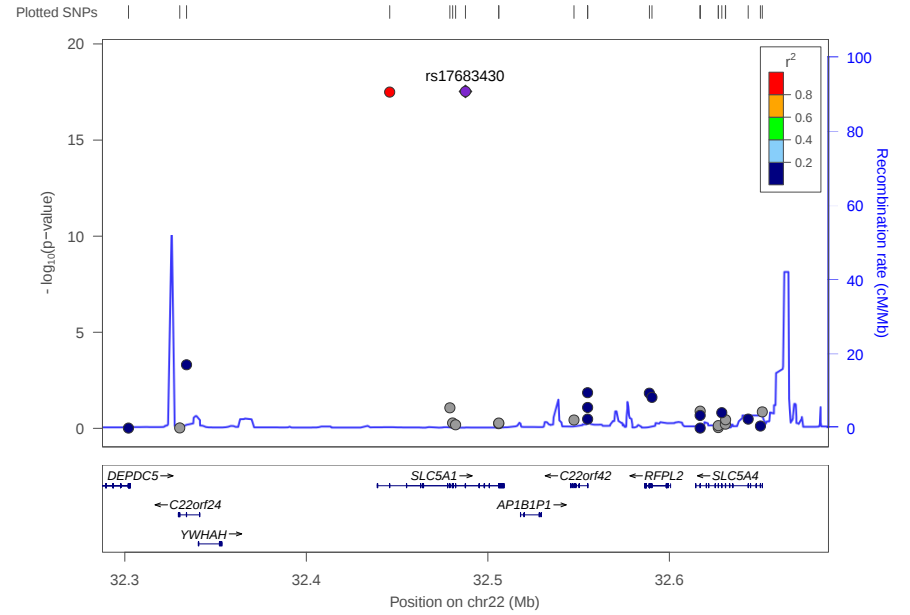
G



F



H



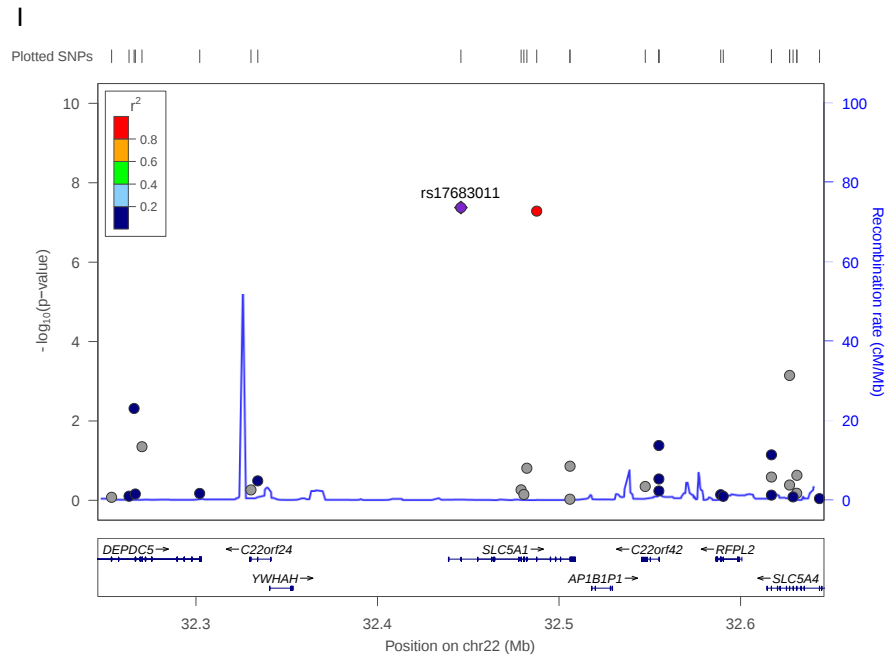


Figure S3. Regional association plots showing 200kb intervals surrounding the top SNP of each genome-wide significant locus in meta-analysis of the MDC and PPP Cohorts. A) 30 minute insulin, B-C) Fasting GIP (glucose-dependent insulintropic peptide, D-H) 2 hour GIP, I) 2 hour GLP-1 (glucagon-like peptide-1). Association of SNPs with hormone levels was analyzed using linear regression models adjusted for sex and age. Fixed-effects meta-analysis was performed using estimates of the allelic effect size and standard error

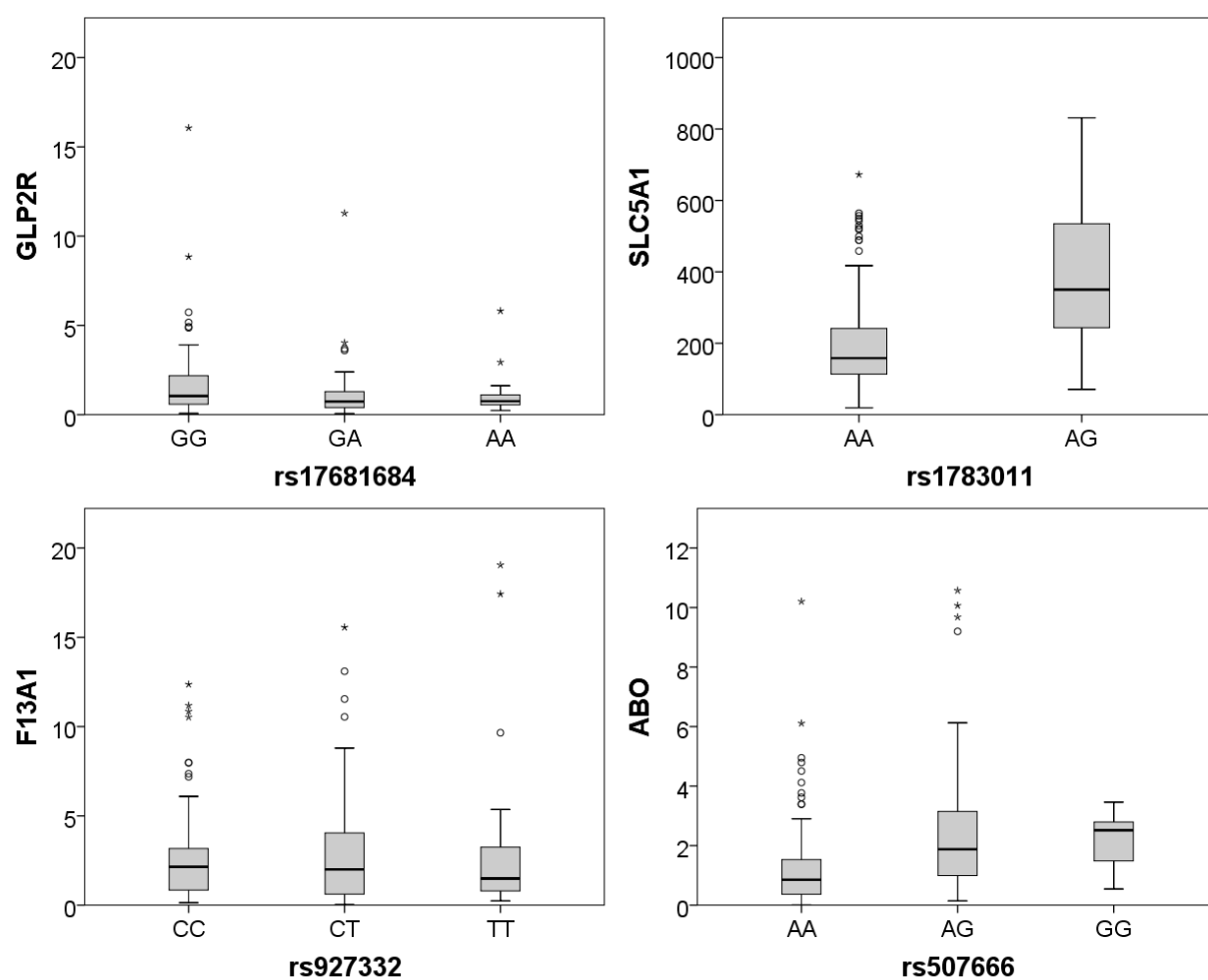


Figure S4. Expression of mRNA in human pancreatic islets by genotype (N=191 donors). Boxes show median and interquartile range. For statistics see Table S4.

Supplemental methods

Genotyping QC

QC filter applied:

Using autocall genotypes:

Samples:

- 1.) Check concordance with GWAS or other external genotypes, if available. Exclude samples with poor concordance.
- 2.) Exclude samples missing >5% of genotypes.
- 3.) Exclude samples that are outliers for inbreeding coefficient ($> 3SD$ away from mean).
- 4.) Exclude samples with discordance between inferred and reported gender.
- 5.) Exclude one from duplicate pairs of samples if phenotypes are identical, keeping sample with lower missing rate.
- 6.) Exclude both samples from duplicate pairs of samples if phenotypes are discordant.
- 7.) Exclude samples with unexpectedly high proportion of IBD sharing, based on high frequency, LD-pruned variants.
- 8.) Exclude samples that are unexpected first/second degree relatives, based on high frequency, LD-pruned variants.
- 9.) Exclude samples that are outliers on first two principal components.

Markers:

- 1.) Remove if monomorphic, i.e. $MAF=0$
- 2.) Remove if missingness across samples is $>5\%$
- 3.) Remove if HWE p-value $<10^{-6}$