

NOTES

(First sheet of the Supplemental Excel spreadsheet)

SUPPLEMENTAL TABLE 1: Baseline clinical and lifestyle characteristics of the analytical cohorts

AIRG: Acute Insulin Response to glucose; eGFR, estimated glomerular filtration rate.

*Comprises race self-reported as ‘White’, ‘American Indian/Alaskan Native’, ‘Asian/Pacific Islander’ or ‘Other.’

†Calculated using serum creatinine and cystatin.

‡Values expressed as median (Q1 – Q3). All other values expressed as mean (SD) or N (%).

SUPPLEMENTAL TABLE 2: Plasma proteins associated with incident type 2 diabetes in the CHS cohort

*Model adjusted for age, gender, race, clinic site, and estimated glomerular filtration rate

†Model adjusted for age, gender, race, clinic site, estimated glomerular filtration rate, BMI, smoking status, alcohol consumption status, and education

HR: Hazard ratio; presents change in risk per standard deviation increase in log₂ protein unit at baseline

‡ Spearman rho (ρ) coefficient for proteins simultaneous assayed using SomaScan® and Olink® on 209 HERITAGE participants (Katz et al. 2022a).

Supporting literature: 1-7 are published proteomic associations with incident diabetes, 8-11 are published proteomic associations with prevalent diabetes.

1, 8: Gudmundsdottir, et al. (2020); 2: Williams et al. (2019); 3: Ngo et al. (2021); 4,9: Elhadad et al. (2020); 5: Huth et al. (2019); 6,10: Molvin et al. (2019); 7: Nowak et al (2016); 11: Beijer et al. (2019)

MS evidence: Mass spectrometry-based verification of aptamer-protein binding (Emilsson et al., 2018).

pQTL evidence: A: Emilsson et al. (2018); B: Suhre et al. (2017); C: Sun et al. (2018); D: Benson et al. (2018); E: Katz et al. (2022b); F: Pietzner et al. (2021); G: Ferkingstad et al. (2021); H: Zhang et al. (2022), European cohort; I: Zhang et al. (2022), African American cohort.

Information on protein subcellular location and function retrieved from Uniprot (The UniProt Consortium, 2021; <https://www.uniprot.org/>)

#Two aptamers targeting the same protein

SUPPLEMENTAL TABLE 3: Plasma proteins associated with incident type 2 diabetes in the CHS cohort stratified by sex with test for interaction

All tests were adjusted for age, gender, race, clinic site, and estimated glomerular filtration rate.

HR: Hazard ratio; presents change in risk per standard deviation increase in log₂ protein unit at baseline

*P-value adjusted for false discovery rate of 5%. All other p-values are unadjusted.

SUPPLEMENTAL TABLE 4: Plasma proteins associated with longitudinal fasting glucose in the CHS cohort

Total model N = 4,176. Glucose data points per time point: N=2,285 at baseline, N=274 at +2 years, N=2,113 at +4 years, and N=1,789 at +6 years.

*Model adjusted for age, gender, race, clinic site, and estimated glomerular filtration rate

‡Model adjusted for age, gender, race, clinic site, estimated glomerular filtration rate, BMI, smoking status, alcohol consumption status, and education

Estimates present annual change in fasting glucose concentration per standard deviation increase in log2 protein unit at baseline

‡ Spearman rho (ρ) coefficient for proteins simultaneously assayed using SomaScan® and Olink® on 209 HERITAGE participants (Katz et al. 2022a)

Supporting literature: 1-7 are published proteomic associations with incident diabetes, 8-11 are published proteomic associations with prevalent diabetes.
1, 8: Gudmundsdottir, et al. (2020); 2: Williams et al. (2019); 3: Ngo et al. (2021); 4,9: Elhadad et al. (2020); 5: Huth et al. (2019); 6,10: Molvin et al. (2019);
7: Nowak et al (2016); 11: Beijer et al. (2019)

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SUPPLEMENTAL TABLE 5: Plasma proteins associated with IVGTT traits in the HERITAGE cohort

*Model adjusted for age, gender, race, and family grouping. ‡ Additionally adjusted for BMI, smoking status, and alcohol consumption status

Insulin sensitivity estimates present change in log2 [10^{-4} min/(mU ml)] per standard deviation increase in log2 protein unit

Disposition index estimates present change in log2 ($S_I \times AIR_G$) per standard deviation increase in log2 protein unit

Glucose effectiveness estimates present change per [10^{-4} min/(mU ml)]² per standard deviation increase in log2 protein unit

SUPPLEMENTAL TABLE 6: Two-sample Mendelian Randomization results for the causal effect of proteins on type 2 diabetes.

All aptamers with Bonferroni significant associations in the CHS models with appropriate genetic instruments are shown.

Genetic instruments selected from genome-wide association studies of SomaScan® aptamers, Emilsson et al. (2018); Suhre et al. (2017); Sun et al. (2018); Benson et al. (2018); Pietzner et al. (2021); Ferkingstad et al. (2021); European cohort from Zhang et al. (2022).

Type 2 diabetes genome-wide association summary data for individuals of European Ancestry from the DIAMANTE consortium, Mahajan et al. (2022).

Glycemic trait genome-wide association summary data for individuals of European Ancestry from the MAGIC consortium, Chen et al. (2021)

SUPPLEMENTAL TABLE 7: Aptamer-specific genetic instruments included in Two-sample Mendelian Randomization analysis.

Genetic instruments selected from genome-wide association studies of SomaScan® aptamers, Emilsson et al. (2018); Suhre et al. (2017); Sun et al. (2018); Benson et al. (2018); Pietzner et al. (2021); Ferkingstad et al. (2021); European cohort from Zhang et al. (2022).

Type 2 diabetes genome-wide association summary data for individuals of European Ancestry from the DIAMANTE consortium, Mahajan et al. (2022).

Glycemic trait genome-wide association summary data for individuals of European Ancestry from the MAGIC consortium, Chen et al. (2021)

SUPPLEMENTAL TABLES: REFERENCE LIST

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SUPPLEMENTAL TABLE 1: Baseline clinical and lifestyle characteristics of the analytical cohorts

Characteristic	Cohort	
	CHS	HERITAGE
N	2,631	752
Age , years	74.4 (4.9)	34.5 (13.5)
Sex , female	1,644 (62%)	415 (55%)
Race		
Black	361 (14%)	289 (38%)
Non-Black*	2,270 (86%)	463 (62%)
<i>White</i>	2,258 (86%)	463 (62%)
<i>American Indian/Alaskan Native</i>	3 (0.1%)	
<i>Asian/Pacific Islander</i>	2 (<0.1%)	
<i>Other</i>	7 (0.3%)	
Smoking Status		
Never Smoked	1,227 (47%)	484 (64%)
Former Smoker	1,154 (44%)	155 (21%)
Current Smoker	250 (9.5%)	113 (15%)
Alcohol Use , current consumer	1,288 (49%)	353 (47%)
Education , completed high school	2,028 (77%)	633 (95%)
Body mass index , kg/m ²	26.3 (4.4)	26.5 (5.5)
eGFR , mL/min/1.73 m ^{2†}	70.0 (15.7)	
Fasting Glucose , mg/dL	97.6 (9.6)	91.6 (11.8)
Follow Up , years*	11.6 (6.8–16.9)	
Insulin Sensitivity (SI) , 10 ⁻⁴ min/(mU ml) ^{‡*}		3.1 (1.8–4.9)
AIRG , 10 min/(mU ml) ^{‡*}		671 (401–1,244)
Disposition Index (DI) , SI x AIRG ^{‡*}		2,214 (1,269–3,535)
Glucose Effectiveness (SG) , %/min ^{‡*}		0.016 (0.011–0.024)

SUPPLEMENTAL TABLE 2: Plasma proteins associated with incident type 2 diabetes in the CHS cohort (Columns A-H)

Aptamer ID	UniProt ID	Gene Symbol	Target Protein Name	HR (95% CI)*	p-value	HR (95% CI) [†]	p-value
10521-10	Q9BRK3	<i>MXRA8</i>	Matrix-remodeling-associated protein 8	0.60 (0.53–0.67)	6.0E-18	0.65 (0.57–0.73)	1.8E-12
8337-65	Q92729	<i>PTPRU</i>	Receptor-type tyrosine-protein phosphatase U	1.35 (1.25–1.45)	1.6E-15	1.32 (1.21–1.43)	2.4E-11
15562-24	P08236	<i>GUSB</i>	Beta-glucuronidase	1.54 (1.38–1.71)	1.4E-15	1.46 (1.30–1.63)	2.5E-11
5722-78	P42785	<i>PRCP</i>	Lysosomal Pro-X carboxypeptidase	1.54 (1.37–1.72)	4.6E-14	1.46 (1.31–1.64)	5.4E-11
3343-1	Q03154	<i>ACY1</i>	Aminoacylase-1	1.39 (1.27–1.52)	6.4E-13	1.36 (1.24–1.48)	5.6E-11
12370-30	Q13790	<i>APOF</i>	Apolipoprotein F	0.64 (0.58–0.72)	2.1E-16	0.68 (0.61–0.77)	7.2E-11
8469-41	P18065	<i>IGFBP2</i>	Insulin-like growth factor-binding protein 2	0.63 (0.56–0.71)	1.2E-14	0.66 (0.58–0.75)	2.8E-10
3554-24	Q15848	<i>ADIPOQ</i>	Adiponectin	0.65 (0.58–0.72)	8.6E-14	0.68 (0.61–0.77)	4.0E-10
14636-25	P52758	<i>HRSP12</i>	Ribonuclease UK114	1.36 (1.24–1.50)	1.7E-10	1.34 (1.21–1.47)	3.1E-09
19241-31	P82980	<i>RBP5</i>	Retinol-binding protein 5	1.34 (1.23–1.46)	5.6E-11	1.30 (1.19–1.42)	1.1E-08
9416-77	P14384	<i>CPM</i>	Carboxypeptidase M	1.36 (1.24–1.49)	5.0E-11	1.32 (1.20–1.46)	1.9E-08
6408-2	P55103	<i>INHBC</i>	Inhibin beta C chain	1.50 (1.34–1.67)	4.1E-13	1.40 (1.25–1.58)	2.3E-08
17396-23	P07327	<i>ADH1A</i>	Alcohol dehydrogenase 1A	1.33 (1.22–1.45)	2.5E-11	1.28 (1.17–1.40)	3.0E-08
4929-55	P04278	<i>SHBG</i>	Sex hormone-binding globulin	0.67 (0.60–0.75)	3.1E-12	0.72 (0.64–0.81)	3.5E-08
2948-58	P10912	<i>GHR</i>	Growth hormone receptor	1.47 (1.31–1.65)	6.0E-11	1.4 (1.24–1.58)	6.5E-08
3362-61	Q9BU40	<i>CHRD1</i>	Chordin-like protein 1	0.67 (0.58–0.76)	5.7E-10	0.69 (0.61–0.79)	7.1E-08
5452-71	P07306	<i>ASGR1</i>	Asialoglycoprotein receptor 1	1.34 (1.22–1.47)	4.8E-10	1.29 (1.17–1.41)	7.4E-08
7206-20	P09467	<i>FBP1</i>	Fructose-1.6-bisphosphatase 1	1.31 (1.20–1.43)	1.1E-09	1.28 (1.17–1.39)	8.9E-08
6379-62	Q86TH1	<i>ADAMTSL2</i>	ADAMTS-like protein 2	1.37 (1.25–1.50)	3.2E-11	1.30 (1.18–1.43)	1.0E-07
7957-2	Q8WXD2	<i>SCG3</i>	Secretogranin-3	0.68 (0.61–0.76)	1.8E-12	0.74 (0.66–0.82)	1.1E-07
10565-19	O94933	<i>SLITRK3</i>	SLIT and NTRK-like protein 3	0.69 (0.63–0.77)	3.5E-12	0.75 (0.67–0.83)	1.2E-07
3009-3	Q03167	<i>TGFBR3</i>	Transforming growth factor beta receptor type 3	0.71 (0.63–0.79)	8.1E-10	0.74 (0.66–0.83)	1.3E-07
15487-164	P23141	<i>CES1</i>	Liver carboxylesterase 1	1.33 (1.21–1.47)	3.2E-09	1.29 (1.17–1.43)	2.1E-07
15525-294	P00326	<i>ADH1C</i>	Alcohol dehydrogenase 1C	1.32 (1.20–1.45)	4.8E-09	1.28 (1.16–1.40)	3.1E-07
16307-22	Q6UXZ4	<i>UNC5D</i>	Netrin receptor UNC5D	0.66 (0.58–0.74)	1.5E-12	0.72 (0.63–0.82)	3.1E-07
5105-2	Q9BZR6	<i>RTN4R</i>	Reticulon-4 receptor	1.39 (1.25–1.55)	1.3E-09	1.34 (1.20–1.50)	3.9E-07
13998-26	Q8N142	<i>ADSSL1</i>	Adenylosuccinate synthetase isozyme 1	1.27 (1.17–1.39)	3.8E-08	1.26 (1.15–1.37)	3.9E-07

18185-118	P05062	<i>ALDOB</i>	Fructose-bisphosphate aldolase B	1.28 (1.17–1.40)	1.5E-07	1.27 (1.16–1.40)	4.3E-07
13460-4	O15335	<i>CHAD</i>	Chondroadherin	0.75 (0.67–0.83)	6.6E-08	0.76 (0.68–0.84)	4.6E-07
9216-100	O15031	<i>PLXNB2</i>	Plexin-B2	1.36 (1.21–1.54)	6.1E-07	1.36 (1.21–1.54)	6.1E-07
6462-12	Q99727	<i>TIMP4</i>	Metalloproteinase inhibitor 4	0.76 (0.68–0.86)	4.3E-06	0.74 (0.66–0.84)	6.2E-07
11241-8	P04424	<i>ASL</i>	Argininosuccinate lyase	1.25 (1.14–1.36)	1.1E-06	1.25 (1.15–1.37)	8.7E-07
7179-69	O94856	<i>NFASC</i>	Neurofascin	1.23 (1.13–1.32)	2.7E-07	1.22 (1.13–1.33)	9.4E-07
8325-37	P08319	<i>ADH4</i>	Alcohol dehydrogenase 4	1.30 (1.19–1.42)	6.0E-09	1.26 (1.15–1.38)	9.9E-07
15426-5	Q99519	<i>NEU1</i>	Sialidase-1	1.21 (1.14–1.29)	3.6E-09	1.18 (1.11–1.27)	1.1E-06
5632-6	Q9NQ79	<i>CRTAC1</i>	Cartilage acidic protein 1	0.77 (0.69–0.85)	4.3E-07	0.77 (0.69–0.86)	1.1E-06
15447-45	Q00796	<i>SORD</i>	Sorbitol dehydrogenase	1.31 (1.19–1.45)	9.7E-08	1.29 (1.16–1.42)	1.2E-06
9213-24	O95954	<i>FTCD</i>	Formimidoyltransferase-cyclodeaminase	1.31 (1.19–1.45)	5.3E-08	1.28 (1.16–1.41)	1.4E-06
3331-8	Q6NW40	<i>RGMB</i>	RGM domain family member B	0.67 (0.60–0.76)	3.8E-10	0.73 (0.64–0.83)	1.5E-06
7050-5 [#]	Q7Z3B1	<i>NEGR1</i>	Neuronal growth regulator 1 [#]	0.70 (0.62–0.79)	7.3E-09	0.74 (0.65–0.84)	1.7E-06
13109-82 [#]	Q7Z3B1	<i>NEGR1</i>	Neuronal growth regulator 1 [#]	0.72 (0.65–0.81)	6.0E-09	0.77 (0.69–0.86)	3.8E-06
6388-21	Q96EE4	<i>CCDC126</i>	Coiled-coil domain-containing protein 126	0.70 (0.63–0.78)	1.5E-10	0.76 (0.68–0.85)	1.7E-06
15483-377	O00468	<i>AGRN</i>	Agrin	1.35 (1.23–1.48)	7.7E-10	1.27 (1.15–1.41)	2.4E-06
5708-1	Q969E1	<i>LEAP2</i>	Liver-expressed antimicrobial peptide 2	1.35 (1.22–1.50)	2.0E-08	1.29 (1.16–1.44)	2.4E-06
16558-2	Q99972	<i>MYOC</i>	Myocilin	0.75 (0.67–0.83)	2.3E-07	0.77 (0.69–0.86)	2.9E-06
14079-14	Q13478	<i>IL18R1</i>	Interleukin-18 receptor 1	1.22 (1.13–1.32)	2.4E-07	1.21 (1.12–1.32)	3.6E-06
6049-64	Q13332	<i>PTPRS</i>	Receptor-type tyrosine-protein phosphatase S	0.75 (0.68–0.84)	9.4E-08	0.78 (0.7–0.87)	3.7E-06
13496-19	Q01581	<i>HMGCS1</i>	Hydroxymethylglutaryl-CoA synthase. cytoplasmic	1.28 (1.16–1.41)	7.5E-07	1.27 (1.15–1.4)	3.9E-06
18342-2	Q9Y617	<i>PSAT1</i>	Phosphoserine aminotransferase	1.27 (1.16–1.39)	3.9E-07	1.25 (1.14–1.37)	4.0E-06
3339-33	P35442	<i>THBS2</i>	Thrombospondin-2	1.31 (1.19–1.44)	4.6E-08	1.26 (1.14–1.39)	4.5E-06
6557-50	Q8TF66	<i>LRRC15</i>	Leucine-rich repeat-containing protein 15	0.76 (0.68–0.85)	7.4E-07	0.77 (0.69–0.86)	4.8E-06
17366-6	Q96GG9	<i>DCUNID1</i>	DCN1-like protein 1	1.28 (1.18–1.38)	7.9E-10	1.22 (1.12–1.34)	9.4E-06
13697-51	P21695	<i>GPD1</i>	Glycerol-3-phosphate dehydrogenase [NAD(+)].	1.36 (1.23–1.50)	1.4E-09	1.27 (1.14–1.41)	1.0E-05
16907-3	Q8N3J6	<i>CADM2</i>	Cell adhesion molecule 2	0.68 (0.60–0.77)	6.3E-10	0.75 (0.66–0.85)	1.2E-05
5078-82	O15197	<i>EPHB6</i>	Ephrin type-B receptor 6	0.69 (0.60–0.79)	1.4E-07	0.73 (0.64–0.84)	1.2E-05
18398-1	P51857	<i>AKR1D1</i>	3-oxo-5-beta-steroid 4-dehydrogenase	1.23 (1.14–1.33)	1.2E-07	1.20 (1.11–1.31)	1.6E-05

5939-42	O43508	<i>TNFSF12</i>	Tumor necrosis factor ligand superfamily member 12	0.71 (0.61–0.81)	1.5E-06	0.74 (0.64–0.85)	1.9E-05
7638-30	Q12907	<i>LMAN2</i>	Vesicular integral-membrane protein VIP36	1.35 (1.22–1.49)	9.0E-09	1.26 (1.13–1.41)	2.1E-05
18893-26	Q9Y653	<i>GPR56</i>	Adhesion G-protein coupled receptor G1	1.24 (1.14–1.35)	2.6E-07	1.20 (1.10–1.31)	2.7E-05
11278-4	P13942	<i>COL11A2</i>	Collagen alpha-2(XI) chain	0.79 (0.71–0.87)	7.0E-06	0.80 (0.71–0.89)	3.0E-05
15594-47	Q92743	<i>HTRA1</i>	Serine protease HTRA1	1.33 (1.21–1.45)	7.9E-10	1.23 (1.11–1.36)	4.3E-05
4125-52	Q15109	<i>AGER</i>	Advanced glycosylation end product-specific receptor.	0.75 (0.67–0.83)	1.5E-07	0.79 (0.71–0.89)	4.4E-05
16916-19	Q9H5Y7	<i>SLITRK6</i>	SLIT and NTRK-like protein 6	0.71 (0.62–0.81)	5.3E-07	0.76 (0.66–0.87)	4.5E-05
18397-5	P17516	<i>AKR1C4</i>	Aldo-keto reductase family 1 member C4	1.25 (1.14–1.37)	1.3E-06	1.21 (1.10–1.33)	5.0E-05
18841-1	Q9UIV8	<i>SERPINB13</i>	Serpin B13	0.73 (0.64–0.84)	6.9E-06	0.76 (0.66–0.87)	5.1E-05
5000-52	Q08380	<i>LGALS3BP</i>	Galectin-3-binding protein	1.29 (1.17–1.42)	3.9E-07	1.23 (1.11–1.36)	5.1E-05
15511-37	O95502	<i>NPTXR</i>	Neuronal pentraxin receptor	0.72 (0.64–0.80)	1.3E-08	0.78 (0.70–0.88)	5.3E-05
5353-89	P18510	<i>IL1RN</i>	Interleukin-1 receptor antagonist protein	1.20 (1.12–1.28)	2.5E-07	1.17 (1.08–1.26)	6.1E-05
5036-50	P98066	<i>TNFAIP6</i>	Tumor necrosis factor-inducible gene 6 protein	0.76 (0.68–0.86)	3.2E-06	0.79 (0.71–0.89)	6.1E-05
2580-83	P05164	<i>MPO</i>	Myeloperoxidase	1.27 (1.15–1.41)	2.1E-06	1.23 (1.11–1.36)	6.6E-05
13501-10	Q8TBE7	<i>SLC35G2</i>	Solute carrier family 35 member G2	1.21 (1.12–1.31)	1.1E-06	1.18 (1.09–1.28)	6.9E-05
5843-60	Q96KQ7	<i>EHMT2</i>	Histone-lysine N-methyltransferase EHMT2	0.73 (0.65–0.81)	3.6E-08	0.79 (0.70–0.89)	6.9E-05
7198-197	O75063	<i>FAM20B</i>	Glycosaminoglycan xylosylkinase	0.73 (0.65–0.82)	2.1E-07	0.78 (0.69–0.88)	8.7E-05
15559-5	P58335	<i>ANTXR2</i>	Anthrax toxin receptor 2	0.75 (0.67–0.83)	1.4E-07	0.80 (0.72–0.89)	8.9E-05
18917-53	P04746	<i>AMY2A</i>	Pancreatic alpha-amylase	0.74 (0.67–0.82)	7.8E-09	0.81 (0.72–0.9)	1.2E-04
19553-14	Q16623	<i>STX1A</i>	Syntaxin-1A	0.72 (0.63–0.81)	2.0E-07	0.78 (0.68–0.88)	1.2E-04
15467-10	Q96CG8	<i>CTHRC1</i>	Collagen triple helix repeat-containing protein 1	0.79 (0.71–0.87)	3.4E-06	0.82 (0.74–0.91)	1.3E-04
2212-69	P00750	<i>PLAT</i>	Tissue-type plasminogen activator	1.34 (1.21–1.50)	9.7E-08	1.25 (1.11–1.40)	1.4E-04
14618-26	Q96AW1	<i>VOPPI</i>	Vesicular prosurvival protein 1	0.72 (0.64–0.82)	3.3E-07	0.79 (0.69–0.89)	1.6E-04
11237-49	Q15113	<i>PCOLCE</i>	Procollagen C-endopeptidase enhancer 1	0.79 (0.71–0.87)	6.4E-06	0.82 (0.73–0.91)	1.8E-04
10464-6	Q9H6X2	<i>ANTXR1</i>	Anthrax toxin receptor 1	0.75 (0.67–0.84)	4.0E-07	0.80 (0.72–0.90)	1.8E-04
9377-25	P21583	<i>KITLG</i>	Kit ligand	0.78 (0.70–0.87)	6.0E-06	0.81 (0.73–0.91)	2.1E-04
18411-83	Q9NXU5	<i>ARL15</i>	ADP-ribosylation factor-like protein 15	1.22 (1.12–1.32)	5.2E-06	1.18 (1.08–1.29)	2.1E-04
7210-25	P51693	<i>APLP1</i>	Amyloid-like protein 1	0.76 (0.69–0.84)	6.3E-08	0.82 (0.74–0.91)	2.6E-04
10445-20	O95445	<i>APOM</i>	Apolipoprotein M	0.76 (0.69–0.85)	3.1E-07	0.82 (0.74–0.91)	3.2E-04

14131-37	P52799	<i>EFNB2</i>	Ephrin-B2	0.74 (0.65–0.84)	7.3E-06	0.78 (0.69–0.89)	3.2E-04
9002-36	Q86U17	<i>SERPINA11</i>	Serpin A11	0.77 (0.69–0.87)	8.4E-06	0.81 (0.72–0.91)	3.4E-04
9484-75	Q14126	<i>DSG2</i>	Desmoglein-2	0.79 (0.71–0.88)	7.9E-06	0.83 (0.75–0.92)	3.5E-04
16890-37	Q8N6G6	<i>ADAMTSL1</i>	ADAMTS-like protein 1	0.76 (0.68–0.85)	9.7E-07	0.81 (0.73–0.91)	3.8E-04
11214-40	Q9UBS3	<i>DNAJB9</i>	DnaJ homolog subfamily B member 9	1.29 (1.17–1.43)	8.3E-07	1.21 (1.09–1.34)	4.1E-04
2771-35	P08833	<i>IGFBP1</i>	Insulin-like growth factor-binding protein 1	0.75 (0.68–0.83)	6.8E-09	0.83 (0.74–0.92)	4.2E-04
7970-315	Q13508	<i>ART3</i>	Ecto-ADP-ribosyltransferase 3	0.72 (0.64–0.81)	5.5E-08	0.80 (0.70–0.91)	4.2E-04
8484-24	P41159	<i>LEP</i>	Leptin	1.46 (1.27–1.68)	5.9E-08	1.25 (1.04–1.49)	4.2E-04
19563-3	Q9BYH1	<i>SEZ6L</i>	Seizure 6-like protein	0.74 (0.66–0.83)	8.0E-08	0.83 (0.73–0.93)	4.2E-04
3235-50	Q8TEU8	<i>WFIKK2</i>	WAP. Kazal. immunoglobulin. Kunitz and NTR domain-containing protein 2	0.75 (0.67–0.83)	1.1E-07	0.83 (0.74–0.92)	4.2E-04
9296-15	P23468	<i>PTPRD</i>	Receptor-type tyrosine-protein phosphatase delta	0.76 (0.68–0.84)	4.0E-07	0.83 (0.74–0.94)	4.2E-04
9018-38	Q9P2E7	<i>PCDH10</i>	Protocadherin-10	0.71 (0.63–0.81)	4.2E-07	0.81 (0.7–0.93)	4.2E-04
9312-8	P25311	<i>AZGP1</i>	Zinc-alpha-2-glycoprotein	0.80 (0.74–0.87)	5.1E-07	0.86 (0.78–0.95)	4.2E-04
15556-49	P19961	<i>AMY2B</i>	Alpha-amylase 2B	0.76 (0.69–0.85)	5.9E-07	0.84 (0.75–0.93)	4.2E-04
8352-26	Q96PQ1	<i>SIGLEC12</i>	Sialic acid-binding Ig-like lectin 12	1.25 (1.14–1.37)	1.9E-06	1.18 (1.07–1.30)	4.2E-04
15539-15	Q96PX8	<i>SLITRK1</i>	SLIT and NTRK-like protein 1	0.74 (0.65–0.84)	2.8E-06	0.83 (0.73–0.95)	4.2E-04
3049-61	P07477	<i>PRSS1</i>	Trypsin-1	0.77 (0.70–0.86)	3.0E-06	0.83 (0.74–0.93)	4.2E-04
15573-110	O14594	<i>NCAN</i>	Neurocan core protein	0.78 (0.70–0.86)	3.1E-06	0.86 (0.77–0.96)	4.2E-04
16908-5	P23515	<i>OMG</i>	Oligodendrocyte-myelin glycoprotein	0.79 (0.71–0.87)	5.9E-06	0.83 (0.75–0.92)	4.2E-04
2950-57	P22692	<i>IGFBP4</i>	Insulin-like growth factor-binding protein 4	1.28 (1.15–1.43)	6.1E-06	1.20 (1.07–1.34)	4.2E-04
4568-17	O94991	<i>SLITRK5</i>	SLIT and NTRK-like protein 5	0.76 (0.68–0.86)	6.7E-06	0.82 (0.73–0.93)	4.2E-04
5657-28	Q11201	<i>ST3GAL1</i>	CMP-N-acetylneuraminate-beta-galactosamide-alpha-2.3-sialyltransferase 1	0.74 (0.65–0.84)	7.1E-06	0.82 (0.71–0.93)	4.2E-04
6383-90	O43897	<i>TLL1</i>	Tolloid-like protein 1	1.28 (1.15–1.42)	7.5E-06	1.21 (1.08–1.34)	4.2E-04
2837-3	P08581	<i>MET</i>	Hepatocyte growth factor receptor	0.80 (0.72–0.88)	7.7E-06	0.85 (0.76–0.94)	4.2E-04
18896-23	Q8IZP7	<i>HS6ST3</i>	Heparan-sulfate 6-O-sulfotransferase 3	0.75 (0.66–0.85)	8.2E-06	0.84 (0.73–0.95)	4.2E-04
4876-32	P00740	<i>F9</i>	Coagulation factor IX	1.32 (1.17–1.49)	8.9E-06	1.22 (1.07–1.38)	4.2E-04

SUPPLEMENTAL TABLE 2: Plasma proteins associated with incident type 2 diabetes in the CHS cohort (Columns C,I-N)

Gene Symbol	ρ^{\ddagger}	MS	pQTL evidence	Supporting literature	Subcellular location	Function
<i>MXRA8</i>			F,G,H,I	1,2,8	Cell membrane, cell junction	Transmembrane protein which can modulate activity of various signaling pathways, probably via binding to integrin. Mediates heterophilic cell-cell interactions in vitro.
<i>PTPRU</i>			F,G,H,I	1,8	Cell junction; cell membrane	Tyrosine-protein phosphatase which dephosphorylates CTNNB1. May function in cell proliferation and migration and play a role in the maintenance of epithelial integrity.
<i>GUSB</i>	0.89		F,G,H,I		Lysosome	Plays an important role in the degradation of dermatan and keratan sulfates.
<i>PRCP</i>	0.68		A,C,F,G,H,I	2,8	Lysosome	Cleaves C-terminal amino acids linked to proline in peptides such as angiotensin II, III and des-Arg9-bradykinin.
<i>ACY1</i>	0.89	DDA, MRM	E,F,G,H,I	1,3,4,8,9	Cytoplasm	Catalyzes the hydrolysis of N-acetylated amino acids to acetate and free amino acids.
<i>APOF</i>			C,F,G,H,I	1,2,8	Secreted	Minor apolipoprotein that associates with LDL. Inhibits cholesteryl ester transfer protein (CETP) activity and appears to be an important regulator of cholesterol transport.
<i>IGFBP2</i>	0.77	DDA	G,H	1,2,3,4,6,8,9,10,11	Secreted	Prolongs IGF half-life. Either inhibits or stimulates the growth promoting effects of the IGFs on cell culture. Alters the interaction of IGFs with their cell surface receptors.
<i>ADIPOQ</i>			D',F,G,H,I	1,3,4,5,8,9	Secreted	Involved in the control of fat metabolism and insulin sensitivity, with direct anti-diabetic, anti-atherogenic and anti-inflammatory activities. Stimulates AMPK phosphorylation and activation in the liver and skeletal muscle, enhancing glucose utilization and fatty-acid combustion.
<i>HRSP12</i>			C,F,G,H,I	1,2,8	Cytoplasm	Catalyzes the hydrolytic deamination of enamine/imine intermediates that form during the course of normal metabolism.
<i>RBP5</i>	0.66		F,G,H,I	2	Cytoplasm	Intracellular transport of retinol.
<i>CPM</i>	0.75	DDA	A,F,G,H,I	1,2,8	Cell membrane	Specifically removes C-terminal basic residues from peptides and proteins. Plays important roles in the control of peptide hormone and growth factor activity at the cell surface, and in the membrane-localized degradation of extracellular proteins.
<i>INHBC</i>	0.40	DDA	A,C',G,H,I	1,2,8	Secreted	Involved in regulation of various functions depending on subunit composition: hypothalamic, pituitary, and gonadal hormone secretion, follitropin and insulin secretion, nerve cell survival.
<i>ADH1A</i>			F,G,H,I	2	Cytoplasm	Oxidizes primary as well as secondary alcohols.
<i>SHBG</i>			F,G,H,I	1,2,3,8,9	Secreted	Functions as an androgen transport protein but may also be involved in receptor mediated processes. Regulates the plasma metabolic clearance rate of steroid hormones.
<i>GHR</i>			C,E,F,G,H,I	1,3,4,8	Cell membrane	Receptor for pituitary gland GH involved in regulating body growth. The soluble form acts as a reservoir of GH in plasma and may be a modulator/inhibitor of GH signaling.
<i>CHRD1</i>	0.33	DDA	F,G	3,8,9	Secreted	Antagonizes BMP4 function by binding to it and preventing its interaction with receptors. Alters the fate commitment of neural stem cells from gliogenesis to neurogenesis. Contributes to neuronal differentiation of neural stem cells by preventing the adoption of a glial fate.
<i>ASGR1</i>	0.49		A',F,G,H,I		Membrane	Mediates the endocytosis of plasma glycoproteins to which the terminal sialic acid residue on their complex carbohydrate moieties has been removed.
<i>FBP1</i>	0.51	DDA, MRM	A,C',F,G,H,I	1,2,8		Plays a role in regulating glucose sensing and insulin secretion of pancreatic beta-cells. Appears to modulate glycerol gluconeogenesis in liver.

<i>ADAMTSL2</i>			F,G,H	1,8	Secreted	
<i>SCG3</i>	0.60	DDA	A,C,F,G,H,I	2,8	Cytoplasmic vesicle	Member of the granin protein family that regulates the biogenesis of secretory granules. Acts as a sorting receptor for intragranular proteins including chromogranin A/CHGA.
<i>SLITRK3</i>			C,F,G,H,I	2,8	Membrane	Suppresses neurite outgrowth.
<i>TGFBR3</i>	0.30		F,G,H,I	3,4,8,9	Secreted	Binds to TGF- β . Could capture and retain TGF- β for presentation to the signaling receptors.
<i>CES1</i>	0.52		F',G',H,I		Endoplasmic reticulum lumen, cytoplasm	Converts monoacylglycerides to free fatty acids and glycerol. Hydrolyzes cellular cholesteryl esters to free cholesterol and promotes reverse cholesterol transport by allowing free cholesterol efflux from macrophages to extracellular cholesterol acceptors and releasing free cholesterol from lipoprotein-delivered cholesteryl esters in the liver for bile acid synthesis or direct secretion into the bile.
<i>ADH1C</i>			F',G,H,I		Cytoplasm	Exhibits high activity for ethanol oxidation and plays a major role in ethanol catabolism.
<i>UNC5D</i>			F,G,H,I	2,3,4,8,9	Cell membrane	Receptor for the netrin NTN4 that promotes neuronal cell survival. Plays a role in cell-cell adhesion and cell guidance. Receptor for netrin involved in cell migration. Plays a role in axon guidance by mediating axon repulsion of neuronal growth cones in the developing nervous system upon ligand binding.
<i>RTN4R</i>	0.65		A,C,D',E,F,G,H,I	1,3,8	Cell membrane	Receptor for RTN4, OMG and MAG. Functions as receptors for the sialylated gangliosides GT1b and GM1, and chondroitin sulfate proteoglycans. Can also bind heparin.
<i>ADSSL1</i>			F,G,H,I	1,8	Cytoplasm	Component of the purine nucleotide cycle, which interconverts IMP and AMP to regulate the nucleotide levels in various tissues, and which contributes to glycolysis and ammoniogenesis. Catalyzes the first committed step in the biosynthesis of AMP from IMP.
<i>ALDOB</i>			F,G,H		Cytoplasm	
<i>CHAD</i>			F,G,H,I	2,8	Secreted	Promotes attachment of chondrocytes, fibroblasts, and osteoblasts. May play an important role in the regulation of chondrocyte growth and proliferation.
<i>PLXNB2</i>	0.44		A,C,E,F,G,H,I	8	Cell membrane	Cell surface receptor for SEMA4C, SEMA4D and SEMA4G that plays an important role in cell-cell signaling. Plays a role in glutamatergic synapse development and is required for SEMA4A-mediated excitatory synapse development.
<i>TIMP4</i>	0.76		A,C,F,G,H,I	2	Secreted	Complexes with metalloproteinases and irreversibly inactivates them by binding to their catalytic zinc cofactor. Known to act on MMP-1, MMP-2, MMP-3, MMP-7 and MMP-9.
<i>ASL</i>			F,G,H,I	1,2,8		Catalyzes the reversible cleavage of L-argininosuccinate to fumarate and L-arginine, an intermediate step reaction in the urea cycle mostly providing for hepatic nitrogen detoxification into excretable urea as well as de novo L-arginine synthesis in nonhepatic tissues.
<i>NFASC</i>	0.65	MRM	A,C,F,G,H,I	8	Cell membrane	Cell adhesion, ankyrin-binding protein which may be involved in neurite extension, axonal guidance, synaptogenesis, myelination and neuron-glial cell interactions.
<i>ADH4</i>	0.92	DDA, MRM	A,F,G,H,I	1,8	Cytoplasm	Catalyzes the NAD-dependent oxidation of either all-trans-retinol or 9-cis-retinol. Also oxidizes long chain omega-hydroxy fatty acids producing both the intermediate aldehyde, 20-oxoarachidonate and the end product (5Z,8Z,11Z,14Z)-eicosatetraenedioate .
<i>NEU1</i>			F',G,H,I	2	Lysosome membrane	Catalyzes the removal of sialic acid moieties from glycoproteins and glycolipids.
<i>CRTAC1</i>	0.66	DDA	A,F,G,H,I	8	Secreted	

<i>SORD</i>	0.77		F,G,H,I		Mitochondrion membrane	Polyol dehydrogenase that catalyzes the reversible NAD(+)-dependent oxidation of various sugar alcohols. Is mostly active with D-sorbitol, L-threitol, xylitol and ribitol as substrates, leading to C2-oxidized products D-fructose, L-erythrulose, D-xylulose, and D-ribulose.
<i>FTCD</i>			E,F,G	1,2,3,8	Cytoplasm	Folate-dependent enzyme, that displays both transferase and deaminase activity. Serves to channel one-carbon units from formiminoglutamate to the folate pool.
<i>RGMB</i>	0.43		C,F,G,H,I	3,9	Cell membrane	Member of the repulsive guidance molecule family that contributes to the patterning of the developing nervous system. Acts as a BMP coreceptor that potentiates BMP signaling.
<i>NEGR1</i>			F,G,H,I	2,3	Cell membrane	May be involved in cell-adhesion. May function as a trans-neural growth-promoting factor in regenerative axon sprouting in the mammalian brain.
<i>NEGR1</i>			F,G,H,I			
<i>CCDC126</i>			C,F,G,H,I	1,8	Secreted	
<i>AGRN</i>	0.37		F,G,H,I		Secreted	Glycoprotein that plays a central role in the formation and the maintenance of the neuromuscular junction and directs key events in postsynaptic differentiation.
<i>LEAP2</i>			F,G,H,I	2,8	Secreted	Has an antimicrobial activity.
<i>MYOC</i>	0.47		F,G,H,I		Secreted	Secreted glycoprotein regulating the activation of different signaling pathways in adjacent cells to control different processes including cell adhesion, cell-matrix adhesion, cytoskeleton organization and cell migration.
<i>IL18R1</i>	0.53		A,C,F,G,H,I	2,3,8	Membrane	Responsible for the binding of the pro-inflammatory cytokine IL18. Contributes to IL18-induced cytokine production, either independently or as a complex with SLC12A3.
<i>PTPRS</i>	0.38	DDA	F',G,H	1,2,8	Cell membrane	Cell surface receptor that binds to glycosaminoglycans, including chondroitin sulfate proteoglycans and heparan sulfate proteoglycan.
<i>HMGCS1</i>			G'	1,8	Cytoplasm	Catalyzes the condensation of acetyl-CoA with acetoacetyl-CoA to form HMG-CoA, which is converted by HMG-CoA reductase into mevalonate, a precursor for cholesterol synthesis.
<i>PSAT1</i>			F,G,H,I	2		Catalyzes the reversible conversion of 3-phosphohydroxypyruvate to phosphoserine and of 3-hydroxy-2-oxo-4-phosphonooxybutanoate to phosphohydroxythreonine.
<i>THBS2</i>	0.49	DDA, MRM	A,B,C,D,E,F, G,H,I	1,3,8		Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Ligand for CD36 mediating antiangiogenic properties.
<i>LRRC15</i>			C,F,G,H,I	8	Cell membrane	
<i>DCUN1D1</i>			F',G'	2	Nucleus, cytoplasm	Part of an E3 ubiquitin ligase complex for neddylation. Promotes neddylation of cullin components of E3 cullin-RING ubiquitin ligase complexes.
<i>GPD1</i>			F,G,H,I	1,8	Cytoplasm	Has glycerol-3-phosphate dehydrogenase activity.
<i>CADM2</i>			F',G',H,I	2	Cell membrane	Adhesion molecule that engages in homo- and heterophilic interactions with the other nectin-like family members, leading to cell aggregation.
<i>EPHB6</i>	0.47		A,C,D,F,G,H,I	3,9	Membrane	Kinase-defective receptor for members of the ephrin-B family. Modulates cell adhesion and migration by exerting both positive and negative effects upon stimulation with ephrin-B2.
<i>AKR1D1</i>			G',H		Cytoplasm	Catalyzes the stereospecific NADPH-dependent reduction of the C4-C5 double bond of bile acid intermediates and steroid hormones carrying a delta(4)-3-one structure to yield an A/B cis-ring junction. This cis-configuration is crucial for bile acid biosynthesis and plays important roles in steroid metabolism.
<i>TNFSF12</i>	0.52		A,C,F,G,H,I	2,8	Cell membrane	Mediates NF-kappa-B activation. Promotes angiogenesis and the proliferation of endothelial cells. Also involved in induction of inflammatory cytokines. Promotes IL8 secretion.

<i>LMAN2</i>			F',G'	2	Endoplasmic reticulum	Plays a role as an intracellular lectin in the early secretory pathway. Involved in the transport and sorting of glycoproteins carrying high mannose-type glycans.
<i>GPR56</i>	0.11		F,G,H	2	Cell membrane	Receptor involved in cell adhesion and probably in cell-cell interactions. Mediates cell matrix adhesion in developing neurons and hematopoietic stem cells.
<i>COL11A2</i>			C,F,G,H,I	2,8	Secreted	May play an important role in fibrillogenesis by controlling lateral growth of collagen II fibrils.
<i>HTRA1</i>			F,G,H,I	2	Secreted, cell membrane	Serine protease with various targets, including ECM proteins like fibronectin. May degrade proteoglycans, thereby releasing soluble FGF-glycosaminoglycan complexes that promote the range and intensity of FGF signals in the extracellular space. Regulates the availability of IGFs by cleaving IGF-binding proteins.
<i>AGER</i>	0.54		C,D,F,G,H,I	3,8	Cell membrane	Mediates interactions of advanced glycosylation end products which plays a role in regulating production/expression of TNF α , oxidative stress, and endothelial dysfunction in T2 diabetes.
<i>SLITRK6</i>	0.38		F,G,H,I		Cell membrane	Regulator of neurite outgrowth required for normal hearing and vision.
<i>AKR1C4</i>	0.09		F,G,H,I	2	Cytoplasm, cytosol	Cytosolic aldo-keto reductase that catalyzes the NADH and NADPH-dependent reduction of ketosteroids to hydroxysteroids.
<i>SERPINB1</i> 3			F,G,H,I		Cytoplasm	May play a role in the proliferation or differentiation of keratinocytes.
<i>LGALS3BP</i>			D',E,F,G,H,I	1,2,3,8,9	Secreted	Promotes integrin-mediated cell adhesion. May stimulate host defense against viruses and tumor cells.
<i>NPTXR</i>	0.61		A,F,G,H,I	2,8	Membrane	May be involved in mediating uptake of synaptic material during synapse remodeling, or synaptic clustering of AMPA glutamate receptors at a subset of excitatory synapses.
<i>IL1RN</i>	0.64		A,C,E,F,G,H,I	3,7,11	Secreted	Anti-inflammatory antagonist of interleukin-1 family. Protects from immune dysregulation and uncontrolled systemic inflammation triggered by IL1.
<i>TNFAIP6</i>			B,C,D,E,F,G,H,I	2,3,8,9	Secreted	Major regulator of ECM organization during tissue remodeling.
<i>MPO</i>	0.54	MRM	A,C,E,F,G,H,I		Lysosome	Part of the host defense system of polymorphonuclear leukocytes. Mediates the proteolytic cleavage of alpha-1-microglobulin to form t-alpha-1-microglobulin, which potently inhibits oxidation of low-density lipoprotein particles and limits vascular damage.
<i>SLC35G2</i>			C',F',G'	2	Cell membrane	May play a role in cell proliferation.
<i>EHMT2</i>			C',F',G'	1,3,8	Nucleus	Histone methyltransferase that specifically mono- and dimethylates 'Lys-9' of histone H3 (H3K9me1 and H3K9me2, respectively) in euchromatin. Also required for DNA methylation.
<i>FAM20B</i>			C',F,G,H,I	2,8	Golgi apparatus membrane	Responsible for the 2-O-phosphorylation of xylose in the glycosaminoglycan-protein linkage region of proteoglycans thereby regulating the amount of mature GAG chains.
<i>ANTXR2</i>			F,G,H,I	2	Endoplasmic reticulum	Necessary for cellular interactions with laminin and the ECM.
<i>AMY2A</i>	0.75		F,G,H,I		Secreted	
<i>STX1A</i>			F',G'	2,8	Cytoplasmic vesicle	Essential for hormone and neurotransmitter calcium-dependent exocytosis and endocytosis. Also involved in the exocytosis of hormones such as insulin or glucagon-like peptide 1.
<i>CTHRC1</i>			F',G'	8	Secreted	May act as a negative regulator of collagen matrix deposition.
<i>PLAT</i>	0.66		A,F,G,H	1,2,3,6,7,8,11	Secreted	By controlling plasmin-mediated proteolysis, it plays an important role in tissue remodeling and degradation, in cell migration and many other physiopathological events.

<i>VOPPI</i>			F',G,H,I	1,2,8	Cytoplasmic vesicle membrane	Increases the transcriptional activity of NFkB1 by facilitating its nuclear translocation, DNA-binding and associated apoptotic response, when overexpressed.
<i>PCOLCE</i>	0.58	DDA	A,C,F,G,H,I		Secreted	Binds to the C-terminal propeptide of type I procollagen and enhances procollagen C-proteinase activity.
<i>ANTXR1</i>			F',G',H	1,8	Cell membrane	Plays a role in cell attachment and migration. Interacts with ECM proteins and with the actin cytoskeleton. Mediates adhesion of cells to type 1 collagen and gelatin, reorganization of the actin cytoskeleton and promotes cell spreading.
<i>KITLG</i>	0.58		A',C',F',G'	2	Cell membrane	Ligand for the receptor-type protein-tyrosine kinase KIT. Plays an essential role in the regulation of cell survival and proliferation, hematopoiesis, stem cell maintenance, gametogenesis, mast cell development, migration and function, and in melanogenesis.
<i>ARL15</i>			G'			
<i>APLP1</i>	0.77		F',G,H	2,8	Cell membrane	May play a role in postsynaptic function. The C-terminal gamma-secretase processed fragment, ALID1, activates transcription activation through APBB1 (Fe65) binding.
<i>APOM</i>	0.36	DDA	A,C,F,G,H,I	1,3,8	Secreted	Probably involved in lipid transport. Can bind sphingosine-1-phosphate, myristic acid, palmitic acid and stearic acid, retinol, all-trans-retinoic acid and 9-cis-retinoic acid.
<i>EFNB2</i>			F',G,H	3	Cell membrane	Cell surface transmembrane ligand for Eph receptors, a family tyrosine kinases crucial for migration, repulsion and adhesion during neuronal, vascular and epithelial development.
<i>SERPINA11</i>	0.60	DDA	A,F,G,H,I		Secreted	
<i>DSG2</i>	0.48	DDA	A,C,F,G,H,I	1,2,8	Cell membrane	Component of intercellular desmosome junctions. Involved in the interaction of plaque proteins and intermediate filaments mediating cell-cell adhesion.
<i>ADAMTSL1</i>			F,G,H	2	Secreted	
<i>DNAJB9</i>			C',F',G,H	8	Endoplasmic reticulum lumen	Co-chaperone for Hsp70 protein HSPA5/BiP, a key repressor of the ERN1/IRE1-mediated unfolded protein response. J domain-containing co-chaperones stimulate the ATPase activity of Hsp70 proteins and are required for efficient substrate recognition by Hsp70 proteins.
<i>IGFBP1</i>	0.83	DDA, MRM	A,D',F,G,H,I	1,3,8	Secreted	Prolong the half-life of the IGFs and have been shown to either inhibit or stimulate the growth promoting effects of the IGFs on cell culture. Promotes cell migration.
<i>ART3</i>	0.63	MRM	A,C,F,G,H,I	1,8	Cell membrane	
<i>LEP</i>	0.94	DDA, MRM	G,H	1,3,8	Secreted	Key player in the regulation of energy balance and body weight control.
<i>SEZ6L</i>	0.54		F,G,H,I		Endoplasmic reticulum membrane	May contribute to specialized endoplasmic reticulum functions in neurons.
<i>WFIKK2</i>	0.56	MRM	A,B,C,D,E,F,G,H,I	1,2,3,8,9	Secreted	Protease-inhibitor that contains multiple distinct protease inhibitor domains. Might have serine- and metallo-protease-inhibitor activity. Inhibits the activity of mature myostatin.
<i>PTPRD</i>			G'	8	Membrane	Bidirectionally induces pre- and post-synaptic neuron differentiation. Involved in pre-synaptic differentiation through interaction with SLITRK2.
<i>PCDH10</i>			G,H,I		Cell membrane	Potential calcium-dependent cell-adhesion protein.

<i>AZGP1</i>			C',F,G,H,I		Secreted	Stimulates lipid degradation in adipocytes. Causes fat losses associated with some cancers.
<i>AMY2B</i>	0.70		A,F,G,H,I	8	Secreted	
<i>SIGLEC12</i>			C',F',G'	2	Membrane	Putative adhesion molecule that mediates sialic-acid dependent binding to cells.
<i>SLITRK1</i>			G,H	2,8	Membrane, secreted	It is involved in synaptogenesis and promotes excitatory synapse differentiation. Enhances neuronal dendrite outgrowth.
<i>PRSS1</i>			F',G,H	3,8,9	Secreted	Has activity against the synthetic substrates Boc-Phe-Ser-Arg-Mec, Boc-Leu-Thr-Arg-Mec, Boc-Gln-Ala-Arg-Mec and Boc-Val-Pro-Arg-Mec.
<i>NCAN</i>	0.60		F,G,H		Secreted	May modulate neuronal adhesion and neurite growth during development by binding to neural cell adhesion molecules.
<i>OMG</i>	0.77		F,G,H	2	Cell membrane	Cell adhesion molecule contributing to the interactive process required for myelination in the central nervous system.
<i>IGFBP4</i>	0.11	DDA	A,G,H,I	1,3,8	Secreted	Prolongs IGF half-life. Either inhibits or stimulates the growth promoting effects of the IGFs on cell culture. Alters the interaction of IGFs with their cell surface receptors.
<i>SLITRK5</i>			F,G,H,I	3,8,9	Membrane	Suppresses neurite outgrowth.
<i>ST3GAL1</i>	0.03		A,C,F,G,H,I	1,2,8	Golgi apparatus	Involved in terminal sialylation of glycoproteins and glycolipids.
<i>TLL1</i>			C',F',G,H	8	Secreted	Protease which processes procollagen C-propeptides, such as chordin.
<i>MET</i>	0.52	MRM	A,B',C',D',E,F,G,H,I	3,8,9	Membrane	Receptor tyrosine kinase that transduces signals from the ECM to the cytoplasm by binding to hepatocyte growth factor/ -ligand. Regulates proliferation, scattering, morphogenesis & survival.
<i>HS6ST3</i>			F,G,H,I	2	Membrane	6-O-sulfation enzyme which catalyzes the transfer of sulfate from 3'-phosphoadenosine 5'-phosphosulfate (PAPS) to position 6 of the N-sulfoglucosamine residue of heparan sulfate.
<i>F9</i>	0.46	DDA	F',G	2,3,8,9	Secreted	Participates in the intrinsic blood coagulation pathway by converting factor X to its active form in the presence of Ca(2+) ions, phospholipids, and factor VIIIa.

SUPPLEMENTAL TABLE 3: Plasma proteins associated with incident type 2 diabetes in the CHS cohort stratified by sex with test for interaction (Col C, E-I, Repeated aptamer information excluded to ease viewing)

Gene Symbol	Sex Interaction p _{fd} * [*]	Male (N = 987. incl. 154 cases)		Female (N = 1.644. incl. 256 cases)	
		HR (95% CI)	p-value	HR (95% CI)	p-value
<i>NEU1</i>	0.173	1.11 (1.00–1.23)	5.6E-02	1.38 (1.26–1.52)	5.1E-11
<i>HS6ST3</i>	0.173	0.58 (0.46–0.72)	8.5E-07	0.86 (0.74–1.00)	5.2E-02
<i>APOF</i>	0.369	0.73 (0.61–0.88)	7.3E-04	0.60 (0.52–0.68)	4.9E-15
<i>AGRN</i>	0.369	1.18 (1.01–1.38)	3.6E-02	1.48 (1.31–1.68)	4.6E-10
<i>ADAMTSL1</i>	0.369	0.89 (0.74–1.07)	2.0E-01	0.70 (0.61–0.80)	2.1E-07
<i>IGFBP2</i>	0.512	0.72 (0.59–0.88)	1.3E-03	0.58 (0.50–0.67)	3.3E-13
<i>EFNB2</i>	0.721	0.81 (0.65–1.00)	5.1E-02	0.69 (0.58–0.82)	2.5E-05
<i>OMG</i>	0.721	0.70 (0.59–0.83)	5.2E-05	0.84 (0.74–0.96)	1.2E-02
<i>TIMP4</i>	0.721	0.88 (0.72–1.08)	2.2E-01	0.71 (0.61–0.82)	2.2E-06
<i>APLP1</i>	0.721	0.67 (0.57–0.79)	2.4E-06	0.82 (0.73–0.93)	1.6E-03
<i>ACY1</i>	0.756	1.60 (1.37–1.88)	7.6E-09	1.32 (1.18–1.47)	8.7E-07
<i>TNFSF12</i>	0.756	0.59 (0.45–0.77)	1.1E-04	0.76 (0.64–0.90)	1.4E-03
<i>MXRA8</i>	0.762	0.66 (0.54–0.80)	2.8E-05	0.56 (0.48–0.64)	1.1E-14
<i>VOPP1</i>	0.762	0.81 (0.66–1.00)	4.7E-02	0.67 (0.57–0.78)	4.9E-07
<i>SLITRK1</i>	0.762	0.81 (0.66–1.00)	4.9E-02	0.70 (0.60–0.82)	1.3E-05
<i>SLITRK6</i>	0.762	0.79 (0.63–0.98)	3.2E-02	0.67 (0.57–0.79)	3.4E-06
<i>TGFBR3</i>	0.762	0.76 (0.63–0.92)	4.9E-03	0.68 (0.59–0.78)	3.6E-08
<i>THBS2</i>	0.762	1.42 (1.20–1.68)	3.5E-05	1.26 (1.12–1.42)	1.7E-04
<i>AGER</i>	0.762	0.80 (0.67–0.95)	9.2E-03	0.72 (0.63–0.83)	2.8E-06
<i>EPHB6</i>	0.762	0.74 (0.60–0.93)	8.5E-03	0.66 (0.55–0.79)	4.4E-06
<i>SERPINA11</i>	0.762	0.87 (0.72–1.05)	1.4E-01	0.72 (0.63–0.83)	5.9E-06
<i>ADH4</i>	0.809	1.43 (1.22–1.68)	7.5E-06	1.25 (1.12–1.39)	7.0E-05
<i>HRSP12</i>	0.815	1.45 (1.23–1.70)	5.9E-06	1.32 (1.18–1.49)	3.5E-06
<i>PSAT1</i>	0.815	1.40 (1.18–1.65)	7.8E-05	1.23 (1.09–1.37)	4.0E-04
<i>AKR1C4</i>	0.815	1.34 (1.16–1.54)	8.9E-05	1.21 (1.07–1.36)	1.6E-03
<i>ARL15</i>	0.815	1.13 (0.96–1.31)	1.3E-01	1.27 (1.15–1.40)	2.8E-06
<i>SIGLEC12</i>	0.815	1.16 (0.98–1.38)	8.2E-02	1.29 (1.16–1.44)	2.9E-06
<i>PCDH10</i>	0.815	0.74 (0.60–0.92)	6.2E-03	0.69 (0.58–0.81)	9.1E-06
<i>PCOLCE</i>	0.832	0.70 (0.59–0.84)	7.6E-05	0.84 (0.74–0.96)	1.1E-02
<i>STX1A</i>	0.832	0.78 (0.63–0.96)	1.8E-02	0.69 (0.59–0.81)	3.3E-06
<i>SLITRK5</i>	0.832	0.81 (0.67–0.98)	3.3E-02	0.74 (0.64–0.86)	5.8E-05
<i>ART3</i>	0.832	0.75 (0.61–0.91)	3.2E-03	0.70 (0.60–0.81)	3.2E-06
<i>FTCD</i>	0.832	1.23 (1.04–1.45)	1.7E-02	1.38 (1.22–1.56)	2.2E-07
<i>WFIKKN2</i>	0.888	0.68 (0.57–0.82)	7.1E-05	0.78 (0.69–0.89)	2.2E-04
<i>LGALS3BP</i>	0.888	1.20 (1.01–1.41)	3.3E-02	1.34 (1.19–1.51)	2.3E-06
<i>TNFAIP6</i>	0.888	0.81 (0.67–0.97)	2.5E-02	0.73 (0.64–0.84)	1.9E-05

<i>DCUN1D1</i>	0.905	1.19 (1.04–1.37)	1.2E-02	1.32 (1.20–1.45)	4.5E-09
<i>PTPRD</i>	0.905	0.69 (0.57–0.82)	5.0E-05	0.80 (0.70–0.92)	1.2E-03
<i>ASL</i>	0.906	1.38 (1.17–1.64)	1.4E-04	1.21 (1.08–1.34)	6.3E-04
<i>APOM</i>	0.913	0.74 (0.62–0.89)	1.3E-03	0.78 (0.68–0.88)	9.7E-05
<i>ANTXR1</i>	0.913	0.81 (0.67–0.98)	2.7E-02	0.72 (0.62–0.82)	2.8E-06
<i>DNAJB9</i>	0.913	1.35 (1.15–1.60)	3.1E-04	1.26 (1.11–1.44)	4.0E-04
<i>COL11A2</i>	0.913	0.83 (0.68–1.01)	6.9E-02	0.77 (0.68–0.87)	2.9E-05
<i>CESI</i>	0.913	1.42 (1.20–1.69)	6.1E-05	1.30 (1.16–1.47)	7.9E-06
<i>NPTXR</i>	0.913	0.67 (0.55–0.82)	7.7E-05	0.75 (0.65–0.86)	4.9E-05
<i>ANTXR2</i>	0.913	0.74 (0.62–0.88)	7.5E-04	0.75 (0.65–0.86)	5.4E-05
<i>NCAN</i>	0.913	0.74 (0.63–0.88)	6.9E-04	0.80 (0.70–0.92)	1.5E-03
<i>UNC5D</i>	0.913	0.65 (0.54–0.79)	1.9E-05	0.65 (0.56–0.76)	1.5E-08
<i>MYOC</i>	0.913	0.69 (0.57–0.82)	5.1E-05	0.78 (0.68–0.90)	4.8E-04
<i>ALDOB</i>	0.913	1.36 (1.15–1.61)	3.7E-04	1.26 (1.13–1.41)	5.3E-05
<i>SERPINB13</i>	0.913	0.76 (0.62–0.94)	1.2E-02	0.71 (0.59–0.84)	1.1E-04
<i>SEZ6L</i>	0.913	0.68 (0.57–0.82)	5.8E-05	0.77 (0.67–0.88)	1.7E-04
<i>MPO</i>	0.913	1.17 (0.99–1.39)	6.3E-02	1.32 (1.17–1.50)	1.1E-05
<i>MET</i>	0.913	0.75 (0.63–0.88)	5.2E-04	0.82 (0.72–0.93)	1.8E-03
<i>ADIPOQ</i>	0.913	0.67 (0.55–0.83)	1.5E-04	0.63 (0.55–0.72)	9.6E-11
<i>F9</i>	0.913	1.39 (1.11–1.73)	3.6E-03	1.29 (1.11–1.49)	8.4E-04
<i>SHBG</i>	0.913	0.72 (0.58–0.90)	4.0E-03	0.65 (0.57–0.74)	6.5E-11
<i>RTN4R</i>	0.913	1.41 (1.17–1.70)	3.4E-04	1.37 (1.20–1.56)	2.1E-06
<i>ASGR1</i>	0.913	1.36 (1.17–1.59)	8.5E-05	1.33 (1.18–1.49)	1.6E-06
<i>PTPRS</i>	0.913	0.77 (0.65–0.92)	3.8E-03	0.74 (0.65–0.84)	5.8E-06
<i>TLL1</i>	0.913	1.23 (1.05–1.45)	1.0E-02	1.30 (1.13–1.50)	3.1E-04
<i>INHBC</i>	0.913	1.43 (1.18–1.73)	2.3E-04	1.55 (1.35–1.77)	2.0E-10
<i>LRRC15</i>	0.913	0.79 (0.65–0.95)	1.5E-02	0.75 (0.66–0.86)	2.1E-05
<i>NEGR1</i>	0.913	0.72 (0.59–0.88)	1.2E-03	0.69 (0.59–0.80)	1.6E-06
<i>FAM20B</i>	0.913	0.77 (0.62–0.94)	9.8E-03	0.71 (0.61–0.82)	4.8E-06
<i>FBP1</i>	0.913	1.41 (1.21–1.64)	8.4E-06	1.27 (1.14–1.41)	1.1E-05
<i>LMAN2</i>	0.913	1.31 (1.09–1.57)	4.4E-03	1.38 (1.22–1.57)	2.6E-07
<i>SCG3</i>	0.913	0.64 (0.54–0.77)	1.9E-06	0.70 (0.61–0.80)	2.4E-07
<i>LEP</i>	0.913	1.36 (1.11–1.66)	3.1E-03	1.56 (1.29–1.89)	5.5E-06
<i>PLXNB2</i>	0.913	1.46 (1.19–1.78)	2.3E-04	1.31 (1.12–1.53)	5.6E-04
<i>KITLG</i>	0.913	0.74 (0.61–0.88)	1.0E-03	0.80 (0.70–0.92)	1.2E-03
<i>CHAD</i>	0.917	0.77 (0.64–0.94)	8.4E-03	0.74 (0.65–0.84)	2.2E-06
<i>SLC35G2</i>	0.917	1.29 (1.10–1.52)	2.1E-03	1.19 (1.09–1.31)	1.2E-04
<i>AKR1D1</i>	0.917	1.20 (1.06–1.35)	2.8E-03	1.26 (1.14–1.40)	1.3E-05
<i>SLITRK3</i>	0.917	0.67 (0.57–0.79)	1.9E-06	0.71 (0.62–0.81)	4.8E-07
<i>GUSB</i>	0.917	1.51 (1.26–1.82)	9.0E-06	1.57 (1.38–1.79)	1.3E-11
<i>RGMB</i>	0.917	0.66 (0.54–0.80)	2.8E-05	0.68 (0.58–0.80)	2.7E-06
<i>CHRDLI</i>	0.917	0.66 (0.53–0.81)	1.3E-04	0.67 (0.57–0.78)	8.4E-07

<i>GPD1</i>	0.919	1.36 (1.16–1.60)	1.9E-04	1.38 (1.22–1.57)	5.1E-07
<i>ADH1A</i>	0.919	1.38 (1.18–1.60)	4.0E-05	1.32 (1.19–1.46)	1.0E-07
<i>RBP5</i>	0.919	1.33 (1.16–1.52)	3.5E-05	1.36 (1.21–1.53)	2.2E-07
<i>PLAT</i>	0.919	1.30 (1.08–1.56)	5.9E-03	1.39 (1.21–1.59)	2.3E-06
<i>GHR</i>	0.919	1.47 (1.20–1.81)	2.4E-04	1.48 (1.28–1.70)	5.0E-08
<i>PTPRU</i>	0.919	1.38 (1.21–1.57)	1.0E-06	1.34 (1.23–1.47)	1.8E-10
<i>AZGP1</i>	0.919	0.79 (0.65–0.97)	2.6E-02	0.80 (0.73–0.88)	6.3E-06
<i>DSG2</i>	0.919	0.76 (0.64–0.90)	1.7E-03	0.81 (0.71–0.92)	1.5E-03
<i>IL18R1</i>	0.920	1.23 (1.06–1.44)	7.7E-03	1.22 (1.11–1.33)	1.6E-05
<i>IL1RN</i>	0.921	1.16 (1.03–1.31)	1.4E-02	1.22 (1.12–1.32)	3.4E-06
<i>ST3GAL1</i>	0.921	0.76 (0.61–0.94)	1.2E-02	0.72 (0.61–0.86)	1.5E-04
<i>EHMT2</i>	0.922	0.76 (0.63–0.92)	4.5E-03	0.71 (0.61–0.81)	1.5E-06
<i>HMGCS1</i>	0.953	1.34 (1.13–1.60)	9.6E-04	1.26 (1.12–1.42)	1.4E-04
<i>ADSSL1</i>	0.953	1.28 (1.12–1.46)	2.3E-04	1.28 (1.15–1.44)	1.7E-05
<i>LEAP2</i>	0.953	1.31 (1.11–1.55)	1.3E-03	1.38 (1.21–1.59)	3.5E-06
<i>SORD</i>	0.965	1.37 (1.15–1.64)	5.3E-04	1.30 (1.15–1.46)	3.2E-05
<i>HTRA1</i>	0.970	1.32 (1.15–1.53)	1.4E-04	1.31 (1.17–1.47)	2.9E-06
<i>ADH1C</i>	0.973	1.35 (1.15–1.58)	2.0E-04	1.31 (1.17–1.47)	3.4E-06
<i>AMY2B</i>	0.973	0.75 (0.63–0.89)	1.0E-03	0.76 (0.67–0.87)	7.8E-05
<i>GPR56</i>	0.973	1.24 (1.11–1.39)	1.7E-04	1.23 (1.09–1.38)	8.6E-04
<i>AMY2A</i>	0.973	0.72 (0.61–0.86)	2.0E-04	0.74 (0.65–0.84)	4.7E-06
<i>IGFBP1</i>	0.973	0.72 (0.62–0.84)	4.8E-05	0.77 (0.68–0.87)	2.4E-05
<i>IGFBP4</i>	0.973	1.27 (1.05–1.53)	1.2E-02	1.29 (1.13–1.47)	1.7E-04
<i>PRSS1</i>	0.973	0.75 (0.64–0.88)	5.0E-04	0.78 (0.68–0.91)	1.0E-03
<i>CRTAC1</i>	0.973	0.77 (0.65–0.91)	2.4E-03	0.76 (0.67–0.87)	5.9E-05
<i>PRCP</i>	0.973	1.55 (1.27–1.88)	1.0E-05	1.53 (1.34–1.76)	1.0E-09
<i>ADAMTSL2</i>	0.973	1.35 (1.16–1.59)	1.8E-04	1.37 (1.23–1.54)	3.8E-08
<i>CCDC126</i>	0.973	0.69 (0.58–0.83)	7.8E-05	0.70 (0.61–0.80)	3.3E-07
<i>NFASC</i>	0.973	1.23 (1.08–1.40)	1.6E-03	1.22 (1.10–1.35)	9.2E-05
<i>CADM2</i>	0.983	0.64 (0.52–0.79)	4.2E-05	0.70 (0.60–0.81)	3.4E-06
<i>CPM</i>	0.983	1.36 (1.18–1.56)	1.3E-05	1.37 (1.21–1.56)	4.8E-07

SUPPLEMENTAL TABLE 4: Plasma proteins associated with longitudinal fasting glucose in the CHS cohort (Columns C, E-L)

Gene Symbol	Estimate (95% CI)*	p-value	Estimate (95% CI)†	p-value	Spearman rho‡	MS-verified	pQTL evidence	Supporting literature
<i>APOM</i>	−2.15 (−2.96 ; −1.33)	2,52E-07	−1.54 (−2.38 ; −0.70)	3,45E-04	0.36	DDA	A,C,F,G,H,I	1,3,8
<i>FABP3</i>	2.44 (1.39 ; 3.48)	5,49E-06	1.18 (−0.01 ; 2.37)	4,21E-04			F',G',I	3,8
<i>GUSB</i>	2.21 (1.34 ; 3.08)	6,52E-07	1.61 (0.72 ; 2.51)	4,08E-04	0.88		F,G,H,I	
<i>GHR</i>	2.34 (1.45 ; 3.23)	2,74E-07	1.74 (0.80 ; 2.69)	3,00E-04			C,E,F,G,H,I	1,3,4,8
<i>CPM</i>	2.09 (1.24 ; 2.94)	1,57E-06	1.69 (0.83 ; 2.55)	1,27E-04	0.74	DDA	A,F,G,H,I	1,2,8
<i>IGFBP2</i>	−2.50 (−3.42 ; −1.59)	9,03E-08	−1.77 (−2.78 ; −0.76)	4,21E-04	0.76	DDA	G,H	1,2,3,4,6,8,9,10,11
<i>PRCP</i>	2.61 (1.72 ; 3.50)	8,89E-09	2.19 (1.30 ; 3.08)	1,64E-06	0.68		A,C,F,G,H,I	2,8
<i>INHBC</i>	2.23 (1.42 ; 3.04)	6,58E-08	1.52 (0.64 ; 2.39)	4,21E-04	0.40	DDA	A,C',G,H,I	1,2,8
<i>IL18R1</i>	1.93 (1.10 ; 2.77)	5,38E-06	1.72 (0.89 ; 2.55)	4,99E-05	0.53		A,C,F,G,H,I	2,3,8
<i>APOF</i>	−3.09 (−3.99 ; −2.20)	1,53E-11	−2.43 (−3.39 ; −1.46)	8,88E-07			C,F,G,H,I	1,2,8
<i>ADIPOQ</i>	−2.34 (−3.23 ; −1.45)	2,60E-07	−1.69 (−2.60 ; −0.77)	3,15E-04			D',F,G,H,I	1,3,4,5,8,9
<i>PTPRU</i>	2.19 (1.35 ; 3.02)	3,41E-07	1.73 (0.88 ; 2.59)	6,72E-05			G'	1,8
<i>HTRA1</i>	1.85 (1.05 ; 2.66)	6,01E-06	1.13 (0.29 ; 1.97)	4,21E-04			F,G,H,I	2
<i>MXRA8</i>	−2.17 (−3.01 ; −1.33)	4,42E-07	−1.47 (−2.35 ; −0.6)	4,21E-04			F,G,H,I	1,2,8
<i>CHRDLI</i>	−2.14 (−3.08 ; −1.19)	9,53E-06	−1.58 (−2.56 ; −0.61)	4,21E-04	0.33	DDA	F,G	3,8,9
<i>RTN4R</i>	2.52 (1.68 ; 3.37)	5,70E-09	2.03 (1.16 ; 2.91)	5,29E-06	0.65		A,C,D',E,F,G,H,I	1,3,8
<i>TMEM9</i>	1.80 (1.00 ; 2.59)	9,61E-06	1.82 (1.03 ; 2.61)	5,89E-06			F,G,H	

SUPPLEMENTAL TABLE 4: Plasma proteins associated with longitudinal fasting glucose in the CHS cohort (Columns C, M, N)

Gene Symbol	Subcellular location	Function
<i>APOM</i>	Secreted	Probably involved in lipid transport. Can bind sphingosine-1-phosphate, myristic acid, palmitic acid and stearic acid, retinol, all-trans-retinoic acid and 9-cis-retinoic acid.
<i>FABP3</i>	Cytoplasm	FABP are thought to play a role in the intracellular transport of long-chain fatty acids and their acyl-CoA esters.
<i>GUSB</i>	Lysosome	Plays an important role in the degradation of dermatan and keratan sulfates.
<i>GHR</i>	Cell membrane	Receptor for pituitary gland growth hormone involved in regulating postnatal body growth. The soluble form (GHBP) acts as a reservoir of growth hormone in plasma and may be a modulator/inhibitor of GH signaling.
<i>CPM</i>	Cell membrane	Specifically removes C-terminal basic residues (Arg or Lys) from peptides and proteins. It is believed to play important roles in the control of peptide hormone and growth factor activity at the cell surface, and in the membrane-localized degradation of extracellular proteins.
<i>IGFBP2</i>	Secreted	Prolongs the half-life of the IGFs and have been shown to either inhibit or stimulate the growth promoting effects of the IGFs on cell culture. Alters the interaction of IGFs with their cell surface receptors.
<i>PRCP</i>	Lysosome	Cleaves C-terminal amino acids linked to proline in peptides such as angiotensin II, III and des-Arg9-bradykinin.
<i>INHBC</i>	Secreted	Inhibits the secretion of follitropin by the pituitary gland. Involved in regulation of a number of diverse functions such as hypothalamic and pituitary hormone secretion, gonadal hormone secretion, insulin secretion, nerve cell survival, depending on their subunit composition.
<i>IL18R1</i>	Membrane	Responsible for the binding of the pro-inflammatory cytokine IL18. Contributes to IL18-induced cytokine production, either independently of SLC12A3, or as a complex with SLC12A3.
<i>APOF</i>	Secreted	Associates with LDL. Inhibits cholesteryl ester transfer protein activity and appears to be an important regulator of cholesterol transport.
<i>ADIPOQ</i>	Secreted	Involved in the control of fat metabolism and insulin sensitivity, with direct anti-diabetic, anti-atherogenic and anti-inflammatory activities. Stimulates AMPK phosphorylation and activation in the liver and skeletal muscle, enhancing glucose utilization and fatty-acid combustion.
<i>PTPRU</i>	Cell junction	Tyrosine-protein phosphatase which dephosphorylates CTNNB1. May function in cell proliferation and migration and play a role in the maintenance of epithelial integrity.
<i>HTRA1</i>	Secreted, cell membrane	Serine protease with a variety of targets, including ECM proteins such as fibronectin. May also degrade proteoglycans. Through cleavage of proteoglycans, may release soluble FGF-glycosaminoglycan complexes that promote the range and intensity of FGF signals in the extracellular space. Regulates the availability of insulin-like growth factors (IGFs) by cleaving IGF-binding proteins.
<i>MXRA8</i>	Cell membrane	Transmembrane protein which can modulate activity of various signaling pathways, probably via binding to integrin. Mediates heterophilic cell-cell interactions in vitro.
<i>CHRD1</i>	Secreted	Antagonizes BMP4 function by binding to it and preventing its interaction with receptors. Alters the fate commitment of neural stem cells from gliogenesis to neurogenesis. Contributes to neuronal differentiation of neural stem cells by preventing the adoption of a glial fate.
<i>RTN4R</i>	Cell membrane	Receptor for RTN4, OMG and MAG. Functions as receptor for the sialylated gangliosides GT1b and GM1. Functions as receptor for chondroitin sulfate proteoglycans. Can also bind heparin.
<i>TMEM9</i>	Lysosome, membrane	Transmembrane protein that binds to and facilitates the assembly of lysosomal proton-transporting V-type ATPase, resulting in enhanced lysosomal acidification and trafficking.

SUPPLEMENTAL TABLE 5: Plasma proteins associated with IVGTT traits in the HERITAGE cohort (Columns D, F-O)

Gene Symbol	Insulin sensitivity (S_I)					Acute insulin response to glucose (AIR_G)				
	N	Beta*	p*	Beta [†]	p [†]	N	Beta*	p*	Beta [†]	p [†]
<i>MXRA8</i>	670	0,45	1E-20	0,29	1E-09	672	-0,10	5E-02	0,00	1E+00
<i>PTPRU</i>	670	-0,27	2E-09	-0,16	2E-04	672	0,06	2E-01	0,00	9E-01
<i>GUSB</i>	670	-0,34	2E-13	-0,21	2E-06	672	0,04	4E-01	-0,03	5E-01
<i>PRCP</i>	670	-0,14	3E-03	-0,05	3E-01	672	-0,03	6E-01	-0,07	1E-01
<i>ACY1</i>	668	-0,36	6E-15	-0,25	7E-09	670	0,13	4E-03	0,07	1E-01
<i>APOF</i>	670	0,50	7E-26	0,33	1E-11	672	-0,23	1E-06	-0,15	4E-03
<i>IGFBP2</i>	670	0,59	1E-33	0,44	9E-18	672	-0,22	6E-06	-0,14	1E-02
<i>ADIPOQ</i>	670	0,40	2E-15	0,24	1E-06	672	-0,10	5E-02	0,00	1E+00
<i>HRSP12</i>	668	-0,21	7E-07	-0,16	5E-05	670	0,07	1E-01	0,04	3E-01
<i>RBP5</i>	669	-0,26	1E-08	-0,19	6E-06	671	0,06	2E-01	0,03	6E-01
<i>CPM</i>	670	-0,26	5E-08	-0,15	1E-03	672	0,06	2E-01	0,00	1E+00
<i>INHBC</i>	670	-0,24	9E-08	-0,12	5E-03	672	0,09	4E-02	0,03	5E-01
<i>ADH1A</i>	670	-0,31	2E-13	-0,22	4E-08	672	0,14	8E-04	0,09	3E-02
<i>SHBG</i>	669	0,34	7E-11	0,13	1E-02	671	-0,18	6E-04	-0,08	1E-01
<i>GHR</i>	670	-0,39	3E-17	-0,22	2E-06	672	0,13	3E-03	0,04	4E-01
<i>CHRD1</i>	670	0,24	2E-07	0,10	2E-02	672	-0,14	2E-03	-0,07	1E-01
<i>ASGR1</i>	669	-0,17	5E-04	-0,11	1E-02	671	-0,01	9E-01	-0,04	4E-01
<i>FBP1</i>	666	-0,31	2E-11	-0,21	1E-06	668	0,10	2E-02	0,05	3E-01
<i>ADAMTSL2</i>	669	-0,20	8E-06	-0,13	1E-03	671	-0,06	2E-01	-0,10	2E-02
<i>SCG3</i>	670	0,35	2E-11	0,10	6E-02	672	-0,10	5E-02	0,04	5E-01
<i>SLITRK3</i>	670	0,43	5E-20	0,26	6E-08	672	-0,17	2E-04	-0,08	1E-01
<i>TGFBR3</i>	670	0,37	5E-15	0,24	3E-07	672	-0,17	3E-04	-0,10	4E-02
<i>CES1</i>	670	-0,23	1E-06	-0,13	4E-03	672	0,03	5E-01	-0,03	6E-01
<i>ADH1C</i>	670	-0,23	6E-07	-0,17	3E-05	672	0,07	1E-01	0,04	3E-01
<i>UNC5D</i>	670	0,30	4E-10	0,09	9E-02	672	-0,09	5E-02	0,03	6E-01
<i>RTN4R</i>	670	-0,26	2E-08	-0,13	2E-03	672	-0,01	9E-01	-0,07	1E-01
<i>ADSSL1</i>	669	-0,19	3E-05	-0,10	2E-02	671	0,05	3E-01	0,01	9E-01
<i>ALDOB</i>	668	-0,28	7E-10	-0,19	1E-05	670	0,10	3E-02	0,05	3E-01
<i>CHAD</i>	670	0,26	1E-06	0,13	1E-02	672	-0,06	2E-01	0,01	9E-01
<i>PLXNB2</i>	670	0,11	2E-02	0,07	8E-02	672	-0,14	3E-03	-0,12	9E-03
<i>TIMP4</i>	670	0,00	1E+00	0,06	2E-01	672	0,19	7E-05	0,16	6E-04
<i>ASL</i>	668	-0,26	3E-09	-0,18	7E-06	670	0,11	9E-03	0,08	8E-02
<i>NFASC</i>	669	-0,04	4E-01	-0,08	6E-02	671	-0,08	8E-02	-0,06	2E-01
<i>ADH4</i>	669	-0,36	7E-17	-0,25	8E-10	671	0,17	1E-04	0,11	1E-02
<i>NEU1</i>	669	-0,23	8E-07	-0,20	5E-06	671	0,03	5E-01	0,01	8E-01
<i>CRTAC1</i>	670	0,23	1E-06	0,14	1E-03	672	-0,06	2E-01	-0,02	7E-01
<i>SORD</i>	669	-0,23	3E-07	-0,18	9E-06	671	0,09	3E-02	0,07	9E-02
<i>FTCD</i>	667	-0,18	7E-05	-0,15	2E-04	670	0,03	6E-01	0,01	8E-01
<i>RGMB</i>	670	0,32	5E-10	0,16	9E-04	672	-0,10	4E-02	-0,02	7E-01
<i>NEGR1</i>	669	0,31	7E-11	0,21	3E-06	671	-0,09	5E-02	-0,04	4E-01
<i>CCDC126</i>	670	0,38	2E-15	0,21	8E-06	672	-0,11	2E-02	-0,02	7E-01
<i>AGRN</i>	670	-0,18	3E-04	-0,09	4E-02	672	-0,03	5E-01	-0,08	9E-02
<i>LEAP2</i>	670	0,01	8E-01	0,02	5E-01	672	0,03	6E-01	0,02	7E-01

<i>MYOC</i>	670	0,09	6E-02	0,06	2E-01	672	0,03	6E-01	0,04	4E-01
<i>IL18R1</i>	670	-0,09	4E-02	-0,07	1E-01	672	-0,05	2E-01	-0,06	1E-01
<i>PTPRS</i>	670	0,28	4E-10	0,20	2E-06	672	-0,09	3E-02	-0,05	3E-01
<i>HMGC51</i>	669	-0,06	2E-01	-0,12	9E-03	671	-0,01	8E-01	0,02	7E-01
<i>PSAT1</i>	670	-0,32	1E-13	-0,24	2E-09	672	0,12	4E-03	0,08	5E-02
<i>THBS2</i>	669	0,08	7E-02	0,01	7E-01	671	-0,21	4E-06	-0,18	9E-05
<i>LRRC15</i>	668	0,16	2E-03	0,08	9E-02	670	-0,01	9E-01	0,04	4E-01
<i>DCUN1D1</i>	669	-0,19	3E-05	-0,07	8E-02	671	0,08	7E-02	0,03	6E-01
<i>GPD1</i>	670	-0,32	1E-13	-0,17	9E-05	672	0,11	9E-03	0,03	5E-01
<i>CADM2</i>	668	0,29	2E-09	0,10	5E-02	670	-0,11	2E-02	-0,01	9E-01
<i>EPHB6</i>	669	0,31	6E-09	0,14	7E-03	671	-0,10	6E-02	-0,01	9E-01
<i>AKR1D1</i>	670	-0,27	8E-11	-0,21	1E-07	672	0,09	3E-02	0,05	2E-01
<i>TNFSF12</i>	668	0,22	8E-07	0,11	9E-03	670	-0,09	4E-02	-0,03	5E-01
<i>LMAN2</i>	668	-0,19	4E-05	-0,11	1E-02	670	0,10	3E-02	0,06	2E-01
<i>GPR56</i>	669	-0,07	1E-01	-0,05	2E-01	671	-0,03	4E-01	-0,05	3E-01
<i>COL11A2</i>	669	0,20	2E-04	0,05	4E-01	671	-0,11	4E-02	-0,03	6E-01
<i>HTRA1</i>	669	-0,30	1E-11	-0,16	2E-04	671	0,07	1E-01	-0,01	8E-01
<i>AGER</i>	670	0,24	6E-06	0,05	3E-01	672	-0,07	2E-01	0,03	6E-01
<i>SLITRK6</i>	669	0,24	2E-07	0,15	4E-04	671	-0,08	9E-02	-0,03	5E-01
<i>AKR1C4</i>	668	-0,25	2E-08	-0,18	8E-06	670	0,10	3E-02	0,06	2E-01
<i>SERPINB13</i>	668	0,25	1E-07	0,13	5E-03	670	-0,05	3E-01	0,01	9E-01
<i>LGALS3BP</i>	670	-0,33	3E-12	-0,20	7E-06	672	0,07	1E-01	0,00	1E+00
<i>NPTXR</i>	670	0,21	3E-05	0,01	9E-01	672	-0,05	3E-01	0,05	3E-01
<i>IL1RN</i>	669	-0,35	1E-14	-0,17	3E-04	671	0,14	2E-03	0,05	4E-01
<i>TNFAIP6</i>	669	0,23	1E-06	0,07	1E-01	671	-0,16	6E-04	-0,09	7E-02
<i>MPO</i>	670	0,01	8E-01	0,04	4E-01	672	0,01	8E-01	0,00	9E-01
<i>SLC35G2</i>	670	-0,21	7E-06	-0,12	6E-03	672	0,09	5E-02	0,05	3E-01
<i>EHMT2</i>	669	0,38	5E-17	0,22	8E-07	671	-0,16	3E-04	-0,08	7E-02
<i>FAM20B</i>	670	0,27	1E-09	0,15	2E-04	672	-0,13	4E-03	-0,07	1E-01
<i>ANTXR2</i>	670	0,37	1E-16	0,25	6E-09	672	-0,15	5E-04	-0,10	4E-02
<i>AMY2A</i>	669	0,22	4E-06	0,07	1E-01	671	-0,02	7E-01	0,06	2E-01
<i>STX1A</i>	668	0,29	1E-10	0,17	1E-04	670	-0,08	6E-02	-0,01	8E-01
<i>CTHRC1</i>	670	0,20	1E-05	0,12	5E-03	672	-0,05	3E-01	-0,01	8E-01
<i>PLAT</i>	670	-0,13	1E-02	0,00	9E-01	672	0,04	4E-01	-0,02	7E-01
<i>VOPPI</i>	670	0,38	1E-16	0,20	4E-05	672	-0,15	9E-04	-0,06	3E-01
<i>PCOLCE</i>	669	0,19	5E-05	0,12	7E-03	671	-0,04	4E-01	0,00	9E-01
<i>ANTXR1</i>	670	0,36	9E-15	0,21	3E-06	672	-0,15	1E-03	-0,07	1E-01
<i>KITLG</i>	668	0,24	4E-08	0,16	8E-05	670	-0,02	6E-01	0,02	6E-01
<i>ARL15</i>	669	-0,21	2E-06	-0,08	7E-02	671	0,06	2E-01	-0,01	8E-01
<i>APLP1</i>	670	0,32	4E-11	0,11	2E-02	672	-0,09	6E-02	0,03	6E-01
<i>APOM</i>	669	0,11	2E-02	0,06	1E-01	671	0,06	2E-01	0,08	7E-02
<i>EFNB2</i>	670	0,20	5E-05	0,10	3E-02	672	-0,12	1E-02	-0,08	1E-01
<i>SERPINA11</i>	670	0,16	9E-04	0,05	2E-01	672	-0,08	1E-01	-0,02	6E-01
<i>DSG2</i>	670	0,34	4E-13	0,20	7E-06	672	-0,10	4E-02	-0,02	6E-01
<i>ADAMTSL1</i>	670	0,30	4E-10	0,13	4E-03	672	-0,17	2E-04	-0,10	5E-02
<i>DNAJB9</i>	670	-0,26	2E-08	-0,12	4E-03	672	0,02	6E-01	-0,05	3E-01
<i>IGFBP1</i>	668	0,57	7E-33	0,38	5E-12	670	-0,40	1E-17	-0,40	1E-11
<i>ART3</i>	670	0,31	4E-10	0,11	3E-02	672	-0,10	4E-02	0,01	9E-01
<i>LEP</i>	670	-0,72	4E-32	-0,48	6E-11	672	0,50	4E-17	0,50	4E-11

<i>SEZ6L</i>	670	0,35	2E-11	0,08	2E-01	672	-0,11	4E-02	0,05	4E-01
<i>WFIKKN2</i>	670	0,33	1E-12	0,14	4E-03	671	-0,13	4E-03	-0,03	5E-01
<i>PTPRD</i>	670	0,29	7E-09	0,07	2E-01	672	-0,13	6E-03	-0,03	6E-01
<i>PCDH10</i>	669	0,27	3E-08	0,06	2E-01	671	-0,06	2E-01	0,05	3E-01
<i>AZGP1</i>	669	0,32	2E-10	0,19	9E-05	671	-0,08	1E-01	-0,01	8E-01
<i>AMY2B</i>	670	0,21	1E-05	0,06	2E-01	672	-0,03	6E-01	0,06	3E-01
<i>SIGLEC12</i>	669	-0,23	3E-07	-0,15	2E-04	671	0,07	1E-01	0,03	5E-01
<i>SLITRK1</i>	669	0,28	2E-09	0,09	7E-02	671	-0,05	3E-01	0,06	2E-01
<i>PRSS1</i>	669	0,19	1E-04	0,07	1E-01	671	-0,07	2E-01	-0,01	8E-01
<i>NCAN</i>	670	0,27	5E-08	0,04	4E-01	672	-0,16	1E-03	-0,05	4E-01
<i>OMG</i>	670	0,13	6E-03	-0,02	7E-01	672	-0,02	7E-01	0,06	2E-01
<i>IGFBP4</i>	669	-0,21	8E-07	-0,11	5E-03	671	0,06	1E-01	0,01	8E-01
<i>SLITRK5</i>	670	0,20	2E-05	0,08	9E-02	672	-0,12	9E-03	-0,06	2E-01
<i>ST3GAL1</i>	669	0,28	2E-09	0,13	4E-03	671	-0,14	2E-03	-0,07	1E-01
<i>TLL1</i>	669	0,01	9E-01	-0,03	4E-01	671	-0,02	6E-01	-0,01	9E-01
<i>MET</i>	670	0,27	2E-08	0,20	2E-06	672	-0,19	3E-05	-0,17	3E-04
<i>HS6ST3</i>	670	0,35	7E-12	0,10	7E-02	672	-0,14	6E-03	-0,01	9E-01
<i>F9</i>	670	-0,26	1E-09	-0,13	3E-03	672	0,07	1E-01	-0,01	9E-01
<i>TMEM9</i>	668	0,00	9E-01	-0,04	3E-01	670	-0,01	8E-01	0,01	8E-01
<i>FABP3</i>	670	-0,45	8E-18	-0,14	2E-02	672	0,27	9E-08	0,17	1E-02

SUPPLEMENTAL TABLE 5: Plasma proteins associated with IVGTT traits in the HERITAGE cohort (Columns D, P-Y)

Gene Symbol	Disposition index (DI)					Glucose effectiveness (S _G)				
	N	Beta*	p*	Beta [†]	p [†]	N	Beta*	p*	Beta [†]	p [†]
<i>MXRA8</i>	665	0,35	2E-09	0,28	6E-06	677	4E-03	6E-03	4E-03	1E-02
<i>PTPRU</i>	665	-0,21	7E-05	-0,15	5E-03	677	3E-03	6E-02	4E-03	2E-02
<i>GUSB</i>	665	-0,31	1E-08	-0,25	5E-06	677	-4E-03	1E-02	-4E-03	1E-02
<i>PRCP</i>	665	-0,18	2E-03	-0,14	1E-02	677	1E-03	5E-01	1E-03	4E-01
<i>ACY1</i>	663	-0,23	2E-05	-0,18	1E-03	675	5E-04	7E-01	7E-04	7E-01
<i>APOF</i>	665	0,27	2E-06	0,18	4E-03	677	-1E-03	4E-01	-3E-03	1E-01
<i>IGFBP2</i>	665	0,39	1E-11	0,33	5E-07	677	2E-03	2E-01	1E-03	5E-01
<i>ADIPOQ</i>	665	0,30	4E-07	0,23	2E-04	677	4E-03	1E-02	4E-03	1E-02
<i>HRSP12</i>	663	-0,14	6E-03	-0,11	3E-02	675	-4E-05	1E+00	3E-04	8E-01
<i>RBP5</i>	664	-0,19	3E-04	-0,16	2E-03	676	7E-04	7E-01	9E-04	6E-01
<i>CPM</i>	665	-0,21	1E-04	-0,16	6E-03	677	-2E-03	1E-01	-2E-03	2E-01
<i>INHBC</i>	665	-0,14	8E-03	-0,07	2E-01	677	-1E-03	4E-01	-7E-04	7E-01
<i>ADH1A</i>	665	-0,17	7E-04	-0,13	1E-02	677	2E-03	2E-01	2E-03	2E-01
<i>SHBG</i>	664	0,20	2E-03	0,08	2E-01	676	2E-03	3E-01	1E-03	6E-01
<i>GHR</i>	665	-0,28	2E-07	-0,21	4E-04	677	-1E-03	4E-01	-9E-04	6E-01
<i>CHRD1</i>	665	0,10	6E-02	0,03	6E-01	677	2E-03	2E-01	2E-03	2E-01
<i>ASGR1</i>	664	-0,17	3E-03	-0,14	1E-02	676	-2E-03	2E-01	-2E-03	2E-01
<i>FBP1</i>	661	-0,21	1E-04	-0,17	3E-03	673	1E-03	5E-01	1E-03	4E-01
<i>ADAMTSL2</i>	664	-0,23	2E-05	-0,20	2E-04	676	6E-04	7E-01	8E-04	6E-01
<i>SCG3</i>	665	0,25	3E-05	0,14	4E-02	677	2E-03	3E-01	2E-03	4E-01
<i>SLITRK3</i>	665	0,25	5E-06	0,17	5E-03	677	-6E-04	7E-01	-1E-03	4E-01
<i>TGFBR3</i>	665	0,21	3E-04	0,14	2E-02	677	-2E-04	9E-01	-6E-04	7E-01

<i>CESI</i>	665	-0,21	2E-04	-0,16	4E-03	677	-5E-04	8E-01	-3E-04	9E-01
<i>ADH1C</i>	665	-0,16	3E-03	-0,13	1E-02	677	2E-03	3E-01	2E-03	2E-01
<i>UNC5D</i>	665	0,21	2E-04	0,11	9E-02	677	4E-04	8E-01	-3E-06	1E+00
<i>RTN4R</i>	665	-0,25	4E-06	-0,19	6E-04	677	-3E-03	5E-02	-2E-03	1E-01
<i>ADSSL1</i>	664	-0,16	4E-03	-0,11	5E-02	676	1E-03	4E-01	2E-03	3E-01
<i>ALDOB</i>	663	-0,18	7E-04	-0,13	1E-02	675	2E-03	2E-01	2E-03	1E-01
<i>CHAD</i>	665	0,19	2E-03	0,13	4E-02	677	-2E-03	2E-01	-3E-03	2E-01
<i>PLXNB2</i>	665	-0,02	8E-01	-0,04	4E-01	677	1E-03	4E-01	1E-03	5E-01
<i>TIMP4</i>	665	0,19	7E-04	0,23	6E-05	677	3E-03	6E-02	3E-03	7E-02
<i>ASL</i>	663	-0,15	5E-03	-0,10	5E-02	675	2E-04	9E-01	6E-04	7E-01
<i>NFASC</i>	664	-0,08	1E-01	-0,11	4E-02	676	3E-03	2E-02	3E-03	2E-02
<i>ADH4</i>	664	-0,20	1E-04	-0,15	6E-03	676	2E-03	2E-01	2E-03	1E-01
<i>NEU1</i>	664	-0,21	2E-04	-0,19	6E-04	676	-6E-04	7E-01	-5E-04	7E-01
<i>CRTAC1</i>	665	0,16	3E-03	0,12	3E-02	677	4E-03	1E-02	4E-03	1E-02
<i>SORD</i>	664	-0,12	2E-02	-0,09	7E-02	676	-1E-04	9E-01	1E-04	9E-01
<i>FTCD</i>	663	-0,15	7E-03	-0,13	1E-02	674	8E-04	6E-01	9E-04	6E-01
<i>RGMB</i>	665	0,21	4E-04	0,14	3E-02	677	2E-03	1E-01	3E-03	1E-01
<i>NEGR1</i>	664	0,23	4E-05	0,18	2E-03	676	3E-03	4E-02	3E-03	4E-02
<i>CCDC126</i>	665	0,26	3E-06	0,18	2E-03	677	4E-03	1E-02	4E-03	3E-02
<i>AGRN</i>	665	-0,23	3E-05	-0,19	5E-04	677	4E-04	8E-01	6E-04	7E-01
<i>LEAP2</i>	665	0,04	5E-01	0,04	4E-01	677	2E-03	2E-01	2E-03	2E-01
<i>MYOC</i>	665	0,11	6E-02	0,09	9E-02	677	1E-03	4E-01	1E-03	4E-01
<i>IL18R1</i>	665	-0,13	1E-02	-0,12	2E-02	677	-1E-04	9E-01	1E-05	1E+00
<i>PTPRS</i>	665	0,19	5E-04	0,14	8E-03	677	-6E-04	7E-01	-7E-04	7E-01
<i>HMGCS1</i>	664	-0,06	3E-01	-0,09	9E-02	676	3E-03	8E-02	3E-03	9E-02
<i>PSAT1</i>	665	-0,20	1E-04	-0,16	2E-03	677	3E-03	7E-02	3E-03	5E-02
<i>THBS2</i>	664	-0,10	8E-02	-0,14	1E-02	676	-1E-03	4E-01	-1E-03	4E-01
<i>LRRC15</i>	663	0,16	6E-03	0,13	3E-02	675	-1E-03	4E-01	-1E-03	5E-01
<i>DCUN1D1</i>	664	-0,10	7E-02	-0,03	6E-01	676	-3E-04	8E-01	2E-04	9E-01
<i>GPD1</i>	665	-0,22	3E-05	-0,14	1E-02	677	1E-03	4E-01	2E-03	2E-01
<i>CADM2</i>	663	0,21	2E-04	0,11	7E-02	675	1E-03	4E-01	1E-03	4E-01
<i>EPHB6</i>	664	0,23	3E-04	0,15	2E-02	676	-9E-04	6E-01	-1E-03	5E-01
<i>AKR1D1</i>	665	-0,19	1E-04	-0,16	1E-03	677	1E-03	5E-01	1E-03	4E-01
<i>TNFSF12</i>	663	0,12	2E-02	0,07	2E-01	675	-2E-03	1E-01	-2E-03	1E-01
<i>LMAN2</i>	663	-0,09	9E-02	-0,05	4E-01	675	-9E-04	5E-01	-7E-04	6E-01
<i>GPR56</i>	664	-0,08	1E-01	-0,08	1E-01	676	1E-03	3E-01	1E-03	4E-01
<i>COL11A2</i>	664	0,10	1E-01	0,01	8E-01	676	-1E-03	4E-01	-2E-03	4E-01
<i>HTRA1</i>	664	-0,24	6E-06	-0,17	1E-03	676	-3E-03	5E-02	-3E-03	1E-01
<i>AGER</i>	665	0,18	4E-03	0,09	2E-01	677	2E-03	3E-01	2E-03	4E-01
<i>SLITRK6</i>	664	0,18	8E-04	0,13	1E-02	676	3E-03	8E-02	3E-03	9E-02
<i>AKR1C4</i>	663	-0,15	6E-03	-0,12	3E-02	675	4E-04	8E-01	5E-04	7E-01
<i>SERPINB13</i>	663	0,20	3E-04	0,13	2E-02	675	4E-03	2E-02	3E-03	3E-02
<i>LGALS3BP</i>	665	-0,26	4E-06	-0,20	5E-04	677	-1E-03	4E-01	-1E-03	5E-01
<i>NPTXR</i>	665	0,15	7E-03	0,05	4E-01	677	2E-03	3E-01	1E-03	4E-01
<i>ILIRN</i>	664	-0,22	7E-05	-0,12	4E-02	676	-3E-03	5E-02	-3E-03	9E-02
<i>TNFAIP6</i>	664	0,09	1E-01	-0,01	9E-01	676	-5E-04	7E-01	-1E-03	4E-01
<i>MPO</i>	665	0,02	7E-01	0,03	5E-01	677	-3E-03	3E-02	-3E-03	4E-02
<i>SLC35G2</i>	665	-0,12	3E-02	-0,07	2E-01	677	2E-04	9E-01	4E-04	8E-01
<i>EHMT2</i>	664	0,20	1E-04	0,12	4E-02	676	4E-03	4E-03	4E-03	1E-02

<i>FAM20B</i>	665	0,15	4E-03	0,09	1E-01	677	3E-05	1E+00	-4E-04	8E-01
<i>ANTXR2</i>	665	0,22	5E-05	0,15	6E-03	677	5E-03	1E-03	5E-03	3E-03
<i>AMY2A</i>	664	0,20	3E-04	0,13	3E-02	676	2E-03	3E-01	1E-03	4E-01
<i>STX1A</i>	663	0,20	2E-04	0,15	9E-03	675	1E-03	4E-01	1E-03	4E-01
<i>CTHRC1</i>	665	0,15	6E-03	0,11	4E-02	677	1E-03	4E-01	1E-03	5E-01
<i>PLAT</i>	665	-0,10	9E-02	-0,04	5E-01	677	3E-03	4E-02	4E-03	2E-02
<i>VOPPI</i>	665	0,22	5E-05	0,12	4E-02	677	1E-03	5E-01	5E-04	8E-01
<i>PCOLCE</i>	664	0,15	5E-03	0,12	2E-02	676	3E-03	6E-02	3E-03	8E-02
<i>ANTXR1</i>	665	0,21	2E-04	0,13	2E-02	677	4E-03	1E-02	4E-03	3E-02
<i>KITLG</i>	663	0,22	3E-05	0,18	5E-04	675	2E-04	9E-01	2E-04	9E-01
<i>ARL15</i>	664	-0,17	2E-03	-0,10	7E-02	676	-2E-03	2E-01	-2E-03	2E-01
<i>APLP1</i>	665	0,22	9E-05	0,12	5E-02	677	3E-03	6E-02	3E-03	8E-02
<i>APOM</i>	664	0,14	7E-03	0,12	2E-02	676	9E-04	5E-01	6E-04	7E-01
<i>EFNB2</i>	665	0,08	2E-01	0,02	7E-01	677	-3E-04	8E-01	-5E-04	8E-01
<i>SERPINA11</i>	665	0,10	8E-02	0,04	4E-01	677	2E-04	9E-01	5E-05	1E+00
<i>DSG2</i>	665	0,25	4E-06	0,19	1E-03	677	2E-03	3E-01	1E-03	4E-01
<i>ADAMTSL1</i>	665	0,14	1E-02	0,04	4E-01	677	1E-03	5E-01	7E-04	7E-01
<i>DNAJB9</i>	665	-0,26	5E-07	-0,20	2E-04	677	-4E-03	3E-03	-4E-03	7E-03
<i>IGFBP1</i>	663	0,19	1E-03	0,01	9E-01	675	-3E-04	8E-01	-2E-03	3E-01
<i>ART3</i>	665	0,20	7E-04	0,10	1E-01	677	2E-03	2E-01	2E-03	2E-01
<i>LEP</i>	665	-0,23	2E-03	0,01	9E-01	677	1E-03	6E-01	4E-03	1E-01
<i>SEZ6L</i>	665	0,25	5E-05	0,14	6E-02	677	1E-03	4E-01	1E-03	5E-01
<i>WFIKKN2</i>	665	0,21	1E-04	0,12	6E-02	676	3E-03	4E-02	3E-03	4E-02
<i>PTPRD</i>	665	0,16	6E-03	0,05	5E-01	677	9E-04	6E-01	6E-04	8E-01
<i>PCDH10</i>	664	0,21	1E-04	0,12	5E-02	676	2E-03	2E-01	2E-03	3E-01
<i>AZGP1</i>	664	0,24	6E-05	0,17	5E-03	676	-1E-03	5E-01	-2E-03	2E-01
<i>AMY2B</i>	665	0,19	7E-04	0,12	4E-02	677	2E-03	1E-01	2E-03	2E-01
<i>SIGLEC12</i>	664	-0,16	3E-03	-0,12	2E-02	676	-1E-03	4E-01	-1E-03	4E-01
<i>SLITRK1</i>	664	0,24	1E-05	0,15	1E-02	676	2E-03	3E-01	2E-03	3E-01
<i>PRSSI</i>	664	0,12	4E-02	0,05	4E-01	676	2E-03	1E-01	2E-03	2E-01
<i>NCAN</i>	665	0,12	3E-02	0,00	1E+00	677	5E-04	8E-01	3E-04	9E-01
<i>OMG</i>	665	0,12	3E-02	0,04	4E-01	677	4E-03	3E-03	5E-03	3E-03
<i>IGFBP4</i>	664	-0,16	2E-03	-0,11	4E-02	676	7E-04	6E-01	9E-04	5E-01
<i>SLITRK5</i>	665	0,08	2E-01	0,02	8E-01	677	5E-04	8E-01	8E-04	7E-01
<i>ST3GAL1</i>	664	0,15	7E-03	0,06	3E-01	676	2E-03	1E-01	2E-03	2E-01
<i>TLL1</i>	664	-0,01	8E-01	-0,04	4E-01	676	2E-04	9E-01	-5E-05	1E+00
<i>MET</i>	665	0,06	3E-01	0,02	7E-01	677	-1E-03	5E-01	-1E-03	4E-01
<i>HS6ST3</i>	665	0,20	7E-04	0,07	3E-01	677	3E-03	5E-02	4E-03	5E-02
<i>F9</i>	665	-0,20	7E-05	-0,14	1E-02	677	-5E-03	3E-04	-6E-03	3E-04
<i>TMEM9</i>	663	-0,01	8E-01	-0,04	5E-01	675	-1E-03	5E-01	-1E-03	4E-01
<i>FABP3</i>	665	-0,20	2E-03	0,00	1E+00	677	-1E-03	4E-01	-4E-04	9E-01

SUPPLEMENTAL TABLE 6: Two-sample Mendelian randomization results for the causal effect of proteins on type 2 diabetes (Columns C, E-N)

Gene Symbol	CHS Incident diabetes			DIAMANTE Diabetes GWAS						
	HR	p	Concordant with MR	SNPs	IVW or Wald Ratio			MR Egger		
					Beta	SE	p	Beta	SE	p
<i>NCAN</i>	0,78	3E-06	Yes	1	-0,20	0,04	5E-08			
<i>PLXNB2</i>	1,36	6E-07	No	3	-0,04	0,01	8E-05	-0,05	0,02	2E-01
<i>NEGR1</i>	0,70	7E-09	Yes	1	-0,15	0,04	1E-04			
<i>SHBG</i>	0,67	3E-12	Yes	1	-0,14	0,04	2E-04			
<i>OMG</i>	0,79	6E-06	Yes	1	-0,28	0,08	4E-04			
<i>NEGR1</i>	0,72	6E-09	Yes	2	-0,10	0,03	8E-04			
<i>TGFBR3</i>	0,71	8E-10	No	1	0,26	0,08	2E-03			
<i>AMY2B</i>	0,76	6E-07	No	7	0,04	0,01	4E-03	0,04	0,03	2E-01
<i>IGFBP4</i>	1,28	6E-06	No	1	-0,28	0,11	1E-02			
<i>TNFAIP6</i>	0,76	3E-06	Yes	4	-0,02	0,01	2E-02	-0,05	0,03	2E-01
<i>ADH1C</i>	1,32	5E-09	No	1	-0,03	0,01	2E-02			
<i>ALDOB</i>	1,28	1E-07	Yes	1	0,07	0,03	3E-02			
<i>TNFSF12</i>	0,71	1E-06	Yes	2	-0,02	0,01	3E-02			
<i>IGFBP1</i>	0,75	7E-09	No	1	0,16	0,08	4E-02			
<i>INHBC</i>	1,50	4E-13	Yes	1	0,12	0,07	1E-01			
<i>LEAP2</i>	1,35	2E-08	No	1	-0,04	0,02	6E-02			
<i>PRCP</i>	1,54	5E-14	Yes	1	0,01	0,04	8E-01			
<i>ADSSL1</i>	1,27	4E-08	Yes	2	0,02	0,01	1E-01			
<i>AGRN</i>	1,35	8E-10	Yes	1	0,00	0,03	9E-01			
<i>ASL</i>	1,25	1E-06	No	1	-0,10	0,06	8E-02			
<i>GUSB</i>	1,54	1E-15	Yes	1	0,07	0,04	1E-01			
<i>WFIKK2</i>	0,75	1E-07	Yes	2	-0,02	0,01	5E-02			
<i>PCOLCE</i>	0,79	6E-06	No	2	0,01	0,04	7E-01			
<i>IL1RN</i>	1,20	2E-07	Yes	2	0,02	0,02	3E-01			
<i>APOF</i>	0,64	2E-16	No	2	0,05	0,04	2E-01			
<i>ACY1</i>	1,39	6E-13	Yes	1	0,05	0,05	3E-01			
<i>CCDC126</i>	0,70	2E-10	No	2	0,10	0,06	8E-02			
<i>ART3</i>	0,72	5E-08	No	2	0,05	0,05	3E-01			
<i>ADAMTSL2</i>	1,37	3E-11	Yes	3	0,04	0,04	3E-01	-0,06	0,16	8E-01
<i>CADM2</i>	0,68	6E-10	Yes	1	-0,01	0,05	8E-01			
<i>RTN4R</i>	1,39	1E-09	No	5	-0,01	0,02	5E-01	-0,03	0,09	8E-01
<i>ADH4</i>	1,30	6E-09	Yes	1	0,01	0,02	5E-01			
<i>TLL1</i>	1,28	7E-06	No	1	-0,01	0,11	1E+00			
<i>AKR1C4</i>	1,25	1E-06	Yes	1	0,00	0,01	9E-01			
<i>SERPINA11</i>	0,77	8E-06	No	4	0,02	0,02	4E-01	0,04	0,08	7E-01

<i>NPTXR</i>	0,72	1E-08	No	3	0,00	0,01	1E+00	0,00	0,02	9E-01
<i>HRSP12</i>	1,36	2E-10	Yes	1	0,02	0,02	4E-01			
<i>MYOC</i>	0,75	2E-07	Yes	4	-0,02	0,02	4E-01	0,04	0,04	5E-01
<i>APOM</i>	0,76	3E-07	Yes	3	-0,01	0,15	1E+00	-0,03	0,29	9E-01
<i>HTRA1</i>	1,33	8E-10	No	2	-0,11	0,07	1E-01			
<i>DSG2</i>	0,79	8E-06	Yes	3	-0,05	0,04	2E-01	0,05	0,07	6E-01
<i>IGFBP2</i>	0,63	1E-14	Yes	2	-0,09	0,06	9E-02			
<i>SLITRK5</i>	0,76	7E-06	Yes	3	-0,02	0,04	6E-01	0,13	0,25	7E-01
<i>SLITRK3</i>	0,69	4E-12	No	4	0,00	0,02	1E+00	0,01	0,03	7E-01
<i>CPM</i>	1,36	5E-11	Yes	3	0,06	0,05	2E-01	-0,15	0,19	6E-01
<i>CHAD</i>	0,75	7E-08	Yes	1	-0,17	0,12	1E-01			
<i>SCG3</i>	0,68	2E-12	Yes	2	-0,01	0,01	3E-01			
<i>MET</i>	0,80	8E-06	No	2	0,00	0,04	1E+00			
<i>SEZ6L</i>	0,74	8E-08	Yes	3	-0,09	0,07	2E-01	0,15	0,61	8E-01
<i>EFNB2</i>	0,74	7E-06	No	2	0,03	0,07	7E-01			
<i>THBS2</i>	1,31	5E-08	Yes	8	0,01	0,02	7E-01	0,00	0,02	1E+00
<i>SLITRK6</i>	0,71	5E-07	Yes	1	-0,05	0,04	2E-01			
<i>FBP1</i>	1,31	1E-09	Yes	2	0,01	0,03	8E-01			
<i>PTPRU</i>	1,35	2E-15	Yes	2	0,01	0,03	7E-01			
<i>CRTAC1</i>	0,77	4E-07	Yes	6	0,00	0,02	1E+00	-0,11	0,04	4E-02
<i>VOPPI</i>	0,72	3E-07	No	2	0,05	0,04	2E-01			
<i>LGALS3BP</i>	1,29	4E-07	No	3	-0,05	0,03	1E-01	-0,01	0,08	9E-01
<i>PLAT</i>	1,34	1E-07	Yes	1	0,02	0,04	5E-01			
<i>COL11A2</i>	0,79	7E-06	Yes	2	-0,01	0,04	7E-01			
<i>PTPRS</i>	0,75	9E-08	Yes	1	-0,04	0,08	6E-01			
<i>SLITRK1</i>	0,74	3E-06	No	1	0,18	0,11	1E-01			
<i>TMEM9</i>	0,99	8E-01	Yes	1	-0,07	0,10	5E-01			
<i>MXRA8</i>	0,60	6E-18	No	1	0,11	0,08	2E-01			
<i>SORD</i>	1,31	1E-07	No	3	-0,01	0,04	9E-01	0,39	0,20	3E-01
<i>FTCD</i>	1,31	5E-08	No	1	-0,02	0,02	3E-01			
<i>EPHB6</i>	0,69	1E-07	Yes	1	-0,02	0,01	7E-02			
<i>ANTXR2</i>	0,75	1E-07	Yes	2	0,00	0,05	9E-01			
<i>ADIPOQ</i>	0,65	9E-14	No	5	0,02	0,02	3E-01	0,07	0,03	1E-01
<i>TIMP4</i>	0,76	4E-06	No	3	0,06	0,09	5E-01	-0,18	0,20	5E-01
<i>GPR56</i>	1,24	3E-07	Yes	1	0,05	0,10	6E-01			
<i>SERPINB13</i>	0,73	7E-06	Yes	1	-0,03	0,04	4E-01			
<i>ST3GAL1</i>	0,74	7E-06	Yes	3	-0,03	0,02	3E-01	0,04	0,06	6E-01
<i>GHR</i>	1,47	6E-11	Yes	2	0,01	0,06	9E-01			
<i>IL18R1</i>	1,22	2E-07	Yes	2	0,03	0,02	3E-01			
<i>APLP1</i>	0,76	6E-08	No	1	0,04	0,06	5E-01			

<i>GPD1</i>	1,36	1E-09	Yes	1	0,01	0,06	8E-01				
<i>MPO</i>	1,27	2E-06	Yes	3	0,03	0,02	2E-01	-0,02	0,04	7E-01	
<i>RGMB</i>	0,67	4E-10	Yes	2	-0,01	0,02	6E-01				
<i>PCDH10</i>	0,71	4E-07	Yes	2	-0,02	0,05	7E-01				
<i>UNC5D</i>	0,66	2E-12	No	2	0,04	0,02	1E-01				
<i>FAM20B</i>	0,73	2E-07	Yes	2	-0,07	0,04	1E-01				
<i>ASGR1</i>	1,34	5E-10	No	2	-0,03	0,03	3E-01				
<i>AMY2A</i>	0,74	8E-09	No	3	0,03	0,02	2E-01	0,06	0,03	3E-01	
<i>LRRC15</i>	0,76	7E-07	Yes	3	-0,03	0,02	1E-01	-0,01	0,04	8E-01	
<i>ADAMTSL1</i>	0,76	1E-06	No	8	0,01	0,03	8E-01	0,03	0,04	5E-01	
<i>CES1</i>	1,33	3E-09	No	1	-0,02	0,03	6E-01				
<i>NFASC</i>	1,23	3E-07	Yes	4	0,01	0,04	8E-01	0,06	0,06	4E-01	

SUPPLEMENTAL TABLE 6: Two-sample Mendelian randomization results for the causal effect of proteins on type 2 diabetes (Columns C, O-AB)

MAGIC Fasting Glucose GWAS								MAGIC HbA1c GWAS												
Gene Symbol	SNPs	IVW or Wald Ratio			MR Egger			SNPs	IVW or Wald Ratio			MR Egger								
		Beta	SE	p	Beta	SE	p		Beta	SE	p	Beta	SE	p						
NCAN	1	-0,013	0,01	2E-01				1	0,000	0,007	1E+00									
PLXNB2	3	-0,001	0,00	8E-01				-0,005	0,007	6E-01	3				-0,001	0,002	6E-01	-0,003	0,004	7E-01
NEGR1	1	0,016	0,01	1E-01				1	0,003	0,008	7E-01									
SHBG	1	-0,019	0,01	9E-02				1	-0,045	0,008	6E-08									
OMG	1	-0,018	0,02	4E-01				1	0,002	0,017	9E-01									
NEGR1	2	-0,001	0,02	9E-01				2	-0,003	0,007	7E-01									
TGFBR3	1	0,057	0,03	3E-02				1	0,038	0,018	4E-02									
AMY2B	7	0,002	0,00	6E-01				0,010	0,011	4E-01	7				0,003	0,004	4E-01	-0,002	0,010	9E-01
IGFBP4	1	-0,005	0,03	9E-01				1	0,013	0,025	6E-01									
TNFAIP6	4	-0,002	0,00	5E-01				0,004	0,007	7E-01	4				-0,005	0,004	2E-01	-0,017	0,006	1E-01
ADH1C	1	-0,004	0,00	2E-01				1	0,001	0,002	8E-01									
ALDOB	1	-0,017	0,01	9E-02				1	-0,001	0,009	9E-01									
TNFSF12	2	-0,001	0,00	8E-01				2	-0,006	0,002	5E-03									
IGFBP1	1	0,010	0,02	7E-01				1	0,009	0,018	6E-01									
INHBC	1	0,050	0,02	8E-03				1	0,020	0,015	2E-01									
LEAP2	1	-0,016	0,01	9E-03				1	-0,007	0,005	1E-01									
PRCP	2	0,021	0,01	4E-02				2	0,001	0,008	9E-01									
ADSSL1	2	0,003	0,00	5E-01				2	0,008	0,003	4E-03									
AGRN	2	-0,007	0,01	5E-01				2	-0,018	0,007	2E-02									
ASL	1	-0,012	0,02	5E-01				1	-0,028	0,012	2E-02									
GUSB	1	0,002	0,01	9E-01				1	0,019	0,009	3E-02									
WFIKKN2	2	-0,004	0,01	5E-01				2	-0,006	0,003	4E-02									
PCOLCE	2	0,014	0,01	2E-01				2	-0,017	0,008	4E-02									

IL1RN	2	0,009	0,01	1E-01				2	-0,002	0,003	6E-01			
APOF	2	-0,009	0,01	4E-01				2	0,012	0,009	2E-01			
ACY1	1	0,022	0,03	4E-01				1	0,019	0,019	3E-01			
CCDC126	2	0,005	0,01	5E-01				2	0,010	0,005	8E-02			
ART3	3	0,002	0,01	8E-01	-0,010	0,009	5E-01	3	0,001	0,004	8E-01	-0,002	0,007	8E-01
ADAMTSL2	4	-0,028	0,02	7E-02	-0,016	0,060	8E-01	4	0,004	0,012	7E-01	0,046	0,045	4E-01
CADM2	1	0,013	0,01	3E-01				1	0,011	0,010	3E-01			
RTN4R	6	-0,002	0,01	7E-01	-0,003	0,035	9E-01	6	-0,001	0,003	8E-01	0,025	0,017	2E-01
ADH4	1	-0,003	0,00	5E-01				1	0,002	0,003	6E-01			
TLL1	1	0,002	0,03	1E+00				1	-0,032	0,025	2E-01			
AKR1C4	1	0,002	0,00	4E-01				1	0,002	0,002	3E-01			
SERPINA11	4	-0,007	0,01	2E-01	-0,025	0,022	4E-01	4	-0,006	0,004	1E-01	-0,016	0,016	4E-01
NPTXR	3	0,000	0,01	9E-01	0,005	0,005	5E-01	3	0,001	0,003	7E-01	0,003	0,003	6E-01
HRSP12	1	-0,009	0,00	6E-02				1	-0,006	0,003	1E-01			
MYOC	4	-0,006	0,00	2E-01	-0,012	0,013	5E-01	4	-0,002	0,004	6E-01	-0,001	0,010	9E-01
APOM	3	0,004	0,01	7E-01	-0,009	0,023	8E-01	3	0,004	0,008	6E-01	-0,001	0,019	1E+00
HTRA1	2	0,021	0,01	1E-01				2	0,007	0,008	4E-01			
DSG2	3	0,000	0,01	1E+00	0,019	0,020	5E-01	3	0,000	0,006	1E+00	-0,011	0,015	6E-01
IGFBP2	2	-0,011	0,02	5E-01				2	0,005	0,019	8E-01			
SLITRK5	4	-0,007	0,02	7E-01	-0,082	0,112	5E-01	4	-0,008	0,008	3E-01	-0,062	0,041	3E-01
SLITRK3	4	-0,002	0,01	7E-01	-0,005	0,008	6E-01	4	0,006	0,004	2E-01	0,008	0,006	3E-01
CPM	3	0,004	0,01	8E-01	-0,020	0,056	8E-01	3	-0,006	0,010	6E-01	0,012	0,040	8E-01
CHAD	1	0,042	0,03	2E-01				1	-0,018	0,023	4E-01			
SCG3	2	0,001	0,00	6E-01				2	0,001	0,002	6E-01			
MET	2	0,003	0,02	9E-01				2	0,003	0,009	8E-01			
SEZ6L	4	-0,038	0,02	7E-02	-0,085	0,062	3E-01	4	-0,015	0,015	3E-01	0,019	0,045	7E-01
EFNB2	2	-0,007	0,01	6E-01				2	0,008	0,014	6E-01			

THBS2	8	-0,002	0,00	6E-01	-0,004	0,005	5E-01	8	-0,001	0,004	8E-01	0,003	0,006	6E-01
SLITRK6	1	-0,001	0,01	1E+00				1	0,004	0,009	6E-01			
FBP1	2	0,001	0,01	9E-01				2	0,011	0,006	7E-02			
PTPRU	3	-0,007	0,01	5E-01	-0,029	0,049	7E-01	3	-0,011	0,006	5E-02	-0,024	0,021	5E-01
CRTAC1	6	-0,004	0,00	5E-01	-0,002	0,013	9E-01	6	-0,002	0,003	5E-01	-0,007	0,008	4E-01
VOPP1	2	-0,016	0,01	2E-01				2	0,008	0,008	3E-01			
LGALS3BP	4	0,002	0,02	9E-01	0,011	0,046	8E-01	4	-0,008	0,014	6E-01	0,005	0,035	9E-01
PLAT	1	0,006	0,01	6E-01				1	0,009	0,008	3E-01			
COL11A2	2	-0,002	0,00	6E-01				2	0,001	0,003	8E-01			
PTPRS	1	-0,005	0,03	9E-01				1	0,011	0,028	7E-01			
SLITRK1	1	-0,039	0,03	2E-01				1	0,001	0,023	1E+00			
TMEM9	1	-0,031	0,03	2E-01				1	0,001	0,020	9E-01			
MXRA8	1	-0,011	0,02	6E-01				1	0,024	0,020	2E-01			
SORD	3	0,009	0,01	4E-01	-0,012	0,075	9E-01	3	0,016	0,009	7E-02	0,059	0,067	5E-01
FTCD	1	-0,003	0,01	7E-01				1	0,002	0,006	8E-01			
EPHB6	1	-0,001	0,00	9E-01				1	-0,002	0,003	4E-01			
ANTXR2	2	-0,002	0,01	8E-01				2	0,000	0,006	1E+00			
ADIPOQ	5	-0,002	0,01	7E-01	-0,002	0,009	9E-01	5	0,002	0,005	7E-01	-0,005	0,007	5E-01
TIMP4	3	0,002	0,01	8E-01	-0,017	0,011	4E-01	3	-0,003	0,013	8E-01	-0,005	0,043	9E-01
GPR56	1	0,036	0,03	2E-01				1	0,000	0,021	1E+00			
SERPINB13	1	-0,007	0,01	6E-01				1	0,002	0,010	8E-01			
ST3GAL1	3	0,005	0,01	7E-01	-0,013	0,029	7E-01	3	-0,003	0,007	7E-01	-0,015	0,020	6E-01
GHR	2	0,004	0,01	6E-01				2	-0,010	0,009	3E-01			
IL18R1	2	-0,005	0,01	5E-01				2	-0,003	0,007	6E-01			
APLP1	1	0,012	0,02	5E-01				1	-0,005	0,013	7E-01			
GPD1	1	-0,016	0,02	4E-01				1	-0,011	0,016	5E-01			
MPO	4	0,003	0,01	6E-01	-0,017	0,015	4E-01	4	0,007	0,005	2E-01	0,014	0,012	4E-01

RGMB	2	0,008	0,01	1E-01				2	-0,003	0,004	4E-01			
PCDH10	2	0,002	0,01	9E-01				2	-0,009	0,006	1E-01			
UNC5D	2	0,006	0,01	5E-01				2	-0,001	0,005	8E-01			
FAM20B	2	-0,021	0,01	9E-02				2	0,008	0,015	6E-01			
ASGR1	2	-0,026	0,02	1E-01				2	0,014	0,008	1E-01			
AMY2A	4	0,002	0,00	6E-01	0,005	0,006	5E-01	4	0,002	0,003	6E-01	0,000	0,005	1E+00
LRRC15	3	-0,008	0,01	1E-01	-0,008	0,013	6E-01	3	0,002	0,004	7E-01	0,002	0,010	9E-01
ADAMTSL1	8	-0,004	0,01	5E-01	-0,001	0,008	9E-01	8	-0,004	0,004	3E-01	-0,002	0,006	8E-01
CES1	1	0,006	0,01	7E-01				1	-0,007	0,010	5E-01			
NFASC	4	-0,004	0,00	4E-01	-0,002	0,008	9E-01	4	0,000	0,003	9E-01	-0,003	0,006	6E-01

SUPPLEMENTAL TABLE 6: Two-sample Mendelian randomization results for the causal effect of proteins on type 2 diabetes (Columns C, AC-AP)

MAGIC 2-Hour Glucose GWAS								MAGIC Fasting Insulin GWAS						
Gene Symbol	SNPs	IVW or Wald Ratio			MR Egger			SNPs	IVW or Wald Ratio			MR Egger		
		Beta	SE	p	Beta	SE	p		Beta	SE	p	Beta	SE	p
<i>NCAN</i>	1	0,021	0,045	6E-01				1	-0,012	0,012	3E-01			
<i>PLXNB2</i>	3	-0,013	0,019	5E-01	-0,042	0,040	5E-01	3	0,000	0,004	1E+00	0,004	0,008	7E-01
<i>NEGR1</i>	1	-0,072	0,048	1E-01				1	0,001	0,012	1E+00			
<i>SHBG</i>	1	-0,111	0,054	4E-02				1	-0,031	0,012	1E-02			
<i>OMG</i>	1	-0,057	0,112	6E-01				1	-0,008	0,028	8E-01			
<i>NEGR1</i>	2	-0,058	0,032	7E-02				2	-0,007	0,009	4E-01			
<i>TGFBR3</i>	1	-0,006	0,118	1E+00				1	0,019	0,028	5E-01			
<i>AMY2B</i>	7	0,010	0,018	6E-01	0,005	0,049	9E-01	7	-0,006	0,007	3E-01	0,015	0,016	4E-01
<i>IGFBP4</i>	1	0,003	0,163	1E+00				1	0,067	0,038	8E-02			
<i>TNFAIP6</i>	4	-0,015	0,013	3E-01	-0,031	0,036	5E-01	4	-0,003	0,004	4E-01	-0,020	0,008	1E-01
<i>ADH1C</i>	1	-0,019	0,016	2E-01				1	-0,002	0,004	6E-01			

<i>ALDOB</i>	1	0,032	0,044	5E-01				1	0,008	0,011	5E-01			
<i>TNFSF12</i>	2	-0,021	0,027	4E-01				2	-0,003	0,008	7E-01			
<i>IGFBP1</i>	1	0,219	0,109	4E-02				1	0,063	0,025	1E-02			
<i>INHBC</i>	1	0,150	0,084	7E-02				1	0,028	0,020	2E-01			
<i>LEAP2</i>	1	-0,016	0,030	6E-01				1	-0,005	0,007	5E-01			
<i>PRCP</i>	2	-0,001	0,051	1E+00				2	0,021	0,012	9E-02			
<i>ADSSL1</i>	2	-0,001	0,020	1E+00				2	-0,004	0,005	3E-01			
<i>AGRN</i>	2	-0,035	0,047	4E-01				2	-0,017	0,012	2E-01			
<i>ASL</i>	1	-0,008	0,076	9E-01				1	-0,003	0,018	9E-01			
<i>GUSB</i>	1	-0,037	0,061	5E-01				1	0,031	0,014	3E-02			
<i>WFIKK2</i>	2	0,011	0,018	5E-01				2	-0,007	0,004	1E-01			
<i>PCOLCE</i>	2	0,081	0,055	1E-01				2	-0,010	0,012	4E-01			
<i>IL1RN</i>	2	0,060	0,021	5E-03				2	0,003	0,005	5E-01			
<i>APOF</i>	2	-0,133	0,053	1E-02				2	0,018	0,021	4E-01			
<i>ACY1</i>	1	0,279	0,120	2E-02				1	0,025	0,027	4E-01			
<i>CCDC126</i>	2	0,076	0,033	2E-02				2	0,003	0,008	7E-01			
<i>ART3</i>	3	-0,058	0,026	2E-02	-0,046	0,043	5E-01	3	0,002	0,010	8E-01	-0,015	0,010	4E-01
<i>ADAMTSL2</i>	4	-0,145	0,068	3E-02	-0,449	0,255	2E-01	4	0,034	0,019	7E-02	0,004	0,073	1E+00
<i>CADM2</i>	1	-0,136	0,063	3E-02				1	-0,028	0,015	6E-02			
<i>RTN4R</i>	6	-0,047	0,023	4E-02	-0,160	0,110	2E-01	6	-0,003	0,005	6E-01	-0,004	0,027	9E-01
<i>ADH4</i>	1	-0,005	0,021	8E-01				1	-0,017	0,005	4E-04			
<i>TLL1</i>	1	-0,062	0,155	7E-01				1	0,095	0,037	1E-02			
<i>AKR1C4</i>	1	-0,013	0,012	3E-01				1	0,006	0,003	3E-02			
<i>SERPINA11</i>	4	-0,008	0,027	8E-01	0,134	0,106	3E-01	4	-0,013	0,006	3E-02	-0,004	0,025	9E-01
<i>NPTXR</i>	3	0,014	0,018	4E-01	0,006	0,021	8E-01	3	0,007	0,004	7E-02	0,004	0,005	5E-01
<i>HRSP12</i>	1	-0,034	0,023	1E-01				1	0,008	0,005	1E-01			
<i>MYOC</i>	4	0,011	0,024	6E-01	0,094	0,042	2E-01	4	-0,007	0,004	1E-01	-0,004	0,012	8E-01

<i>APOM</i>	3	-0,041	0,045	4E-01	0,018	0,077	9E-01	3	-0,024	0,016	1E-01	-0,026	0,039	6E-01
<i>HTRA1</i>	2	-0,035	0,057	5E-01				2	-0,019	0,013	2E-01			
<i>DSG2</i>	3	-0,005	0,042	9E-01	-0,091	0,098	5E-01	3	-0,013	0,010	2E-01	-0,004	0,023	9E-01
<i>IGFBP2</i>	2	0,093	0,168	6E-01				2	-0,023	0,019	2E-01			
<i>SLITRK5</i>	4	0,050	0,048	3E-01	0,140	0,259	6E-01	4	-0,013	0,011	3E-01	-0,003	0,060	1E+00
<i>SLITRK3</i>	4	-0,030	0,025	2E-01	-0,041	0,037	4E-01	4	-0,012	0,010	3E-01	-0,011	0,019	6E-01
<i>CPM</i>	3	-0,075	0,093	4E-01	-0,119	0,510	9E-01	3	0,018	0,016	3E-01	0,065	0,063	5E-01
<i>CHAD</i>	1	-0,150	0,158	3E-01				1	-0,040	0,037	3E-01			
<i>SCG3</i>	2	0,000	0,012	1E+00				2	0,004	0,004	3E-01			
<i>MET</i>	2	-0,062	0,068	4E-01				2	0,017	0,016	3E-01			
<i>SEZ6L</i>	4	-0,013	0,110	9E-01	0,091	0,385	8E-01	4	0,025	0,024	3E-01	-0,019	0,071	8E-01
<i>EFNB2</i>	2	-0,028	0,044	5E-01				2	0,011	0,011	3E-01			
<i>THBS2</i>	8	-0,019	0,018	3E-01	-0,008	0,024	7E-01	8	-0,004	0,004	4E-01	-0,006	0,005	3E-01
<i>SLITRK6</i>	1	-0,014	0,054	8E-01				1	-0,012	0,013	4E-01			
<i>FBP1</i>	2	0,063	0,038	9E-02				2	-0,008	0,009	4E-01			
<i>PTPRU</i>	3	0,009	0,037	8E-01	-0,072	0,118	7E-01	3	-0,007	0,009	4E-01	-0,039	0,032	4E-01
<i>CRTAC1</i>	6	0,007	0,025	8E-01	-0,088	0,051	2E-01	6	-0,004	0,005	4E-01	0,008	0,012	5E-01
<i>VOPPI</i>	2	0,089	0,061	1E-01				2	0,018	0,022	4E-01			
<i>LGALS3BP</i>	4	0,066	0,081	4E-01	0,250	0,134	2E-01	4	-0,012	0,015	4E-01	0,010	0,036	8E-01
<i>PLAT</i>	1	0,009	0,056	9E-01				1	-0,011	0,014	4E-01			
<i>COL11A2</i>	2	-0,011	0,021	6E-01				2	0,004	0,005	4E-01			
<i>PTPRS</i>	1	-0,120	0,135	4E-01				1	-0,026	0,037	5E-01			
<i>SLITRK1</i>	1	-0,026	0,153	9E-01				1	0,025	0,036	5E-01			
<i>TMEM9</i>	1	-0,046	0,131	7E-01				1	0,019	0,030	5E-01			
<i>MXRA8</i>	1	-0,109	0,124	4E-01				1	0,019	0,030	5E-01			
<i>SORD</i>	3	0,066	0,057	2E-01	-0,341	0,419	6E-01	3	0,007	0,011	5E-01	0,005	0,083	1E+00
<i>FTCD</i>	1	-0,036	0,036	3E-01				1	-0,005	0,009	5E-01			

<i>EPHB6</i>	1	0,003	0,017	9E-01				1	-0,002	0,004	6E-01			
<i>ANTXR2</i>	2	-0,007	0,075	9E-01				2	-0,004	0,009	7E-01			
<i>ADIPOQ</i>	5	-0,040	0,028	1E-01	-0,031	0,049	6E-01	5	0,003	0,007	7E-01	0,016	0,010	2E-01
<i>TIMP4</i>	3	0,075	0,048	1E-01	-0,040	0,099	8E-01	3	0,010	0,023	7E-01	-0,046	0,050	5E-01
<i>GPR56</i>	1	0,084	0,140	5E-01				1	-0,013	0,031	7E-01			
<i>SERPINB13</i>	1	0,008	0,070	9E-01				1	-0,007	0,017	7E-01			
<i>ST3GAL1</i>	3	0,000	0,033	1E+00	0,058	0,079	6E-01	3	0,003	0,008	7E-01	-0,003	0,019	9E-01
<i>GHR</i>	2	-0,004	0,038	9E-01				2	-0,003	0,008	7E-01			
<i>IL18R1</i>	2	0,021	0,081	8E-01				2	-0,006	0,018	7E-01			
<i>APLP1</i>	1	0,031	0,087	7E-01				1	-0,007	0,020	7E-01			
<i>GPD1</i>	1	-0,044	0,077	6E-01				1	0,006	0,018	8E-01			
<i>MPO</i>	4	0,031	0,036	4E-01	-0,080	0,067	4E-01	4	0,002	0,008	8E-01	-0,015	0,017	5E-01
<i>RGMB</i>	2	-0,009	0,026	7E-01				2	-0,001	0,006	8E-01			
<i>PCDH10</i>	2	-0,016	0,036	7E-01				2	-0,002	0,008	8E-01			
<i>UNC5D</i>	2	0,013	0,029	7E-01				2	-0,001	0,007	9E-01			
<i>FAM20B</i>	2	0,134	0,096	2E-01				2	0,002	0,014	9E-01			
<i>ASGR1</i>	2	0,000	0,066	1E+00				2	-0,002	0,013	9E-01			
<i>AMY2A</i>	4	0,004	0,018	8E-01	0,006	0,030	9E-01	4	-0,001	0,004	9E-01	0,007	0,007	4E-01
<i>LRRC15</i>	3	0,032	0,024	2E-01	0,056	0,057	5E-01	3	-0,001	0,008	9E-01	0,017	0,019	5E-01
<i>ADAMTSL1</i>	8	0,004	0,030	9E-01	-0,041	0,038	3E-01	8	0,000	0,006	9E-01	0,006	0,009	6E-01
<i>CES1</i>	1	0,040	0,063	5E-01				1	0,000	0,015	1E+00			
<i>NFASC</i>	4	-0,019	0,023	4E-01	-0,014	0,040	8E-01	4	0,000	0,006	1E+00	0,006	0,010	6E-01

SUPPLEMENTAL TABLE 7: Aptamer-specific genetic instruments included in Two-sample Mendelian Randomization analysis

Aptamer ID	Gene Symbol	Target Protein Name	SNP	SNP incorporated as an instrument in analysis of:				
				Diabetes*	Fasting Glucose [†]	HbA1c [†]	2-Hour Glucose [†]	Fasting Insulin [†]
3343-1	ACY1	Aminoacylase-1	rs150416778	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs10963680	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs146084664	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs1755286	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs1856894	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs35264941	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs575507	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs702208	yes	yes	yes	yes	yes
16890-37	ADAMTSL1	ADAMTS-like protein 1	rs776760	yes	yes	yes	yes	yes
6379-62	ADAMTSL2	ADAMTS-like protein 2	rs10120207	yes	yes	yes	yes	yes
6379-62	ADAMTSL2	ADAMTS-like protein 2	rs11534419	yes	yes	yes	yes	yes
6379-62	ADAMTSL2	ADAMTS-like protein 2	rs56355857	yes	yes	yes	yes	yes
6379-62	ADAMTSL2	ADAMTS-like protein 2	rs62574238	no	yes	yes	yes	yes
15525-294	ADH1C	Alcohol dehydrogenase 1C	rs283415	yes	yes	yes	yes	yes
8325-37	ADH4	Alcohol dehydrogenase 4	rs6858148	yes	yes	yes	yes	yes
3554-24	ADIPOQ	Adiponectin	rs143257534	yes	yes	yes	yes	yes
3554-24	ADIPOQ	Adiponectin	rs17300539	yes	yes	yes	yes	yes
3554-24	ADIPOQ	Adiponectin	rs17366653	yes	yes	yes	yes	yes
3554-24	ADIPOQ	Adiponectin	rs266770	yes	yes	yes	yes	yes
3554-24	ADIPOQ	Adiponectin	rs7616259	yes	yes	yes	yes	yes
13998-26	ADSSL1	Adenylosuccinate synthetase isozyme 1	rs3001371	yes	yes	yes	yes	yes
13998-26	ADSSL1	Adenylosuccinate synthetase isozyme 1	rs72715968	yes	yes	yes	yes	yes
15483-377	AGRN	Agrin	rs4970394	yes	yes	yes	yes	yes
15483-377	AGRN	Agrin	rs189343112	no	yes	yes	yes	yes

18397-5	AKR1C4	Aldo-keto reductase family 1 member C4	rs75811842	yes	yes	yes	yes	yes
18185-118	ALDOB	Fructose-bisphosphate aldolase B	rs142540788	yes	yes	yes	yes	yes
18917-53	AMY2A	Pancreatic alpha-amylase	rs77729677	yes	yes	yes	yes	yes
18917-53	AMY2A	Pancreatic alpha-amylase	rs78245241	yes	yes	yes	yes	yes
18917-53	AMY2A	Pancreatic alpha-amylase	rs7524694	yes	yes	yes	yes	yes
18917-53	AMY2A	Pancreatic alpha-amylase	rs191765977	no	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs114922930	yes	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs12751859	yes	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs140942684	yes	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs150062710	yes	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs77729677	yes	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs78245241	yes	yes	yes	yes	yes
15556-49	AMY2B	Alpha-amylase 2B	rs79456674	yes	yes	yes	yes	yes
15559-5	ANTXR2	Anthrax toxin receptor 2	rs11098925	yes	yes	yes	yes	yes
15559-5	ANTXR2	Anthrax toxin receptor 2	rs7674623	yes	yes	yes	yes	yes
7210-25	APLP1	Amyloid-like protein 1	rs58291714	yes	yes	yes	yes	yes
12370-30	APOF	Apolipoprotein F	rs11575222	yes	yes	yes	yes	yes
12370-30	APOF	Apolipoprotein F	rs2020854	yes	yes	yes	yes	yes
10445-20	APOM	Apolipoprotein M	rs2260000	yes	yes	yes	yes	yes
10445-20	APOM	Apolipoprotein M	rs2894186	yes	no	no	no	no
10445-20	APOM	Apolipoprotein M	rs805295	yes	yes	yes	yes	yes
10445-20	APOM	Apolipoprotein M	rs550671	no	yes	yes	yes	yes
7970-315	ART3	Ecto-ADP-ribosyltransferase 3	rs4599438	yes	yes	yes	yes	yes
7970-315	ART3	Ecto-ADP-ribosyltransferase 3	rs4859610	yes	yes	yes	yes	yes
7970-315	ART3	Ecto-ADP-ribosyltransferase 3	rs187119299	no	yes	yes	yes	yes
5452-71	ASGR1	Asialoglycoprotein receptor 1	rs552653	yes	yes	yes	yes	yes
5452-71	ASGR1	Asialoglycoprotein receptor 1	rs62061425	yes	yes	yes	yes	yes
11241-8	ASL	Argininosuccinate lyase	rs10255397	yes	yes	yes	yes	yes

16907-3	CADM2	Cell adhesion molecule 2	rs9880919	yes	yes	yes	yes	yes
6388-21	CCDC126	Coiled-coil domain-containing protein 126	rs76363413	yes	yes	yes	yes	yes
6388-21	CCDC126		rs7781145	yes	yes	yes	yes	yes
15487-164	CES1	Liver carboxylesterase 1	rs76336259	yes	yes	yes	yes	yes
13460-4	CHAD	Chondroadherin	rs28590506	yes	yes	yes	yes	yes
11278-4	COL11A2	Collagen alpha-2(XI) chain	rs144092339	yes	yes	yes	yes	yes
11278-4	COL11A2	Collagen alpha-2(XI) chain	rs3129205	yes	yes	yes	yes	yes
9416-77	CPM	Carboxypeptidase M	rs10450797	yes	yes	yes	yes	yes
9416-77	CPM	Carboxypeptidase M	rs10878881	yes	yes	yes	yes	yes
9416-77	CPM	Carboxypeptidase M	rs1908671	yes	yes	yes	yes	yes
5632-6	CRTAC1	Cartilage acidic protein 1	rs117781346	yes	yes	yes	yes	yes
5632-6	CRTAC1	Cartilage acidic protein 1	rs505699	yes	yes	yes	yes	yes
5632-6	CRTAC1	Cartilage acidic protein 1	rs56007204	yes	yes	yes	yes	yes
5632-6	CRTAC1	Cartilage acidic protein 1	rs684225	yes	yes	yes	yes	yes
5632-6	CRTAC1	Cartilage acidic protein 1	rs79737742	yes	yes	yes	yes	yes
5632-6	CRTAC1	Cartilage acidic protein 1	rs894376	yes	yes	yes	yes	yes
9484-75	DSG2	Desmoglein-2	rs12373441	yes	yes	yes	yes	yes
9484-75	DSG2	Desmoglein-2	rs147145691	yes	yes	yes	yes	yes
9484-75	DSG2	Desmoglein-2	rs9304098	yes	yes	yes	yes	yes
14131-37	EFNB2	Ephrin-B2	rs2774201	yes	yes	yes	yes	yes
14131-37	EFNB2	Ephrin-B2	rs59166663	yes	yes	yes	yes	yes
5078-82	EPHB6	Ephrin type-B receptor 6	rs7789303	yes	yes	yes	yes	yes
7198-197	FAM20B	Glycosaminoglycan xylosylkinase	rs45499094	yes	yes	yes	yes	yes
7198-197	FAM20B	Glycosaminoglycan xylosylkinase	rs67498652	yes	yes	yes	yes	yes
7206-20	FBP1	Fructose-1,6-bisphosphatase 1	rs2987899	yes	yes	yes	yes	yes
7206-20	FBP1	Fructose-1,6-bisphosphatase 1	rs4743962	yes	yes	yes	yes	yes
9213-24	FTCD	Formimidoyltransferase-cyclodeaminase	rs61735836	yes	yes	yes	yes	yes
2948-58	GHR	Growth hormone receptor	rs4610468	yes	yes	yes	yes	yes

2948-58	GHR	Growth hormone receptor	rs62372052	yes	yes	yes	yes	yes
13697-51	GPD1	Glycerol-3-phosphate dehydrogenase [NAD(+)], cytoplasmic	rs78089413	yes	yes	yes	yes	yes
18893-26	GPR56	Adhesion G-protein coupled receptor G1	rs11076197	yes	yes	yes	yes	yes
15562-24	GUSB	Beta-glucuronidase	rs9530	yes	yes	yes	yes	yes
14636-25	HRSP12	Ribonuclease UK114	rs10955148	yes	yes	yes	yes	yes
15594-47	HTRA1	Serine protease HTRA1	rs61871680	yes	yes	yes	yes	yes
15594-47	HTRA1	Serine protease HTRA1	rs76579910	yes	yes	yes	yes	yes
2771-35	IGFBP1	Insulin-like growth factor-binding protein 1	rs3828998	yes	yes	yes	yes	yes
8469-41	IGFBP2	Insulin-like growth factor-binding protein 2	rs4674091	yes	yes	yes	yes	yes
8469-41	IGFBP2	Insulin-like growth factor-binding protein 2	rs4674100	yes	yes	yes	yes	yes
2950-57	IGFBP4	Insulin-like growth factor-binding protein 4	rs4890114	yes	yes	yes	yes	yes
14079-14	IL18R1	Interleukin-18 receptor 1	rs13014644	yes	yes	yes	yes	yes
14079-14	IL18R1	Interleukin-18 receptor 1	rs3752659	yes	yes	yes	yes	yes
5353-89	IL1RN	Interleukin-1 receptor antagonist protein	rs1530552	yes	yes	yes	yes	yes
5353-89	IL1RN	Interleukin-1 receptor antagonist protein	rs55709272	yes	yes	yes	yes	yes
6408-2	INHBC	Inhibin beta C chain	rs3809113	yes	yes	yes	yes	yes
5708-1	LEAP2	Liver-expressed antimicrobial peptide 2	rs12515756	yes	yes	yes	yes	yes
5000-52	LGALS3BP	Galectin-3-binding protein	rs3826311	yes	yes	yes	yes	yes
5000-52	LGALS3BP	Galectin-3-binding protein	rs4789938	yes	yes	yes	yes	yes
5000-52	LGALS3BP	Galectin-3-binding protein	rs60653700	yes	yes	yes	yes	yes
5000-52	LGALS3BP	Galectin-3-binding protein	rs566419452	no	yes	yes	yes	yes
6557-50	LRRC15	Leucine-rich repeat-containing protein 15	rs4974524	yes	yes	yes	yes	yes
6557-50	LRRC15	Leucine-rich repeat-containing protein 15	rs58182031	yes	yes	yes	yes	yes
6557-50	LRRC15	Leucine-rich repeat-containing protein 15	rs73081778	yes	yes	yes	yes	yes
2837-3	MET	Hepatocyte growth factor receptor	rs10435378	yes	yes	yes	yes	yes
2837-3	MET	Hepatocyte growth factor receptor	rs79326908	yes	yes	yes	yes	yes
2580-83	MPO	Myeloperoxidase	rs2333227	yes	yes	yes	yes	yes

2580-83	MPO	Myeloperoxidase	rs34097845	yes	yes	yes	yes	yes
2580-83	MPO	Myeloperoxidase	rs79141987	yes	yes	yes	yes	yes
2580-83	MPO	Myeloperoxidase	rs146148297	no	yes	yes	yes	yes
10521-10	MXRA8	Matrix-remodeling-associated protein 8	rs181929025	yes	yes	yes	yes	yes
16558-2	MYOC	Myocilin	rs2232826	yes	yes	yes	yes	yes
16558-2	MYOC	Myocilin	rs235922	yes	yes	yes	yes	yes
16558-2	MYOC	Myocilin	rs7547721	yes	yes	yes	yes	yes
16558-2	MYOC	Myocilin	rs79495172	yes	yes	yes	yes	yes
15573-110	NCAN	Neurocan core protein	rs2228603	yes	yes	yes	yes	yes
13109-82	NEGR1	Neuronal growth regulator 1	rs11209871	yes	yes	yes	yes	yes
13109-82	NEGR1	Neuronal growth regulator 1	rs1194278	yes	yes	yes	yes	yes
7050-5	NEGR1	Neuronal growth regulator 1	rs1194282	yes	yes	yes	yes	yes
7179-69	NFASC	Neurofascin	rs12036722	yes	yes	yes	yes	yes
7179-69	NFASC	Neurofascin	rs16854533	yes	yes	yes	yes	yes
7179-69	NFASC	Neurofascin	rs3892308	yes	yes	yes	yes	yes
7179-69	NFASC	Neurofascin	rs6667532	yes	yes	yes	yes	yes
15511-37	NPTXR	Neuronal pentraxin receptor	rs12628473	yes	yes	yes	yes	yes
15511-37	NPTXR	Neuronal pentraxin receptor	rs74925227	yes	yes	yes	yes	yes
15511-37	NPTXR	Neuronal pentraxin receptor	rs9607582	yes	yes	yes	yes	yes
16908-5	OMG	Oligodendrocyte-myelin glycoprotein	rs12449302	yes	yes	yes	yes	yes
9018-38	PCDH10	Protocadherin-10	rs28477738	yes	yes	yes	yes	yes
9018-38	PCDH10	Protocadherin-10	rs4864200	yes	yes	yes	yes	yes
11237-49	PCOLCE	Procollagen C-endopeptidase enhancer 1	rs7385804	yes	yes	yes	yes	yes
11237-49	PCOLCE	Procollagen C-endopeptidase enhancer 1	rs77227535	yes	yes	yes	yes	yes
2212-69	PLAT	Tissue-type plasminogen activator	rs2020921	yes	yes	yes	yes	yes
9216-100	PLXNB2	Plexin-B2	rs11547731	yes	yes	yes	yes	yes
9216-100	PLXNB2	Plexin-B2	rs28540713	yes	yes	yes	yes	yes
9216-100	PLXNB2	Plexin-B2	rs28573806	yes	yes	yes	yes	yes

5722-78	PRCP	Lysosomal Pro-X carboxypeptidase	rs2229437	yes	yes	yes	yes	yes
5722-78	PRCP	Lysosomal Pro-X carboxypeptidase	rs188172480	no	yes	yes	yes	yes
6049-64	PTPRS	Receptor-type tyrosine-protein phosphatase S	rs55763631	yes	yes	yes	yes	yes
8337-65	PTPRU	Receptor-type tyrosine-protein phosphatase U	rs2179795	yes	yes	yes	yes	yes
8337-65	PTPRU	Receptor-type tyrosine-protein phosphatase U	rs67827535	yes	yes	yes	yes	yes
8337-65	PTPRU	Receptor-type tyrosine-protein phosphatase U	rs2377362	no	yes	yes	yes	yes
3331-8	RGMB	RGM domain family member B	rs17663317	yes	yes	yes	yes	yes
3331-8	RGMB	RGM domain family member B	rs2368553	yes	yes	yes	yes	yes
5105-2	RTN4R	Reticulon-4 receptor	rs665780	yes	yes	yes	yes	yes
5105-2	RTN4R	Reticulon-4 receptor	rs696880	yes	yes	yes	yes	yes
5105-2	RTN4R	Reticulon-4 receptor	rs75765	yes	yes	yes	yes	yes
5105-2	RTN4R	Reticulon-4 receptor	rs8142885	yes	yes	yes	yes	yes
5105-2	RTN4R	Reticulon-4 receptor	rs9606293	yes	yes	yes	yes	yes
5105-2	RTN4R	Reticulon-4 receptor	rs73153000	no	yes	yes	yes	yes
7957-2	SCG3	Secretogranin-3	rs2305710	yes	yes	yes	yes	yes
7957-2	SCG3	Secretogranin-3	rs2607116	yes	yes	yes	yes	yes
9002-36	SERPINA11	Serpin A11	rs1956713	yes	yes	yes	yes	yes
9002-36	SERPINA11	Serpin A11	rs2038499	yes	yes	yes	yes	yes
9002-36	SERPINA11	Serpin A11	rs4900235	yes	yes	yes	yes	yes
9002-36	SERPINA11	Serpin A11	rs72631635	yes	yes	yes	yes	yes
18841-1	SERPINB13	Serpin B13	rs77157727	yes	yes	yes	yes	yes
19563-3	SEZ6L	Seizure 6-like protein	rs117966464	yes	yes	yes	yes	yes
19563-3	SEZ6L	Seizure 6-like protein	rs188357839	yes	yes	yes	yes	yes
19563-3	SEZ6L	Seizure 6-like protein	rs73158619	yes	yes	yes	yes	yes
19563-3	SEZ6L	Seizure 6-like protein	rs7293127	no	yes	yes	yes	yes
4929-55	SHBG	Sex hormone-binding globulin	rs858519	yes	yes	yes	yes	yes
15539-15	SLITRK1	SLIT and NTRK-like protein 1	rs2876803	yes	yes	yes	yes	yes
10565-19	SLITRK3	SLIT and NTRK-like protein 3	rs114097740	yes	yes	yes	yes	yes

10565-19	SLITRK3	SLIT and NTRK-like protein 3	rs4858792	yes	yes	yes	yes	yes
10565-19	SLITRK3	SLIT and NTRK-like protein 3	rs62282372	yes	yes	yes	yes	yes
10565-19	SLITRK3	SLIT and NTRK-like protein 3	rs78729408	yes	yes	yes	yes	yes
4568-17	SLITRK5	SLIT and NTRK-like protein 5	rs117858373	yes	yes	yes	yes	yes
4568-17	SLITRK5	SLIT and NTRK-like protein 5	rs12877225	yes	yes	yes	yes	yes
4568-17	SLITRK5	SLIT and NTRK-like protein 5	rs9588027	yes	yes	yes	yes	yes
4568-17	SLITRK5	SLIT and NTRK-like protein 5	rs9523380	no	yes	yes	yes	yes
16916-19	SLITRK6	SLIT and NTRK-like protein 6	rs9547175	yes	yes	yes	yes	yes
15447-45	SORD	Sorbitol dehydrogenase	rs111459698	yes	yes	yes	yes	yes
15447-45	SORD	Sorbitol dehydrogenase	rs11638723	yes	yes	yes	yes	yes
15447-45	SORD	Sorbitol dehydrogenase	rs72722045	yes	yes	yes	yes	yes
5657-28	ST3GAL1	CMP-N-acetylneuraminate-beta-galactosamide-alpha-2,3-sialyltransferase 1	rs4736683	yes	yes	yes	yes	yes
5657-28	ST3GAL1		rs62520289	yes	yes	yes	yes	yes
5657-28	ST3GAL1		rs9643300	yes	yes	yes	yes	yes
3009-3	TGFBR3	Transforming growth factor beta receptor type 3	rs55649112	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs12174547	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs3252	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs35239983	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs62435801	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs73234350	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs74507247	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs78362595	yes	yes	yes	yes	yes
3339-33	THBS2	Thrombospondin-2	rs8089	yes	yes	yes	yes	yes
6462-12	TIMP4	Metalloproteinase inhibitor 4	rs184262	yes	yes	yes	yes	yes
6462-12	TIMP4	Metalloproteinase inhibitor 4	rs2120825	yes	yes	yes	yes	yes
6462-12	TIMP4	Metalloproteinase inhibitor 4	rs3773364	yes	yes	yes	yes	yes
6383-90	TLL1	Tolloid-like protein 1	rs1903176	yes	yes	yes	yes	yes
9249-17	TMEM9	Transmembrane protein 9	rs4915486	yes	yes	yes	yes	yes

5036-50	TNFAIP6	Tumor necrosis factor-inducible gene 6 protein	rs114322406	yes	yes	yes	yes	yes
5036-50	TNFAIP6	Tumor necrosis factor-inducible gene 6 protein	rs12621525	yes	yes	yes	yes	yes
5036-50	TNFAIP6	Tumor necrosis factor-inducible gene 6 protein	rs2278089	yes	yes	yes	yes	yes
5036-50	TNFAIP6	Tumor necrosis factor-inducible gene 6 protein	rs77964389	yes	yes	yes	yes	yes
5939-42	TNFSF12	Tumor necrosis factor ligand superfamily	rs77711855	yes	yes	yes	yes	yes
5939-42	TNFSF12	member 12	rs80067372	yes	yes	yes	yes	yes
16307-22	UNC5D	Netrin receptor UNC5D	rs3108622	yes	yes	yes	yes	yes
16307-22	UNC5D	Netrin receptor UNC5D	rs7833421	yes	yes	yes	yes	yes
14618-26	VOPP1	Vesicular, overexpressed in cancer, prosurvival	rs117042408	yes	yes	yes	yes	yes
14618-26	VOPP1	protein 1	rs9642585	yes	yes	yes	yes	yes
3235-50	WFIKKN2	WAP, Kazal, immunoglobulin, Kunitz and NTR	rs11079936	yes	yes	yes	yes	yes
3235-50	WFIKKN2	domain-containing protein 2	rs17564787	yes	yes	yes	yes	yes