Table SI. Sequences of the primers for reverse transcription-quantitative PCR and GLP-1R siRNA.

Name	Primer sequence (5’-3’)
Acyl-CoA oxidase 1	F: GGAATTTGGCATCGCAGACC
	R: ACATGCCCAAGTGAAGGTCC
β-actin	F: ACCTTCTACAATGAGCTGCG
	R: CTGGATGGCTACGTACATGG
GLP-1R siRNA	F: GAGAGAAACUUUCCUGAGGAATT
	R: UUCCUCAGGAAAGUUUCUCUCTT
Control siRNA	F: UUCUCCGAACGUGUCACGUTT
	R: ACGUGACACGUUCGGAGAATT

F, forward; R, reverse; siRNA, small interfering RNA; GLP-1R, glucagon-like peptide-1 receptor.

Table SII. List of the differentially expressed proteins reversed by semaglutide between T2DM/Control and Sema/T2DM.

Accession	Protein Name	Gene name	T2DM/Control	Sema/T2DM
B2RY04	Dedicator of cytokinesis protein 5	Dock5	1.528	0.544
E9Q634	Unconventional myosin-Ie	Myo1e	1.497	0.633
E9Q7G0	Nuclear mitotic apparatus protein 1	Numa1	1.209	0.797
O09164	Extracellular superoxide dismutase [Cu-Zn]	Sod3	0.504	2.719
O35544	Excitatory amino acid transporter 4	Slc1a6	25.288	0.016
O55128	Histone deacetylase complex subunit SAP18	Sap18	1.394	0.434
O70309	Integrin beta-5	Itgb5	1.477	0.380
O70362	Phosphatidylinositol-glycan-specific phospholipase D	Gpld1	1.258	0.632
O70433	Four and a half LIM domains protein 2	Fhl2	0.620	1.881
O88343	Electrogenic sodium bicarbonate cotransporter 1	Slc4a4	1.457	0.548
O88502	High affinity cAMP-specific and IBMX-insensitive 3’,5’-cyclic phosphodiesterase 8A	Pde8a	1.391	0.657
O88967	ATP-dependent zinc metalloprotease YME1L1	Yme1l1	1.226	0.793
O89051	Integral membrane protein 2B	Itm2b	1.398	0.618
P00520	Tyrosine-protein kinase ABL1	Abl1	1.704	0.555
P00920	Carbonic anhydrase 2	Ca2	1.295	0.629
P06728	Apolipoprotein A-IV	Apoa4	1.662	0.671
P06797	Procathepsin L	Ctsl	0.499	4.213
P0C605	cGMP-dependent protein kinase 1	Prkg1	2.471	0.380
P11859	Angiotensinogen	Agt	1.838	0.480
P11881	Inositol 1,4,5-trisphosphate receptor type 1	Itpr1	2.904	0.385
P12658	Calbindin	Calb1	2.435	0.278
P14733	Lamin-B1	Lmnb1	1.374	0.668
P15331	Peripherin	Prph	2.561	0.413
P18653	Ribosomal protein S6 kinase alpha-1	Rps6ka1	1.482	0.540
P19258	Protein Mpv17	Mpv17	0.668	3.569
P20060	Beta-hexosaminidase subunit beta	Hexb	0.795	1.489
P25911	Tyrosine-protein kinase Lyn	Lyn	1.650	0.461
P27546	Microtubule-associated protein 4	Map4	1.246	0.790
P28230	Gap junction beta-1 protein	Gjb1	1.867	0.465
P28651	Carbonic anhydrase-related protein	Ca8	29.200	0.012
P28661	Septin-4	Septin4	1.319	0.588
P28665	Murinoglobulin-1	Mug1	1.471	0.398
P28828	Receptor-type tyrosine-protein phosphatase mu	Ptprm	1.726	0.539
P31786	Acyl-CoA-binding protein	Dbi	1.668	0.291

P34022	Ran-specific GTPase-activating protein	Ranbp1	0.746	1.942
P35436	Glutamate receptor ionotropic, NMDA 2A	Grin2a	0.746	1.323
P39061	Collagen alpha-1(XVIII) chain	Col18a1	1.370	0.611
P46097	Synaptotagmin-2	Syt2	2.368	0.397
P47740	Aldehyde dehydrogenase family 3 member A2	Aldh3a2	1.253	0.783
P48193	Protein 4.1	Epb41	1.701	0.513
P51859	Hepatoma-derived growth factor	Hdgf	1.364	0.539
P52825	Carnitine O-palmitoyltransferase 2, mitochondrial	Cpt2	1.257	0.729
P54763	Ephrin type-B receptor 2	Ephb2	1.471	0.674
P56528	ADP-ribosyl cyclase/cyclic ADP-ribose hydrolase 1	Cd38	2.463	0.160
P56564	Excitatory amino acid transporter 1	Slc1a3	1.275	0.341
P56942	Pro-MCH	Pmch	1.438	0.354
P59114	mRNA (2'-O-methyladenosine-N(6)-)-methyltransferase	Pcif1	1.880	0.418
P62267	Small ribosomal subunit protein uS12	Rps23	0.716	1.863
P63141	Potassium voltage-gated channel subfamily A member 2	Kcna2	1.367	0.467
P63158	High mobility group protein B1	Hmgb1	1.293	0.491
P70377	Fibroblast growth factor 13	Fgf13	0.704	1.500
P70429	Ena/VASP-like protein	Evl	0.821	1.288
P83917	Chromobox protein homolog 1	Cbx1	1.411	0.508
P97290	Plasma protease C1 inhibitor	Serping1	1.318	0.428
P97346	Nucleoredoxin	Nxn	1.468	0.690
P97772	Metabotropic glutamate receptor 1	Grm1	1.837	0.561
P97863	Nuclear factor 1 B-type	Nfib	2.361	0.229
Q00560	Interleukin-6 receptor subunit beta	Il6st	1.331	0.568
Q00899	Transcriptional repressor protein YY1	Yy1	1.650	0.706
Q02257	Junction plakoglobin	Jup	1.321	0.669
Q02357	Ankyrin-1	Ank1	1.988	0.496
Q02780	Nuclear factor 1 A-type	Nfia	2.568	0.356
Q03137	Ephrin type-A receptor 4	Epha4	0.691	1.597
Q04750	DNA topoisomerase 1	Top1	0.756	1.346
Q05512	Serine/threonine-protein kinase MARK2	Mark2	0.767	1.350
Q05BC3	Echinoderm microtubule-associated protein-like 1	Eml1	1.321	0.702
Q0QWG9	Delphilin	Grid2ip	6.512	0.225
Q14BI2	Metabotropic glutamate receptor 2	Grm2	0.787	2.086
Q3TEL6	E3 ubiquitin ligase Rnf157	Rnf157	1.441	0.779
Q3TWN3	Metal transporter CNNM2	Cnnm2	1.236	0.792
Q3V0I2	Proline-rich protein 7	Prr7	0.467	1.802

Q4PZA2	Endothelin-converting enzyme 1	Ece1	1.397	0.584
Q5DU14	Unconventional myosin-XVI	Myo16	0.693	1.847
Q60722	Transcription factor 4	Tcf4	1.748	0.313
Q60770	Syntaxin-binding protein 3	Stxbp3	1.236	0.704
Q60953	Protein PML	Pml	2.114	0.532
Q61481	Dual specificity calcium/calmodulin-dependent 3',5'-cyclic nucleotide phosphodiesterase 1A	Pde1a	0.761	1.471
Q61625	Glutamate receptor ionotropic, delta-2	Grid2	5.728	0.150
Q62092	Neuronal vesicle trafficking-associated protein 1	Nsg1	1.769	0.622
Q64133	Amine oxidase [flavin-containing] A	Maoa	1.304	0.692
Q64444	Carbonic anhydrase 4	Ca4	1.735	0.745
Q64518	Sarcoplasmic/endoplasmic reticulum calcium ATPase 3	Atp2a3	1.333	0.686
Q64524	Histone H2B type 2-E	H2bc21	2.119	0.626
Q65CL1	Catenin alpha-3	Ctnna3	1.954	0.499
Q69ZX8	Actin-binding LIM protein 3	Ablim3	1.490	0.568
Q6DID3	SR-related and CTD-associated factor 8	Scaf8	1.563	0.574
Q6PGC1	ATP-dependent RNA helicase DHX29	Dhx29	1.312	0.424
Q6PHS9	Voltage-dependent calcium channel subunit alpha-2/delta-2	Cacna2d2	1.500	0.511
Q6URW6	Myosin-14	Myh14	1.318	0.722
Q6WQJ1	Diacylglycerol lipase-alpha	Dagla	1.345	0.642
Q6ZWR6	Nesprin-1	Syne1	1.206	0.786
Q71M36	Chondroitin sulfate proteoglycan 5	Cspg5	0.718	1.557
Q7TNC9	Inositol polyphosphate-5-phosphatase A	Inpp5a	1.987	0.422
Q7TPD3	Roundabout homolog 2	Robo2	0.734	1.646
Q80UP8	Sodium-dependent phosphate transporter 2	Slc20a2	1.775	0.535
Q80W54	CAAX prenyl protease 1 homolog	Zmpste24	1.311	0.624
Q80YX1	Tenascin	Tnc	1.456	0.509
Q8BGV8	Mitochondrial dynamics protein MID51	Mief1	1.223	0.823
Q8BKG3	Inactive tyrosine-protein kinase 7	Ptk7	1.210	0.724
Q8BMI0	F-box only protein 38	Fbxo38	1.511	0.418
Q8BT60	Copine-3	Cpne3	1.232	0.744
Q8BX09	Retinoblastoma-binding protein 5	Rbbp5	1.521	0.816
Q8BYR5	Calcium-dependent secretion activator 2	Cadps2	1.250	0.768
Q8C050	Ribosomal protein S6 kinase alpha-5	Rps6ka5	1.428	0.615
Q8C650	Septin-10	Septin10	1.327	0.830
Q8JZM4	Delta and Notch-like epidermal growth factor-related receptor	Dner	1.625	0.530

Q8K0T7	Protein unc-13 homolog C	Unc13c	2.001	0.496
Q8K1S4	Netrin receptor UNC5A	Unc5a	0.824	1.493
Q8K2P7	Sodium-coupled neutral amino acid symporter 1	Slc38a1	1.761	0.576
Q8K4B4	Interleukin-23 receptor	Il23r	1.653	0.066
Q8K4Q7	Ceramide kinase	Cerk	1.876	0.653
Q8QZV7	Integrator complex subunit 13	IntS13	1.469	0.521
Q8R1S4	Protein MTSS 1	Mtss1	3.519	0.329
Q8VDQ8	NAD-dependent protein deacetylase sirtuin-2	Sirt2	1.278	0.671
Q8VHC3	Selenoprotein M	Selenom	1.641	0.325
Q8VHI3	GDP-fucose protein O-fucosyltransferase 2	Pofut2	1.358	0.758
Q8VHL0	Urea transporter 1	Slc14a1	1.670	0.327
Q91VJ2	Caveolae-associated protein 3	Cavin3	1.346	0.396
Q91VR8	Protein BRICK1	Brk1	0.709	1.956
Q91W43	Glycine dehydrogenase (decarboxylating), mitochondrial	Gldc	0.782	1.584
Q91WL8	WW domain-containing oxidoreductase	Wwox	1.238	0.589
Q91XU3	Phosphatidylinositol 5-phosphate 4-kinase type-2 gamma	Pip4k2c	0.798	1.485
Q91YL2	E3 ubiquitin-protein ligase RNF126	Rnf126	0.698	1.701
Q91ZZ3	Beta-synuclein	Sncb	1.270	0.557
Q920N7	Synaptotagmin-12	Syt12	1.344	0.558
Q920R0	Alsin	Als2	1.322	0.612
Q922H1	Protein arginine N-methyltransferase 3	Prmt3	1.288	0.559
Q924X6	Low-density lipoprotein receptor-related protein 8	Lrp8	1.398	0.425
Q99JP6	Homer protein homolog 3	Homer3	8.855	0.086
Q99K30	Epidermal growth factor receptor kinase substrate 8-like protein 2	Eps8l2	3.027	0.161
Q99LI2	Chloride channel CLIC-like protein 1	Clcc1	1.227	0.576
Q99MI1	ELKS/Rab6-interacting/CAST family member 1	Erc1	1.352	0.697
Q99PM3	Transcription initiation factor IIA subunit 1	Gtf2a1	1.528	0.472
Q99PU5	Long-chain-fatty-acid--CoA ligase ACSBG1	Acsbg1	1.357	0.704
Q9CPR4	Large ribosomal subunit protein uL22	Rpl17	0.719	2.134
Q9CW03	Structural maintenance of chromosomes protein 3	Smc3	1.377	0.623
Q9CY34	NEDD8-conjugating enzyme UBE2F	Ube2f	1.226	0.606
Q9DBE0	Cysteine sulfinic acid decarboxylase	Csad	1.374	0.696
Q9DBY5	Chromobox protein homolog 6	Cbx6	2.183	0.689
Q9EP69	Phosphatidylinositol-3-phosphatase SAC1	Sacm1l	1.207	0.793
Q9EPR4	Solute carrier family 23 member 2	Slc23a2	1.255	0.317
Q9EQ61	Pescadillo homolog	Pes1	1.220	0.467

Q9EQK7	Protein-S-isoprenylcysteine O-methyltransferase	Icmt	3.480	0.095
Q9ERQ8	Carbonic anhydrase 7	Ca7	2.352	0.482
Q9JI59	Junctional adhesion molecule B	Jam2	1.356	0.421
Q9JL35	High mobility group nucleosome-binding domain-containing protein 5	Hmgn5	1.822	0.310
Q9QZN1	F-box/LRR-repeat protein 17	Fbxl17	1.408	0.776
Q9R0A1	Chloride channel protein 2	Clcn2	1.871	0.541
Q9R0H0	Peroxisomal acyl-coenzyme A oxidase 1	Acox1	1.235	0.710
Q9R226	KH domain-containing, RNA-binding, signal transduction-associated protein 3	Khdrbs3	0.766	1.671
Q9WVK8	Cholesterol 24-hydroxylase	Cyp46a1	0.795	1.975
Q9Z1M8	Protein Red	Ik	1.279	0.493
Q9Z1Q5	Chloride intracellular channel protein 1	Clic1	1.463	0.378
Q9Z2I8	Succinate--CoA ligase [GDP-forming] subunit beta, mitochondrial	Suclg2	1.330	0.645
Q9Z2W8	Glutamate receptor 4	Gria4	1.337	0.652
A2AHG0	Leucine zipper putative tumor suppressor 3	Lzts3	0.800	1.339
E9Q137	Testis-expressed protein 264 homolog	Tex264	1.312	0.639
P29758	Ornithine aminotransferase, mitochondrial	Oat	1.224	0.736
P59999	Actin-related protein 2/3 complex subunit 4	Arpc4	0.723	1.345
P61971	Nuclear transport factor 2	Nutf2	1.435	0.471
P62956	Voltage-dependent calcium channel gamma-7 subunit	Cacng7	1.632	0.592
P97376	Protein FRG1	Frg1	1.269	0.384
P97429	Annexin A4	Anxa4	1.407	0.616
Q08331	Calretinin	Calb2	2.084	0.472
Q32NY4	Metal transporter CNNM3	Cnnm3	1.267	0.608
Q3TB82	Pleckstrin homology domain-containing family F member 1	Plekhf1	2.161	0.436
Q640R3	Hepatic and glial cell adhesion molecule	Hepacam	1.552	0.433
Q6P1B3	PILR alpha-associated neural protein	Pianp	0.611	2.325
Q76LS9	Ubiquitin carboxyl-terminal hydrolase MINDY-1	Mindy1	1.512	0.660
Q7TNF0	Double C2-like domain-containing protein alpha	Doc2a	0.743	1.586
Q80XA6	RalBP1-associated Eps domain-containing protein 2	Reps2	0.758	1.596
Q80YN3	Breast carcinoma-amplified sequence 1 homolog	Bcas1	1.265	0.595
Q80ZX8	Sperm-associated antigen 1	Spag1	1.984	0.501
Q8BS40	Ceramide-1-phosphate transfer protein	Cptp	1.452	0.587
Q8BTV1	Tumor suppressor candidate 3	Tusc3	0.778	1.293
Q8BWD8	Cyclin-dependent kinase 19	Cdk19	1.576	0.189
Q8BZB3	Transmembrane protein 266	Tmem266	2.581	0.166

Q8CEE7	Retinol dehydrogenase 13	Rdh13	1.328	0.523
Q8JZM0	Dimethyladenosine transferase 1, mitochondrial	Tfb1m	1.294	0.449
Q8K297	Procollagen galactosyltransferase 1	Colgalt1	1.374	0.564
Q8K2T4	Ubiquinol-cytochrome-c reductase complex assembly factor 3	Uqcc3	1.619	0.479
Q8K354	Carbonyl reductase [NADPH] 3	Cbr3	0.788	1.731
Q8R088	Golgi phosphoprotein 3-like	Golph3l	1.604	0.671
Q8VHP7	Leukocyte elastase inhibitor B	Serpinb1b	2.218	0.431
Q91W59	RNA-binding motif, single-stranded-interacting protein 1	Rbms1	1.615	0.391
Q91W92	Cdc42 effector protein 1	Cdc42ep1	1.584	0.473
Q9CQI6	Coactosin-like protein	Cotl1	1.259	0.591
Q9CWP6	Motile sperm domain-containing protein 2	Mospd2	1.406	0.656
Q9D1G3	Protein-cysteine N-palmitoyltransferase HHAT-like protein	Hhatl	2.052	0.391
Q9D385	ADP-ribosylation factor-like protein 2-binding protein	Arl2bp	1.882	0.470
Q9D975	Sulfiredoxin-1	Srxn1	1.255	0.326
Q9D9E0	Solute carrier family 22 member 17	Slc22a17	0.780	1.695
Q9D9V3	Ethylmalonyl-CoA decarboxylase	Echdc1	1.202	0.728
Q9EQK5	Major vault protein	Mvp	1.268	0.618
Q9JHU2	Palmdelphin	Palmd	0.760	1.781
Q9JL62	Glycolipid transfer protein	Gltp	1.387	0.634
Q9QUN9	Dickkopf-related protein 3	Dkk3	0.744	1.314
P17665	Cytochrome c oxidase subunit 7C, mitochondrial	Cox7c	2.002	0.484
P49442	Inositol polyphosphate 1-phosphatase	Inpp1	1.319	0.771
P55099	Tachykinin-3	Tac3	2.127	0.363
P62748	Hippocalcin-like protein 1	Hpcal1	1.859	0.457
Q1RLL3	Copine-9	Cpne9	1.488	0.433
Q3TGF2	Protein FAM107B	Fam107b	5.546	0.143
Q3TH73	Protein tweety homolog 2	Ttyh2	1.656	0.460
Q3TY65	Islet cell autoantigen 1-like protein	Ica1l	1.592	0.553
Q3UFQ8	Capping protein, Arp2/3 and myosin-I linker protein 3	Carmil3	1.365	0.690
Q3V384	AFG1-like ATPase	Afg1l	1.306	0.599
Q6P5H6	FERM domain-containing protein 5	Frmd5	1.967	0.649
Q6ZQ82	Rho GTPase-activating protein 26	Arhgap26	1.288	0.551
Q80XD1	Beta-chimaerin	Chn2	2.174	0.280
Q8BI08	Protein MAL2	Mal2	0.706	1.479
Q8BK62	Olfactomedin-like protein 3	Olfml3	0.540	2.021
Q8BKY8	Transcription termination factor 2, mitochondrial	Mterf2	1.258	0.521

Q8C0Z1	Protein FAM234A	Fam234a	1.293	0.663
Q8R4C2	RUN and FYVE domain-containing protein 2	Rufy2	1.372	0.604
Q8VDN4	Coiled-coil domain-containing protein 92	Ccdc92	1.291	0.714
Q99J25	rRNA methyltransferase 1, mitochondrial	Mrm1	1.919	0.659
Q99LG2	Transportin-2	Tnpo2	0.808	1.613
Q9CQA6	Small ribosomal subunit protein mS37	Chchd1	0.505	2.934
Q9CQE3	Small ribosomal subunit protein uS17m	Mrps17	1.229	0.579
Q9CYL5	Golgi-associated plant pathogenesis-related protein 1	Glipr2	1.809	0.554
Q9D4F8	Gamma-tubulin complex component 4	Tubgcp4	1.311	0.426
P0DN89	Transmembrane protein 254	Tmem254	1.334	0.513
Q3UXZ6	Protein FAM81A	Fam81a	0.765	3.477
Q3UY34	Protein CUSTOS	Custos	1.228	0.335
Q78RX3	Small integral membrane protein 12	Smim12	1.266	0.605
Q80TB8	Synaptic vesicle membrane protein VAT-1 homolog-like	Vat1l	1.359	0.491
Q8BHG2	CXXC motif containing zinc binding protein	Czib	1.318	0.723
Q8BHI4	Kelch repeat and BTB domain-containing protein 3	Kbtbd3	1.488	0.545
Q8BLR2	Copine-4	Cpne4	0.816	1.775
Q8CD26	Solute carrier family 35 member E1	Slc35e1	1.328	0.667
Q8VCA8	Secernin-2	Scrn2	1.320	0.577
Q91W34	RUS family member 1	Rusf1	1.407	0.405
Q9CWN7	CCR4-NOT transcription complex subunit 11	Cnot11	1.409	0.594
Q9D8W7	OCIA domain-containing protein 2	Ociad2	0.778	1.942
Q9DB29	Isoamyl acetate-hydrolyzing esterase 1 homolog	Iah1	1.458	0.684
Q9JJF0	Nucleosome assembly protein 1-like 5	Nap1l5	1.774	0.219

T2DM, type 2 diabetes melitus.

Table SIII. List of the Top 200 differentially expressed genes reversed by semaglutide between T2DM/Control and Sema/T2DM.

RNA ID	T2DM/Control	Sema/T2DM
ENSMUST00000238946	4717.413	0.004
ENSMUST00000232205	2593102.009	0.000
ENSMUST00000230867	12490293.130	0.000
ENSMUST00000228044	3347348.313	0.000
ENSMUST00000227662	116.833	0.325
ENSMUST00000227594	3626.291	0.003
ENSMUST00000225488	4580633.704	0.000
ENSMUST00000224812	687.567	0.000
ENSMUST00000221807	351.225	0.006
ENSMUST00000221074	12.981	0.004
ENSMUST00000212964	66.314	0.000
ENSMUST00000211136	237.320	0.081
ENSMUST00000209206	7.475	0.001
ENSMUST00000207143	517346.151	0.000
ENSMUST00000201723	2.360	0.000
ENSMUST00000199432	1888136.493	0.455
ENSMUST00000198199	1888136.493	0.003
ENSMUST00000195561	2.804	0.390
ENSMUST00000191030	60.126	0.018
ENSMUST00000188111	2.165	0.006
ENSMUST00000181283	2421.865	0.004
ENSMUST00000180081	2.471	0.217
ENSMUST00000177476	2266297.708	0.000
ENSMUST00000177326	415.718	0.002
ENSMUST00000176263	4.756	0.003
ENSMUST00000172002	2.113	0.439
ENSMUST00000170219	126.979	0.253
ENSMUST00000166384	4.292	0.377
ENSMUST00000163257	3.327	0.283
ENSMUST00000163034	65.306	0.011
ENSMUST00000162872	3053450.824	0.000
ENSMUST00000159459	131.674	0.004
ENSMUST00000157040	94.529	0.034
ENSMUST00000150412	2560869.916	0.000
ENSMUST00000148955	2.267	0.007
ENSMUST00000146384	14.777	0.005

ENSMUST00000141516	2.791	0.408
ENSMUST00000140008	1936.550	0.001
ENSMUST00000139699	16.657	0.108
ENSMUST00000135260	2071616.466	0.003
ENSMUST00000132459	2.235	0.001
ENSMUST00000119422	3.608	0.343
ENSMUST00000119398	4.274	0.364
ENSMUST00000118366	2.329	0.256
ENSMUST00000117757	6.243	0.175
ENSMUST00000116403	92.182	0.012
ENSMUST00000115333	2858808.218	0.000
ENSMUST00000114773	3656054.764	0.000
ENSMUST00000114627	1627155.107	0.007
ENSMUST00000114608	1627155.107	0.003
ENSMUST00000114402	640816.882	0.000
ENSMUST00000113698	640816.882	0.000
ENSMUST00000113693	2.832	0.234
ENSMUST00000113686	2.832	0.000
ENSMUST00000113331	168.534	0.005
ENSMUST00000112523	5.126	0.360
ENSMUST00000112424	263.649	0.040
ENSMUST00000111564	163.706	0.433
ENSMUST00000111221	163.886	0.025
ENSMUST00000111219	163.886	0.007
ENSMUST00000110889	79.157	0.025
ENSMUST00000110520	3.241	0.024
ENSMUST00000110382	39.613	0.263
ENSMUST00000110042	707.705	0.445
ENSMUST00000109786	197.776	0.464
ENSMUST00000109492	7.086	0.195
ENSMUST00000109194	2229.911	0.321
ENSMUST00000108508	12.177	0.000
ENSMUST00000107903	797.671	0.001
ENSMUST00000106475	5322378.941	0.000
ENSMUST00000106411	16.657	0.127
ENSMUST00000106059	1215.927	0.006
ENSMUST00000104902	350.346	0.007
ENSMUST00000103033	10107260.550	0.006
ENSMUST00000102903	2560869.916	0.482

ENSMUST00000102752	7.086	0.248
ENSMUST00000101432	60.575	0.030
ENSMUST00000099444	5.228	0.005
ENSMUST00000095521	1850.570	0.053
ENSMUST00000093893	946.188	0.001
ENSMUST00000093106	2.131	0.004
ENSMUST00000092802	1379.513	0.044
ENSMUST00000092227	5165611.631	0.000
ENSMUST00000091325	341.196	0.000
ENSMUST00000088763	284.172	0.005
ENSMUST00000085044	410.799	0.003
ENSMUST00000081162	311.754	0.003
ENSMUST00000079415	6821.709	0.000
ENSMUST00000079086	7.086	0.165
ENSMUST00000077787	268.623	0.005
ENSMUST00000073939	203.057	0.005
ENSMUST00000070174	2017943.443	0.000
ENSMUST00000069187	3.855	0.002
ENSMUST00000067929	2.522	0.366
ENSMUST00000067086	1839232.814	0.000
ENSMUST00000065380	885.027	0.049
ENSMUST00000055528	2.021	0.098
ENSMUST00000048544	10074102.990	0.000
ENSMUST00000047243	387.514	0.005
ENSMUST00000032797	3.653	0.051
ENSMUST00000030806	10225717.790	0.000
ENSMUST00000028335	38.403	0.168
ENSMUST00000017567	324.224	0.003
ENSMUST00000234654	0.000	3253904.593
ENSMUST00000219993	0.421	2.661
ENSMUST00000207077	0.003	131.338
ENSMUST00000206246	0.427	191.084
ENSMUST00000202313	0.005	194.284
ENSMUST00000197134	0.362	3.191
ENSMUST00000183846	0.009	203.545
ENSMUST00000182877	0.004	137.328
ENSMUST00000182559	0.008	6.705
ENSMUST00000182511	0.005	2.182
ENSMUST00000182383	0.008	3.207

ENSMUST00000182213	0.008	176.417
ENSMUST00000177738	0.001	529.714
ENSMUST00000176464	0.020	198.580
ENSMUST00000173078	0.006	97.496
ENSMUST00000171238	0.000	2542185.368
ENSMUST00000170374	0.366	2.066
ENSMUST00000168871	0.271	5.776
ENSMUST00000165786	0.393	2.134
ENSMUST00000164963	0.006	3.986
ENSMUST00000163370	0.476	2180951.535
ENSMUST00000162269	0.037	2.932
ENSMUST00000161938	0.002	456.547
ENSMUST00000161600	0.000	8658198.525
ENSMUST00000161279	0.133	4.038
ENSMUST00000161254	0.005	51.851
ENSMUST00000156177	0.039	2.570
ENSMUST00000155901	0.003	2.042
ENSMUST00000146592	0.006	2.544
ENSMUST00000135344	0.003	498.119
ENSMUST00000133268	0.039	2.767
ENSMUST00000132583	0.008	318.708
ENSMUST00000119211	0.388	135.263
ENSMUST00000114795	0.007	473.870
ENSMUST00000113624	0.000	4278.679
ENSMUST00000112931	0.006	1962541.580
ENSMUST00000112836	0.344	2.196
ENSMUST00000112624	0.070	16.267
ENSMUST00000111213	0.482	1760397.625
ENSMUST00000109556	0.070	2.248
ENSMUST00000109157	0.321	2.379
ENSMUST00000108702	0.366	81.869
ENSMUST00000107906	0.401	4.098
ENSMUST00000106442	0.493	2.307
ENSMUST00000106192	0.069	3.105
ENSMUST00000105915	0.004	1205.681
ENSMUST00000103116	0.001	2159541.664
ENSMUST00000102760	0.393	2.005
ENSMUST00000098521	0.000	3070900.271
ENSMUST00000095076	0.002	2.561

ENSMUST00000094251	0.176	3.058
ENSMUST00000092766	0.002	354.268
ENSMUST00000089874	0.004	210.888
ENSMUST00000084215	0.002	301.159
ENSMUST00000084105	0.037	101.446
ENSMUST00000076224	0.441	2.098
ENSMUST00000071889	0.007	1268.040
ENSMUST00000071087	0.387	1805777.574
ENSMUST00000063607	0.003	303.831
ENSMUST00000059287	0.005	181.081
ENSMUST00000058496	0.000	320.279
ENSMUST00000052449	0.006	327.023
ENSMUST00000045550	0.439	3.280
ENSMUST00000044019	0.007	2.360
ENSMUST00000044009	0.001	470.766
ENSMUST00000042498	0.437	2.093
ENSMUST00000039165	0.002	1649.402
ENSMUST00000038695	0.323	2.571
ENSMUST00000038359	0.022	280.766
ENSMUST00000037547	0.460	2.212
ENSMUST00000035604	0.001	381.681
ENSMUST00000034802	0.001	3564488.140
ENSMUST00000032710	0.377	4.156
ENSMUST00000032192	0.000	658.122
ENSMUST00000032146	0.261	2.547
ENSMUST00000030691	0.490	2.052
ENSMUST00000028178	0.395	2.821
ENSMUST00000026076	0.071	29.266
ENSMUST00000018212	0.002	3324080.777
ENSMUST00000004201	0.048	36.563
ENSMUST00000212430	1.818	0.654
ENSMUST00000195817	1.874	0.563
ENSMUST00000189101	1.886	0.536
ENSMUST00000185343	1.886	0.577
ENSMUST00000171690	1.837	0.509
ENSMUST00000169488	1.947	0.555
ENSMUST00000159910	1.841	0.634
ENSMUST00000116542	1.972	0.565
ENSMUST00000109543	1.841	0.648

ENSMUST00000092425	1.901	0.588
ENSMUST00000067081	1.849	0.619
ENSMUST00000029416	1.836	0.666
ENSMUST00000027760	1.839	0.533
ENSMUST00000017548	1.901	0.687
ENSMUST00000207858	1.732	0.618
ENSMUST00000147076	1.737	0.589
ENSMUST00000137868	1.725	0.603

T2DM, type 2 diabetes melitus.

Table SIV. Conjoint GO enrichment analysis results of T2DM vs. Control and Sema vs. T2DM.

GO DM/NC-Sema/DM in Transcriptome	GO DM/NC-Sema/DM in proteomics
GO:0006468~protein phosphorylation	GO:0006811~monoatomic ion transport
GO:0051963~regulation of synapse assembly	GO:0007216~G protein-coupled glutamate receptor signaling pathway
GO:0050821~protein stabilization	GO:1903861~positive regulation of dendrite extension
GO:2000463~positive regulation of excitatory postsynaptic potential	GO:0035249~synaptic transmission, glutamatergic
GO:0007411~axon guidance	GO:0071277~cellular response to calcium ion
GO:0071108~protein K48-linked deubiquitination	GO:1900271~regulation of long-term synaptic potentiation
GO:0050808~synapse organization	GO:0034220~monoatomic ion transmembrane transport
GO:0008285~negative regulation of cell population proliferation	GO:0008360~regulation of cell shape
GO:0007399~nervous system development	GO:0016601~Rac protein signal transduction
GO:0016310~phosphorylation	GO:0014059~regulation of dopamine secretion
GO:0006915~apoptotic process	GO:0098712~L-glutamate import across plasma membrane
GO:0030036~actin cytoskeleton organization	GO:1905920~positive regulation of CoA-transferase activity
GO:0010976~positive regulation of neuron projection development	GO:0031032~actomyosin structure organization
GO:0043161~proteasome-mediated ubiquitin-dependent protein catabolic process	GO:0030041~actin filament polymerization
GO:0008344~adult locomotory behavior	GO:0010960~magnesium ion homeostasis
GO:0007015~actin filament organization	GO:0006730~one-carbon metabolic process
GO:0007275~multicellular organism development	GO:0048146~positive regulation of fibroblast proliferation
GO:0001933~negative regulation of protein phosphorylation	GO:0007204~positive regulation of cytosolic calcium ion concentration
GO:0051965~positive regulation of synapse assembly	GO:0009410~response to xenobiotic stimulus
GO:0043066~negative regulation of apoptotic process	GO:0010976~positive regulation of neuron projection development
GO:0070536~protein K63-linked deubiquitination	GO:0001881~receptor recycling
GO:0050885~neuromuscular process controlling balance	GO:2000772~regulation of cellular senescence

GO:0090630~activation of GTPase activity	GO:0007611~learning or memory
GO:0001701~in utero embryonic development	GO:0007528~neuromuscular junction development
GO:0015031~protein transport	GO:0006515~protein quality control for misfolded or incompletely synthesized proteins
GO:0007628~adult walking behavior	GO:0050804~modulation of chemical synaptic transmission
GO:0045893~positive regulation of DNA-templated transcription	GO:0045723~positive regulation of fatty acid biosynthetic process
GO:0098609~cell-cell adhesion	GO:0098962~regulation of postsynaptic neurotransmitter receptor activity
GO:0001764~neuron migration	GO:0032469~endoplasmic reticulum calcium ion homeostasis
GO:0007409~axonogenesis	GO:0060041~retina development in camera-type eye
GO:0006513~protein monoubiquitination	GO:0030178~negative regulation of Wnt signaling pathway
GO:0007626~locomotory behavior	GO:0007268~chemical synaptic transmission
GO:0006357~regulation of transcription by RNA polymerase II	GO:0007162~negative regulation of cell adhesion
GO:0015813~L-glutamate transmembrane transport	GO:0030048~actin filament-based movement
GO:0031175~neuron projection development	GO:0015813~L-glutamate transmembrane transport
GO:0070507~regulation of microtubule cytoskeleton organization	GO:0048144~fibroblast proliferation
GO:0016579~protein deubiquitination	GO:0022008~neurogenesis
GO:0043087~regulation of GTPase activity	GO:0031290~retinal ganglion cell axon guidance
GO:0150052~regulation of postsynapse assembly	GO:0099509~regulation of presynaptic cytosolic calcium ion concentration
GO:0022011~myelination in peripheral nervous system	GO:0016082~synaptic vesicle priming
GO:0043524~negative regulation of neuron apoptotic process	GO:0017158~regulation of calcium ion-dependent exocytosis
GO:0019227~neuronal action potential propagation	GO:0043065~positive regulation of apoptotic process
GO:0060079~excitatory postsynaptic potential	GO:0009611~response to wounding
GO:0045944~positive regulation of transcription by RNA polymerase II	GO:0014009~glial cell proliferation
GO:0030335~positive regulation of cell migration	GO:0060292~long-term synaptic depression
GO:0046329~negative regulation of JNK cascade	GO:0006629~lipid metabolic process
GO:0016192~vesicle-mediated transport	GO:0031175~neuron projection development

GO:0007616~long-term memory	GO:0051301~cell division
GO:0007010~cytoskeleton organization	GO:0001676~long-chain fatty acid metabolic process
GO:0071346~cellular response to type II interferon	GO:0061098~positive regulation of protein tyrosine kinase activity
GO:0045785~positive regulation of cell adhesion	GO:0010842~retina layer formation
GO:0008306~associative learning	GO:0050770~regulation of axonogenesis
GO:0043410~positive regulation of MAPK cascade	GO:0007626~locomotory behavior
GO:0010761~fibroblast migration	GO:0048167~regulation of synaptic plasticity
GO:0043065~positive regulation of apoptotic process	GO:0016310~phosphorylation
GO:0010628~positive regulation of gene expression	GO:0006814~sodium ion transport
GO:0035235~ionotropic glutamate receptor signaling pathway	GO:0051453~regulation of intracellular pH
GO:0033674~positive regulation of kinase activity	GO:0048168~regulation of neuronal synaptic plasticity
GO:0034599~cellular response to oxidative stress	GO:0006885~regulation of pH
GO:0006417~regulation of translation	GO:0007399~nervous system development
GO:0045669~positive regulation of osteoblast differentiation	GO:0007155~cell adhesion
GO:0035264~multicellular organism growth	GO:0007605~sensory perception of sound
GO:1902950~regulation of dendritic spine maintenance	GO:0007411~axon guidance
GO:0030951~establishment or maintenance of microtubule cytoskeleton polarity	GO:0008104~protein localization
GO:0051726~regulation of cell cycle	GO:0043087~regulation of GTPase activity
GO:0007049~cell cycle	GO:0032691~negative regulation of interleukin-1 beta production
GO:0045666~positive regulation of neuron differentiation	GO:0070373~negative regulation of ERK1 and ERK2 cascade
GO:0035249~synaptic transmission, glutamatergic	GO:0018108~peptidyl-tyrosine phosphorylation
GO:0018105~peptidyl-serine phosphorylation	GO:0006821~chloride transport
GO:0007169~cell surface receptor protein tyrosine kinase signaling pathway	GO:0055085~transmembrane transport
GO:0030154~cell differentiation	GO:0006816~calcium ion transport
GO:0000226~microtubule cytoskeleton organization	GO:0032849~positive regulation of cellular pH reduction

GO:0007611~learning or memory	GO:0060689~cell differentiation involved in salivary gland development
GO:0035418~protein localization to synapse	GO:0000154~rRNA modification
GO:0051489~regulation of filopodium assembly	GO:0021780~glial cell fate specification
GO:0021702~cerebellar Purkinje cell differentiation	GO:2001238~positive regulation of extrinsic apoptotic signaling pathway
GO:0001958~endochondral ossification	GO:0090314~positive regulation of protein targeting to membrane
GO:0007416~synapse assembly	GO:0007005~mitochondrion organization
GO:0007420~brain development	GO:0051726~regulation of cell cycle
GO:0051968~positive regulation of synaptic transmission, glutamatergic	GO:0070050~neuron cellular homeostasis
GO:0032465~regulation of cytokinesis	GO:0099149~regulation of postsynaptic neurotransmitter receptor internalization
GO:1905606~regulation of presynapse assembly	GO:0051968~positive regulation of synaptic transmission, glutamatergic
GO:0033138~positive regulation of peptidyl-serine phosphorylation	GO:0098609~cell-cell adhesion
GO:0001666~response to hypoxia	GO:2001225~regulation of chloride transport
GO:0007165~signal transduction	GO:1904778~positive regulation of protein localization to cell cortex
GO:0051897~positive regulation of phosphatidylinositol 3-kinase/protein kinase B signal transduction	GO:0016055~Wnt signaling pathway
GO:0051893~regulation of focal adhesion assembly	GO:0016525~negative regulation of angiogenesis
GO:0021987~cerebral cortex development	GO:1900026~positive regulation of substrate adhesion-dependent cell spreading
GO:0050772~positive regulation of axonogenesis	GO:0140009~L-aspartate import across plasma membrane
GO:0031647~regulation of protein stability	GO:0099502~calcium-dependent activation of synaptic vesicle fusion
GO:0032543~mitochondrial translation	GO:1902961~positive regulation of aspartic-type endopeptidase activity involved in amyloid precursor protein catabolic process
GO:0006412~translation	GO:0086073~bundle of His cell-Purkinje myocyte adhesion involved in cell communication
GO:0008380~RNA splicing	GO:0009449~gamma-aminobutyric acid biosynthetic process

GO:0050773~regulation of dendrite development	GO:1905244~regulation of modification of synaptic structure
GO:0007098~centrosome cycle	GO:0070059~intrinsic apoptotic signaling pathway in response to endoplasmic reticulum stress
GO:0051402~neuron apoptotic process	GO:0050853~B cell receptor signaling pathway
GO:0002931~response to ischemia	GO:0099072~regulation of postsynaptic membrane neurotransmitter receptor levels
GO:0016567~protein ubiquitination	GO:0005737~cytoplasm
GO:0032956~regulation of actin cytoskeleton organization	GO:0098978~glutamatergic synapse
GO:0000381~regulation of alternative mRNA splicing, via spliceosome	GO:0045202~synapse
GO:0065003~protein-containing complex assembly	GO:0030425~dendrite
GO:0030501~positive regulation of bone mineralization	GO:0016020~membrane
GO:2000010~positive regulation of protein localization to cell surface	GO:0045211~postsynaptic membrane
GO:0021954~central nervous system neuron development	GO:0030424~axon
GO:1900016~negative regulation of cytokine production involved in inflammatory response	GO:0005886~plasma membrane
GO:0090398~cellular senescence	GO:0042995~cell projection
GO:0008088~axo-dendritic transport	GO:0005829~cytosol
GO:0001702~gastrulation with mouth forming second	GO:0098688~parallel fiber to Purkinje cell synapse
GO:0048814~regulation of dendrite morphogenesis	GO:0043197~dendritic spine
GO:0051247~positive regulation of protein metabolic process	GO:0098839~postsynaptic density membrane
GO:0072593~reactive oxygen species metabolic process	GO:0043005~neuron projection
GO:0006511~ubiquitin-dependent protein catabolic process	GO:0043025~neuronal cell body
GO:0051260~protein homooligomerization	GO:0005856~cytoskeleton
GO:0000122~negative regulation of transcription by RNA polymerase II	GO:0005739~mitochondrion
GO:0070374~positive regulation of ERK1 and ERK2 cascade	GO:0042734~presynaptic membrane

GO:0072583~clathrin-dependent endocytosis	GO:0043204~perikaryon
GO:0043484~regulation of RNA splicing	GO:0043195~terminal bouton
GO:0008542~visual learning	GO:0048471~perinuclear region of cytoplasm
GO:0010629~negative regulation of gene expression	GO:0016323~basolateral plasma membrane
GO:0090129~positive regulation of synapse maturation	GO:0005654~nucleoplasm
GO:1902414~protein localization to cell junction	GO:0016328~lateral plasma membrane
GO:0097107~postsynaptic density assembly	GO:0070161~anchoring junction
GO:1900408~negative regulation of cellular response to oxidative stress	GO:0014069~postsynaptic density
GO:0010669~epithelial structure maintenance	GO:0009986~cell surface
GO:0030182~neuron differentiation	GO:0005912~adherens junction
GO:0016477~cell migration	GO:0005783~endoplasmic reticulum
GO:0007018~microtubule-based movement	GO:0098794~postsynapse
GO:0051262~protein tetramerization	GO:0005634~nucleus
GO:1902894~negative regulation of miRNA transcription	GO:0030027~lamellipodium
GO:0006897~endocytosis	GO:0098793~presynapse
GO:0001938~positive regulation of endothelial cell proliferation	GO:0005794~Golgi apparatus
GO:0008360~regulation of cell shape	GO:0032809~neuronal cell body membrane
GO:0048169~regulation of long-term neuronal synaptic plasticity	GO:0032437~cuticular plate
GO:0048168~regulation of neuronal synaptic plasticity	GO:0016363~nuclear matrix
GO:0006260~DNA replication	GO:0030426~growth cone
GO:0050804~modulation of chemical synaptic transmission	GO:0015629~actin cytoskeleton
GO:0043547~positive regulation of GTPase activity	GO:0031965~nuclear membrane
GO:0007156~homophilic cell adhesion via plasma membrane adhesion molecules	GO:0097431~mitotic spindle pole
GO:0061003~positive regulation of dendritic spine morphogenesis	GO:0016459~myosin complex
GO:0018108~peptidyl-tyrosine phosphorylation	GO:0099092~postsynaptic density, intracellular component
GO:0006397~mRNA processing	GO:0032153~cell division site
GO:0090136~epithelial cell-cell adhesion	GO:0005637~nuclear inner membrane

GO:0043030~regulation of macrophage activation	GO:0034707~chloride channel complex
GO:1900273~positive regulation of long-term synaptic potentiation	GO:0005743~mitochondrial inner membrane
GO:0043523~regulation of neuron apoptotic process	GO:0036477~somatodendritic compartment
GO:0055001~muscle cell development	GO:0009898~cytoplasmic side of plasma membrane
GO:0010467~gene expression	GO:0098686~hippocampal mossy fiber to CA3 synapse
GO:0008283~cell population proliferation	GO:0005769~early endosome
GO:0034614~cellular response to reactive oxygen species	GO:0031410~cytoplasmic vesicle
GO:0016311~dephosphorylation	GO:0032281~AMPA glutamate receptor complex
GO:0051549~positive regulation of keratinocyte migration	GO:0016604~nuclear body
GO:0098884~postsynaptic neurotransmitter receptor internalization	GO:0072686~mitotic spindle
GO:0051093~negative regulation of developmental process	GO:0098796~membrane protein complex
GO:0050806~positive regulation of synaptic transmission	GO:0034702~monoatomic ion channel complex
GO:0007005~mitochondrion organization	GO:0016529~sarcoplasmic reticulum
GO:0010977~negative regulation of neuron projection development	GO:0031090~organelle membrane
GO:0030334~regulation of cell migration	GO:0097513~myosin II filament
GO:0008203~cholesterol metabolic process	GO:0005730~nucleolus
GO:0043406~positive regulation of MAP kinase activity	GO:0005635~nuclear envelope
GO:0048488~synaptic vesicle endocytosis	GO:0005640~nuclear outer membrane
GO:1904706~negative regulation of vascular associated smooth muscle cell proliferation	GO:0044305~calyx of Held
GO:0045892~negative regulation of DNA-templated transcription	GO:0005768~endosome
GO:0009790~embryo development	GO:0005902~microvillus
GO:1904753~negative regulation of vascular associated smooth muscle cell migration	GO:0098982~GABA-ergic synapse
GO:0038202~TORC1 signaling	GO:0032590~dendrite membrane
GO:0006325~chromatin organization	GO:0097427~microtubule bundle
GO:0007160~cell-matrix adhesion	GO:0005615~extracellular space

GO:0051881~regulation of mitochondrial membrane potential	GO:0043679~axon terminus
GO:0007026~negative regulation of microtubule depolymerization	GO:0005694~chromosome
GO:0032526~response to retinoic acid	GO:0005515~protein binding
GO:0045471~response to ethanol	GO:0051015~actin filament binding
GO:0008284~positive regulation of cell population proliferation	GO:0042802~identical protein binding
GO:0050727~regulation of inflammatory response	GO:0003779~actin binding
GO:0070050~neuron cellular homeostasis	GO:0005544~calcium-dependent phospholipid binding
GO:0061635~regulation of protein complex stability	GO:0005524~ATP binding
GO:0070306~lens fiber cell differentiation	GO:0000166~nucleotide binding
GO:0006974~DNA damage response	GO:0004089~carbonate dehydratase activity
GO:0044331~cell-cell adhesion mediated by cadherin	GO:0044877~protein-containing complex binding
GO:0001578~microtubule bundle formation	GO:0003690~double-stranded DNA binding
GO:0050775~positive regulation of dendrite morphogenesis	GO:0016829~lyase activity
GO:0060291~long-term synaptic potentiation	GO:0046872~metal ion binding
GO:2000316~regulation of T-helper 17 type immune response	GO:0015293~symporter activity
GO:0032014~positive regulation of ARF protein signal transduction	GO:0016491~oxidoreductase activity
GO:1904161~DNA synthesis involved in UV-damage excision repair	GO:0003774~cytoskeletal motor activity
GO:0051649~establishment of localization in cell	GO:0019904~protein domain specific binding
GO:0061061~muscle structure development	GO:0048487~beta-tubulin binding
GO:0010633~negative regulation of epithelial cell migration	GO:0097110~scaffold protein binding
GO:0031110~regulation of microtubule polymerization or depolymerization	GO:0005516~calmodulin binding
GO:0001824~blastocyst development	GO:0060090~molecular adaptor activity
GO:0015914~phospholipid transport	GO:0008289~lipid binding
GO:0035176~social behavior	GO:0000400~four-way junction DNA binding
GO:0016322~neuron remodeling	GO:0016740~transferase activity

GO:1902236~negative regulation of endoplasmic reticulum stress-induced intrinsic apoptotic signaling pathway	GO:0005178~integrin binding
GO:0017148~negative regulation of translation	GO:0005216~monoatomic ion channel activity
GO:0048675~axon extension	GO:0000287~magnesium ion binding
GO:2000134~negative regulation of G1/S transition of mitotic cell cycle	GO:0019903~protein phosphatase binding
GO:0009060~aerobic respiration	GO:0005509~calcium ion binding
GO:0043433~negative regulation of DNA-binding transcription factor activity	GO:0008046~axon guidance receptor activity
GO:0042391~regulation of membrane potential	GO:0099534~calcium ion binding involved in regulation of presynaptic cytosolic calcium ion concentration
GO:1902430~negative regulation of amyloid-beta formation	GO:0016209~antioxidant activity
GO:0006376~mRNA splice site recognition	GO:0019905~syntaxin binding
GO:0045859~regulation of protein kinase activity	GO:0005543~phospholipid binding
GO:0060134~prepulse inhibition	GO:0016301~kinase activity
GO:0006979~response to oxidative stress	GO:0004713~protein tyrosine kinase activity
GO:0030534~adult behavior	GO:0017124~SH3 domain binding
GO:0006470~protein dephosphorylation	GO:0004672~protein kinase activity
GO:0090090~negative regulation of canonical Wnt signaling pathway	GO:0005200~structural constituent of cytoskeleton
GO:0007612~learning	GO:0140297~DNA-binding transcription factor binding
GO:0009749~response to glucose	GO:0016807~cysteine-type carboxypeptidase activity
GO:0061564~axon development	GO:0015276~ligand-gated monoatomic ion channel activity
GO:0045214~sarcomere organization	GO:0015631~tubulin binding
GO:0045773~positive regulation of axon extension	GO:0001786~phosphatidylserine binding
GO:0006801~superoxide metabolic process	GO:0005254~chloride channel activity
GO:0051056~regulation of small GTPase mediated signal transduction	GO:0046875~ephrin receptor binding
GO:0002042~cell migration involved in sprouting angiogenesis	GO:0017080~sodium channel regulator activity
GO:0000266~mitochondrial fission	GO:0005314~high-affinity L-glutamate transmembrane transporter activity

GO:0030031~cell projection assembly	GO:0005246~calcium channel regulator activity
GO:0050731~positive regulation of peptidyl-tyrosine phosphorylation	GO:0005262~calcium channel activity
GO:0071363~cellular response to growth factor stimulus	GO:0031267~small GTPase binding
GO:0005737~cytoplasm	GO:0000146~microfilament motor activity
GO:0042995~cell projection	GO:1990269~RNA polymerase II C-terminal domain phosphoserine binding
GO:0098978~glutamatergic synapse	GO:1902387~ceramide 1-phosphate binding
GO:0045202~synapse	GO:0097100~supercoiled DNA binding
GO:0005634~nucleus	GO:1902388~ceramide 1-phosphate transfer activity
GO:0016020~membrane	GO:0015501~glutamate: sodium symporter activity
GO:0005856~cytoskeleton	GO:0003682~chromatin binding
GO:0043197~dendritic spine	GO:0048306~calcium-dependent protein binding
GO:0014069~postsynaptic density	GO:0030295~protein kinase activator activity
GO:0005768~endosome	
GO:0030426~growth cone	
GO:0005886~plasma membrane	
GO:0005829~cytosol	
GO:0005654~nucleoplasm	
GO:0030425~dendrite	
GO:0043025~neuronal cell body	
GO:0098794~postsynapse	
GO:0030424~axon	
GO:0048471~perinuclear region of cytoplasm	
GO:0043005~neuron projection	
GO:0032991~protein-containing complex	
GO:0045211~postsynaptic membrane	
GO:0031410~cytoplasmic vesicle	
GO:0098793~presynapse	
GO:0070161~anchoring junction	
GO:0031594~neuromuscular junction	
GO:0098839~postsynaptic density membrane	
GO:0034451~centriolar satellite	
GO:0008021~synaptic vesicle	
GO:0005794~Golgi apparatus	
GO:0005874~microtubule	
GO:0048787~presynaptic active zone membrane	
GO:0005911~cell-cell junction	

GO:0044297~cell body	
GO:0030027~lamellipodium	
GO:0044304~main axon	
GO:0001725~stress fiber	
GO:1990904~ribonucleoprotein complex	
GO:0005783~endoplasmic reticulum	
GO:0098686~hippocampal mossy fiber to CA3 synapse	
GO:0098843~postsynaptic endocytic zone	
GO:0060076~excitatory synapse	
GO:0005813~centrosome	
GO:0045177~apical part of cell	
GO:0030673~axolemma	
GO:0000139~Golgi membrane	
GO:1990761~growth cone lamellipodium	
GO:0042734~presynaptic membrane	
GO:0016605~PML body	
GO:0005739~mitochondrion	
GO:0098685~Schaffer collateral - CA1 synapse	
GO:0043198~dendritic shaft	
GO:0005938~cell cortex	
GO:0005730~nucleolus	
GO:0098982~GABA-ergic synapse	
GO:0001726~ruffle	
GO:0005622~intracellular anatomical structure	
GO:0000785~chromatin	
GO:0005789~endoplasmic reticulum membrane	
GO:0030018~Z disc	
GO:0005925~focal adhesion	
GO:0015630~microtubule cytoskeleton	
GO:0044307~dendritic branch	
GO:0009986~cell surface	
GO:0012505~endomembrane system	
GO:0005923~bicellular tight junction	
GO:0036477~somatodendritic compartment	
GO:0098688~parallel fiber to Purkinje cell synapse	
GO:0016607~nuclear speck	
GO:0043195~terminal bouton	

GO:0043204~perikaryon	
GO:0055038~recycling endosome membrane	
GO:0010008~endosome membrane	
GO:0030054~cell junction	
GO:0017146~NMDA selective glutamate receptor complex	
GO:0032587~ruffle membrane	
GO:0044306~neuron projection terminus	
GO:0005884~actin filament	
GO:0043679~axon terminus	
GO:0005765~lysosomal membrane	
GO:0035371~microtubule plus-end	
GO:0016528~sarcoplasm	
GO:0005741~mitochondrial outer membrane	
GO:0005815~microtubule organizing center	
GO:0044291~cell-cell contact zone	
GO:0016324~apical plasma membrane	
GO:0005743~mitochondrial inner membrane	
GO:0055037~recycling endosome	
GO:0031466~Cul5-RING ubiquitin ligase complex	
GO:0005769~early endosome	
GO:0044309~neuron spine	
GO:1990635~proximal dendrite	
GO:0005778~peroxisomal membrane	
GO:0005764~lysosome	
GO:0043231~intracellular membrane-bounded organelle	
GO:0005834~heterotrimeric G-protein complex	
GO:0015629~actin cytoskeleton	
GO:0016323~basolateral plasma membrane	
GO:0005758~mitochondrial intermembrane space	
GO:0044305~calyx of Held	
GO:0030864~cortical actin cytoskeleton	
GO:1904115~axon cytoplasm	
GO:0097449~astrocyte projection	
GO:0035253~ciliary rootlet	
GO:0005905~clathrin-coated pit	
GO:0043596~nuclear replication fork	

GO:0005777~peroxisome	
GO:0097060~synaptic membrane	
GO:0030136~clathrin-coated vesicle	
GO:0005840~ribosome	
GO:0005515~protein binding	
GO:0046872~metal ion binding	
GO:0044877~protein-containing complex binding	
GO:0004672~protein kinase activity	
GO:0016740~transferase activity	
GO:0005096~GTPase activator activity	
GO:0042802~identical protein binding	
GO:0000166~nucleotide binding	
GO:0016301~kinase activity	
GO:0008017~microtubule binding	
GO:0005524~ATP binding	
GO:0001222~transcription corepressor binding	
GO:1990380~K48-linked deubiquitinase activity	
GO:0035255~ionotropic glutamate receptor binding	
GO:0004843~cysteine-type deubiquitinase activity	
GO:0019903~protein phosphatase binding	
GO:0005085~guanyl-nucleotide exchange factor activity	
GO:0030674~protein-macromolecule adaptor activity	
GO:0060090~molecular adaptor activity	
GO:0016787~hydrolase activity	
GO:0003677~DNA binding	
GO:0140297~DNA-binding transcription factor binding	
GO:0001540~amyloid-beta binding	
GO:0051015~actin filament binding	
GO:0106310~protein serine kinase activity	
GO:0004842~ubiquitin-protein transferase activity	
GO:0004713~protein tyrosine kinase activity	
GO:0019894~kinesin binding	
GO:0042803~protein homodimerization activity	

GO:0061630~ubiquitin protein ligase activity	
GO:0008234~cysteine-type peptidase activity	
GO:0004674~protein serine/threonine kinase activity	
GO:0031267~small GTPase binding	
GO:0005522~profilin binding	
GO:0030165~PDZ domain binding	
GO:0061578~K63-linked deubiquitinase activity	
GO:0005030~neurotrophin receptor activity	
GO:0003779~actin binding	
GO:0019899~enzyme binding	
GO:0019901~protein kinase binding	
GO:0004714~transmembrane receptor protein tyrosine kinase activity	
GO:0008270~zinc ion binding	
GO:0015631~tubulin binding	
GO:0099186~structural constituent of postsynapse	
GO:0035254~glutamate receptor binding	
GO:0044325~transmembrane transporter binding	
GO:0005102~signaling receptor binding	
GO:0003723~RNA binding	
GO:0098632~cell-cell adhesion mediator activity	
GO:0003676~nucleic acid binding	
GO:0005509~calcium ion binding	
GO:0005543~phospholipid binding	
GO:0019904~protein domain specific binding	
GO:0004683~calmodulin-dependent protein kinase activity	
GO:0004972~NMDA glutamate receptor activity	
GO:0008046~axon guidance receptor activity	
GO:0008092~cytoskeletal protein binding	
GO:0001221~transcription coregulator binding	
GO:0003729~mRNA binding	
GO:0003690~double-stranded DNA binding	
GO:0050839~cell adhesion molecule binding	
GO:0005516~calmodulin binding	
GO:0051020~GTPase binding	
GO:0031698~beta-2 adrenergic receptor binding	

GO:0000981~DNA-binding transcription factor activity, RNA polymerase II-specific	
GO:0004527~exonuclease activity	
GO:0043565~sequence-specific DNA binding	
GO:0098919~structural constituent of postsynaptic density	
GO:0043021~ribonucleoprotein complex binding	
GO:0031625~ubiquitin protein ligase binding	
GO:0010485~histone H4 acetyltransferase activity	
GO:0003682~chromatin binding	
GO:0003924~GTPase activity	
GO:0017124~SH3 domain binding	
GO:0034236~protein kinase A catalytic subunit binding	
GO:0030145~manganese ion binding	
GO:0008134~transcription factor binding	
GO:0051087~protein-folding chaperone binding	
GO:0099508~voltage-gated monoatomic ion channel activity involved in regulation of presynaptic membrane potential	
GO:0101005~deubiquitinase activity	
GO:0042826~histone deacetylase binding	
GO:0003730~mRNA 3'-UTR binding	
GO:0003824~catalytic activity	
GO:0005200~structural constituent of cytoskeleton	
GO:0008233~peptidase activity	
GO:0030695~GTPase regulator activity	
GO:0003697~single-stranded DNA binding	
GO:0030971~receptor tyrosine kinase binding	

Table SV. Expression of differentially expressed genes and differentially expressed proteins with the same trend for proteome and transcriptome in the comparison of T2DM vs. Control and Sema vs. T2DM pathway.

KEGG DM/NC-Sema/DM in Transcriptome	KEGG DM/NC-Sema/DM in proteomics
mmu04360: Axon guidance	mmu04724: Glutamatergic synapse
mmu04724: Glutamatergic synapse	mmu04964: Proximal tubule bicarbonate reclamation
mmu04070: Phosphatidylinositol signaling system	mmu05031: Amphetamine addiction
mmu04728: Dopaminergic synapse	mmu04260: Cardiac muscle contraction
mmu04921: Oxytocin signaling pathway	mmu01100: Metabolic pathways
mmu00562: Inositol phosphate metabolism	mmu04070: Phosphatidylinositol signaling system
mmu04713: Circadian entrainment	mmu04261: Adrenergic signaling in cardiomyocytes
mmu04720: Long-term potentiation	mmu04720: Long-term potentiation
mmu04725: Cholinergic synapse	mmu00071: Fatty acid degradation
mmu04211: Longevity regulating pathway	mmu00910: Nitrogen metabolism
mmu04010: MAPK signaling pathway	mmu04971: Gastric acid secretion
mmu04015: Rap1 signaling pathway	mmu04713: Circadian entrainment
mmu04810: Regulation of actin cytoskeleton	mmu04530: Tight junction
mmu05031: Amphetamine addiction	mmu04970: Salivary secretion
mmu04152: AMPK signaling pathway	mmu00562: Inositol phosphate metabolism
mmu04261: Adrenergic signaling in cardiomyocytes	mmu04721:Synaptic vesicle cycle
mmu05231: Choline metabolism in cancer	mmu04810: Regulation of actin cytoskeleton
mmu04140: Autophagy - animal	mmu04730: Long-term depression
mmu05211: Renal cell carcinoma	mmu05017: Spinocerebellar ataxia
mmu05200: Pathways in cancer	mmu01212: Fatty acid metabolism
mmu04024: cAMP signaling pathway	mmu04925: Aldosterone synthesis and secretion
mmu04510: Focal adhesion	mmu05412: Arrhythmogenic right ventricular cardiomyopathy
mmu04722: Neurotrophin signaling pathway	mmu04911: Insulin secretion
mmu05017: Spinocerebellar ataxia	mmu04024: cAMP signaling pathway
mmu04911: Insulin secretion	mmu04360: Axon guidance
mmu04926: Relaxin signaling pathway	mmu04666: Fc gamma R-mediated phagocytosis
mmu05212: Pancreatic cancer	mmu04918: Thyroid hormone synthesis
mmu04213: Longevity regulating pathway - multiple species	mmu00564: Glycerophospholipid metabolism
mmu04520: Adherens junction	mmu00280: Valine, leucine and isoleucine degradation
mmu04022: cGMP-PKG signaling pathway	mmu00900: Terpenoid backbone biosynthesis

mmu01522: Endocrine resistance	mmu05022: Pathways of neurodegeneration - multiple diseases
mmu05210: Colorectal cancer	mmu00230: Purine metabolism
mmu04928: Parathyroid hormone synthesis, secretion and action	mmu04728: Dopaminergic synapse
mmu04910: Insulin signaling pathway	mmu04022: cGMP-PKG signaling pathway
mmu04935: Growth hormone synthesis, secretion and action	mmu05100: Bacterial invasion of epithelial cells
mmu05213: Endometrial cancer	mmu04820: Cytoskeleton in muscle cells
mmu04371: Apelin signaling pathway	mmu04921: Oxytocin signaling pathway
mmu04922: Glucagon signaling pathway	mmu05414: Dilated cardiomyopathy
mmu05224: Breast cancer	mmu05415: Diabetic cardiomyopathy
mmu05417: Lipid and atherosclerosis	mmu05135: *Yersinia* infection
mmu04120: Ubiquitin mediated proteolysis	
mmu04710: Circadian rhythm	
mmu04020: Calcium signaling pathway	
mmu05214: Glioma	
mmu05220: Chronic myeloid leukemia	
mmu05030: Cocaine addiction	
mmu05223: Non-small cell lung cancer	
mmu04912: GnRH signaling pathway	
mmu04068: FoxO signaling pathway	
mmu04924: Renin secretion	
mmu04721: Synaptic vesicle cycle	
mmu04915: Estrogen signaling pathway	
mmu05218: Melanoma	
mmu05414: Dilated cardiomyopathy	
mmu05135: *Yersinia* infection	
mmu05410: Hypertrophic cardiomyopathy	
mmu04925: Aldosterone synthesis and secretion	
mmu04927: Cortisol synthesis and secretion	
mmu04668: TNF signaling pathway	
mmu05222: Small cell lung cancer	
mmu04930: Type 2 diabetes mellitus	
mmu04918: Thyroid hormone synthesis	
mmu04917: Prolactin signaling pathway	
mmu05217: Basal cell carcinoma	
mmu04380: Osteoclast differentiation	

T2DM, type 2 diabetes melitus; KEGG, Kyoto Encyclopedia of Genes and Genomes.

Table SVI. Expression of differentially expressed genes and differentially expressed proteins reversed by semaglutide in proteome and transcriptome in the comparison of DM vs. NC and Sema vs. DM pathway.

Kyoto Encyclopedia of Genes and Genomes	Transcriptome		Proteome		ACOX1
	DM vs. NC FC	Sema vs. DM FC	DM vs. NC FC	Sema-vs.DM FC	Enrichment
mmu00071: Fatty acid degradation	2.809	2.782	5.734	2.433	Yes
mmu00230: Purine metabolism	3.138	3.320	11.043	2.182	
mmu00280: Valine, leucine and isoleucine degradation	3.161	3.029	6.508	1.547	
mmu00562: Inositol phosphate metabolism	2.533	3.694	5.030	2.590	
mmu00564: Glycerophospholipid metabolism	2.412	2.836	4.290	2.469	
mmu00900: Terpenoid backbone biosynthesis	3.189	2.418	1.501	2.525	
mmu00910: Nitrogen metabolism	2.358	2.686	3.261	2.072	
mmu01100: Metabolic pathways	2.734	2.508	3.977	2.396	Yes
mmu01212:Fatty acid metabolism	3.060	2.452	3.622	2.783	Yes
mmu04022: cGMP-PKG signaling pathway	2.674	2.497	3.115	2.453	Yes
mmu04024: cAMP signaling pathway	2.468	2.247	4.662	2.858	
mmu04070:Phosphatidylinositol signaling system	2.180	1.824	5.340	2.696	
mmu04260: Cardiac muscle contraction	2.642	2.414	10.208	2.805	
mmu04261: Adrenergic signaling in cardiomyocytes	1.810	2.637	4.165	2.125	
mmu04360: Axon guidance	1.954	1.974	3.506	3.178	
mmu04530: Tight junction	1.909	2.583	2.515	1.943	
mmu04666: Fc gamma R-mediated phagocytosis	2.852	2.717	2.323	2.140	
mmu04713: Circadian entrainment	1.822	2.044	2.670	2.951	
mmu04720: Long-term potentiation	2.260	2.300	3.590	4.040	
mmu04721: Synaptic vesicle cycle	2.147	2.371	3.856	2.384	
mmu04724: Glutamatergic synapse	1.876	1.847	2.283	2.765	
mmu04728: Dopaminergic synapse	2.103	2.180	3.606	2.380	
mmu04730: Long-term depression	2.427	3.684	2.244	4.803	

mmu04810: Regulation of actin cytoskeleton	2.013	1.763	4.049	3.578	
mmu04820: Cytoskeleton in muscle cells	2.695	1.810	2.708	2.503	
mmu04911: Insulin secretion	1.889	2.240	3.919	2.069	
mmu04918: Thyroid hormone synthesis	1.990	2.632	3.033	1.722	
mmu04921: Oxytocin signaling pathway	1.497	2.072	3.229	1.912	
mmu04925: Aldosterone synthesis and secretion	1.831	2.782	3.229	2.102	
mmu04964: Proximal tubule bicarbonate reclamation	2.187	2.562	2.169	2.227	
mmu04970: Salivary secretion	2.734	1.832	3.120	2.281	
mmu04971: Gastric acid secretion	1.868	2.247	2.301	2.938	
mmu05017: Spinocerebellar ataxia	2.169	2.616	2.954	2.120	
mmu05022: Pathways of neurodegeneration - multiple diseases	2.441	2.279	3.283	1.660	
mmu05031: Amphetamine addiction	2.369	3.098	2.833	2.108	
mmu05100: Bacterial invasion of epithelial cells	1.743	2.540	3.653	2.750	
mmu05135: *Yersinia* infection	1.972	1.866	2.777	2.535	
mmu05412: Arrhythmogenic right ventricular cardiomyopathy	2.036	1.962	6.036	2.149	
mmu05414: Dilated cardiomyopathy	2.384	2.164	2.314	2.199	
mmu05415: Diabetic cardiomyopathy	2.082	2.434	3.414	3.189	

DM, diabetes mellitus; NC, negative control.