

Supplementary materials

Supplementary Table 1. The most significant obesity genes that are common between the different types of diabetes; T1D, T2D, and MODY.

Genes	Genes	Genes	Genes
<i>VDR</i>	<i>BDNF</i>	<i>PPARGC1A</i>	<i>SERPINC1</i>
<i>ACE</i>	<i>IFNG</i>	<i>SERPINE1</i>	<i>APOA1</i>
<i>HMGCR</i>	<i>ABCA1</i>	<i>CYP19A1</i>	<i>CCK</i>
<i>MMP2</i>	<i>RETN</i>	<i>VCAM1</i>	<i>ADRB2</i>
<i>EDN1</i>	<i>IL4</i>	<i>TP53</i>	<i>GAPDH</i>
<i>ABCB7</i>	<i>BCHE</i>	<i>TNF</i>	<i>APC</i>
<i>GSR</i>	<i>BCL2</i>	<i>INSR</i>	<i>TLR2</i>
<i>FASLG</i>	<i>TNFRSF11B</i>	<i>IFNA1</i>	<i>VEGFA</i>
<i>GGT1</i>	<i>CD36</i>	<i>HNF1B</i>	<i>CDKN2A</i>
<i>CYBA</i>	<i>FGF2</i>	<i>GNRH1</i>	<i>TGFB1</i>
<i>IGF1</i>	<i>CLU</i>	<i>HLA-DRB1</i>	<i>KCNJ11</i>
<i>CCL11</i>	<i>PCK2</i>	<i>IL1A</i>	<i>TFRC</i>
<i>PTEN</i>	<i>HK2</i>	<i>LDLR</i>	<i>ABCC8</i>
<i>HMOX1</i>	<i>G6PD</i>	<i>LPL</i>	<i>GAST</i>
<i>HNF1A</i>	<i>TF</i>	<i>CAT</i>	<i>TSHR</i>
<i>NOS2</i>	<i>GCK</i>	<i>MPO</i>	<i>JUN</i>
<i>INS</i>	<i>IGF1R</i>	<i>TCF7L2</i>	<i>HCRT</i>
<i>FLT1</i>	<i>IRS1</i>	<i>LIPC</i>	<i>SERPINF2</i>
<i>SLC6A4</i>	<i>GHRL</i>	<i>SELP</i>	<i>TIMP1</i>
<i>SOD2</i>	<i>ICAM1</i>	<i>GCG</i>	<i>CSF2</i>
<i>BGLAP</i>	<i>RECK</i>	<i>F5</i>	<i>GHRH</i>
<i>MMP3</i>	<i>RPS27A</i>	<i>IL8</i>	<i>MMP9</i>
<i>PPARA</i>	<i>TNFRSF1B</i>	<i>HLA-A</i>	<i>CD14</i>
<i>NGF</i>	<i>APOB</i>	<i>SLC2A2</i>	<i>ADIPOQ</i>
<i>GATA3</i>	<i>CS</i>	<i>AKT1</i>	
<i>IL2RA</i>	<i>LTF</i>	<i>PIK3R1</i>	
<i>PAX4</i>	<i>IL5</i>	<i>GRP</i>	
<i>TTR</i>	<i>AGT</i>	<i>NR1H2</i>	
<i>LEP</i>	<i>CGA</i>	<i>TNFRSF1A</i>	
<i>PTPRN2</i>	<i>PPARG</i>	<i>STAT3</i>	
<i>OXT</i>	<i>HNF4A</i>	<i>SPP1</i>	
<i>CYP1A2</i>	<i>CRP</i>	<i>F2</i>	
<i>TG</i>	<i>HIF1A</i>	<i>PTGS2</i>	
<i>CYP2C19</i>	<i>CALCA</i>	<i>AHSG</i>	
<i>NOS1</i>	<i>SERPINA1</i>	<i>B2M</i>	
<i>CRH</i>	<i>NOS3</i>	<i>LRP5</i>	
<i>IL10</i>	<i>MAPT</i>	<i>OLR1</i>	
<i>PRL</i>	<i>GLP1R</i>	<i>GH1</i>	
<i>IGF2</i>	<i>CASR</i>	<i>ITGB3</i>	
<i>LAPP</i>	<i>CNR1</i>	<i>CYP2C9</i>	

<i>MTHFR</i>	<i>DKK1</i>	<i>IL1B</i>	
<i>ISL1</i>	<i>NFE2L2</i>	<i>REN</i>	
<i>PAX6</i>	<i>NR3C1</i>	<i>VWF</i>	
<i>TNFSF11</i>	<i>HP</i>	<i>NPY</i>	
<i>GHR</i>	<i>OPRM1</i>	<i>IL18</i>	
<i>DPP4</i>	<i>CYP17A1</i>	<i>GAD2</i>	
<i>NPPB</i>	<i>TLR4</i>	<i>IGFBP2</i>	
<i>APOC3</i>	<i>LEPR</i>	<i>AR</i>	
<i>SOD1</i>	<i>BMP6</i>	<i>GAD1</i>	
<i>IFNA2</i>	<i>NPPA</i>	<i>PCSK9</i>	
<i>CD79A</i>	<i>ESR1</i>	<i>EPO</i>	
<i>FOXM1</i>	<i>SST</i>	<i>ACHE</i>	
<i>PIK3CA</i>	<i>PRF1</i>	<i>CP</i>	
<i>APOE</i>	<i>BMP4</i>	<i>KLK3</i>	
<i>IL2</i>	<i>NEUROD1</i>	<i>IL1R1</i>	
<i>FAS</i>	<i>SPARC</i>	<i>CCL2</i>	
<i>C3</i>	<i>AGTR1</i>	<i>HGF</i>	
<i>PDX1</i>	<i>IGFBP3</i>	<i>IL6</i>	
<i>PON1</i>	<i>ALB</i>	<i>APP</i>	
<i>NEUROG3</i>	<i>PTGS1</i>	<i>CPT2</i>	
<i>FOXA2</i>	<i>LCAT</i>	<i>COMT</i>	
<i>IGFBP1</i>	<i>APOA4</i>	<i>UCP2</i>	
<i>HSPD1</i>	<i>POMC</i>	<i>PROC</i>	

Supplementary Table 2. Involved GO terms from ClueGo enrichment analysis for cluster 1 genes.

GO ID	GO Term	Group p-Value Corrected with Bonferroni step down	% Associated Genes	Nr. Genes	Associated Genes Found
R-HSA:375276	Peptide ligand-binding receptors	7.15293E-47	18.42	35.00	[<i>AGT, AGTR1, APLN, APLNR, APP, BDKRB2, C3, CCK, CCKAR, CCL5, CCR2, CCR5, CX3CR1, CXCL5, CXCL8, CXCR4, EDN1, EDNRA, F2, GAL, GHSR, GRP, HCRT, KNG1, MLN, NPY, NTS, OPRM1, OXT, POMC, PPY, PYY, SST, TAC1, TRH</i>]
R-HSA:373076	Class A/1 (Rhodopsin-like receptors)	7.15293E-47	14.81	48.00	[<i>ADORA1, ADRA2A, ADRA2B, AGT, AGTR1, APLN, APLNR, APP, BDKRB2, C3, CCK, CCKAR, CCL5, CCR2, CCR5, CNR1, CNR2, CX3CR1, CXCL5, CXCL8, CXCR4, DRD2, DRD4, EDN1, EDNRA, F2, GAL, GHSR, GNRH1, GPR39, GRP, HCRT, HTR1A, HTR2A, KNG1, MLN, MTNR1A, MTNR1B, NPY, NTS, OPRM1, OXT, POMC, PPY, PYY, SST, TAC1, TRH</i>]
KEGG:04080	Neuroactive ligand-receptor interaction	7.15293E-47	12.13	41.00	[<i>ADORA1, ADRA2A, ADRA2B, AGT, AGTR1, APLN, APLNR, BDKRB2, C3, CCK, CCKAR, CNR1, CNR2, DRD2, DRD4, EDN1, EDNRA, F2, GAL, GCG, GCGR, GHSR, GNRH1, GRP, HCRT, HTR1A, HTR2A, KNG1, MLN, MTNR1A, MTNR1B, NPY, NTS, OPRM1, OXT, POMC, PPY, PYY, SST, TAC1, TRH</i>]
R-HSA:500792	GPCR ligand binding	7.15293E-47	11.16	51.00	[<i>ADORA1, ADRA2A, ADRA2B, AGT, AGTR1, APLN, APLNR, APP, BDKRB2, C3, CASR, CCK, CCKAR, CCL5, CCR2, CCR5, CNR1, CNR2, CX3CR1, CXCL5, CXCL8, CXCR4, DRD2, DRD4, EDN1, EDNRA, F2, GAL, GCG, GCGR, GHSR, GNRH1, GPR39, GRP, HCRT, HTR1A, HTR2A, KNG1, MLN, MTNR1A, MTNR1B, NPY, NTS, OPRM1, OXT, POMC, PPY, PYY, SST, TAC1, TRH</i>]
R-HSA:418594	G alpha (i) signalling events	7.15293E-47	9.09	37.00	[<i>ADORA1, ADRA2A, ADRA2B, AGT, APLN, APLNR, APOA1, APOA2, APOB, APOE, APP, BDKRB2, C3, CASR, CCL5, CCR2, CCR5, CNR1, CNR2, CX3CR1, CXCL5, CXCL8, CXCR4, DRD2, DRD4, GAL, GNAI1, HTR1A, KNG1, MTNR1A, MTNR1B, NPY, OPRM1, POMC, PPY, PYY, SST</i>]
R-HSA:8957275	Post-translational protein phosphorylation	7.24486E-42	28.70	31.00	[<i>AHSG, ALB, APOA1, APOA2, APOA5, APOB, APOE, APP, BMP4, C3, CP, CSF1, CST3, F5, FGA, FGF23, IGFBP1, IGFBP3, IGFBP5, IGFBP7, IL6, KNG1, PCSK9, PNPLA2, PROC, SERPIN1, SERPINC1, SPP1, TF, TIMP1, TNC</i>]
R-HSA:381426	Regulation of Insulin-like Growth Factor (IGF) transport and uptake by	7.24486E-42	25.60	32.00	[<i>AHSG, ALB, APOA1, APOA2, APOA5, APOB, APOE, APP, BMP4, C3, CP, CSF1, CST3, F2, F5, FGA, FGF23, IGFBP1, IGFBP3,</i>

	Insulin-like Growth Factor Binding Proteins (IGFBPs)				<i>IGFBP5, IGFBP7, IL6, KNG1, PCSK9, PNPLA2, PROC, SERPINA1, SERPINC1, SPP1, TF, TIMP1, TNC]</i>
R-HSA:416476	G alpha (q) signalling events	6.88134E-26	12.44	27.00	<i>[AGT, AGTR1, APP, BDKRB2, CASR, CCK, CCKAR, EDN1, EDNRA, F2, GAST, GCG, GCGR, GHSR, GNRH1, GPR39, GRP, HCRT, HTR2A, KNG1, MLN, NTS, OXT, PIK3CA, PIK3R1, TAC1, TRH]</i>
R-HSA:392023	Adrenaline signalling through Alpha-2 adrenergic receptor	6.72026E-10	66.67	2.00	<i>[ADRA2A, ADRA2B]</i>
R-HSA:390651	Dopamine receptors	6.72026E-10	40.00	2.00	<i>[DRD2, DRD4]</i>
R-HSA:140875	Common Pathway of Fibrin Clot Formation	6.72026E-10	22.73	5.00	<i>[F2, F5, FGA, PROC, SERPINC1]</i>
R-HSA:390696	Adrenoceptors	6.72026E-10	22.22	2.00	<i>[ADRA2A, ADRA2B]</i>
R-HSA:390666	Serotonin receptors	6.72026E-10	16.67	2.00	<i>[HTR1A, HTR2A]</i>
R-HSA:375280	Amine ligand-binding receptors	6.72026E-10	14.29	6.00	<i>[ADRA2A, ADRA2B, DRD2, DRD4, HTR1A, HTR2A]</i>
R-HSA:76009	Platelet Aggregation (Plug Formation)	6.72026E-10	10.26	4.00	<i>[ADRA2A, ADRA2B, F2, FGA]</i>
R-HSA:140875	Common Pathway of Fibrin Clot Formation	1.1004E-08	22.73	5.00	<i>[F2, F5, FGA, PROC, SERPINC1]</i>
R-HSA:159763	Transport of gamma-carboxylated protein precursors from the endoplasmic reticulum to the Golgi apparatus	1.1004E-08	22.22	2.00	<i>[F2, PROC]</i>
R-HSA:159740	Gamma-carboxylation of protein precursors	1.1004E-08	20.00	2.00	<i>[F2, PROC]</i>
R-HSA:159782	Removal of aminoterminal propeptides from gamma-carboxylated proteins	1.1004E-08	20.00	2.00	<i>[F2, PROC]</i>
R-HSA:140837	Intrinsic Pathway of Fibrin Clot Formation	1.1004E-08	18.18	4.00	<i>[F2, KNG1, PROC, SERPINC1]</i>
R-HSA:159854	Gamma-carboxylation, transport, and aminoterminal cleavage of proteins	1.1004E-08	18.18	2.00	<i>[F2, PROC]</i>

R-HSA:140877	Formation of Fibrin Clot (Clotting Cascade)	1.1004E-08	15.38	6.00	[F2, F5, FGA, KNG1, PROC, SERPINC1]
KEGG:04610	Complement and coagulation cascades	1.1004E-08	11.39	9.00	[BDKRB2, C3, F2, F5, FGA, KNG1, PROC, SERPINA1, SERPINC1]
R-HSA:76009	Platelet Aggregation (Plug Formation)	1.1004E-08	10.26	4.00	[ADRA2A, ADRA2B, F2, FGA]
R-HSA:173107	Binding and entry of HIV virion	2.31219E-08	20.00	2.00	[CCR5, CXCR4]
R-HSA:6783783	Interleukin-10 signaling	2.31219E-08	14.89	7.00	[CCL5, CCR2, CCR5, CSF1, CXCL8, IL6, TIMP1]
R-HSA:380108	Chemokine receptors bind chemokines	2.31219E-08	14.58	7.00	[CCL5, CCR2, CCR5, CX3CR1, CXCL5, CXCL8, CXCR4]
R-HSA:162594	Early Phase of HIV Life Cycle	2.31219E-08	10.00	2.00	[CCR5, CXCR4]
KEGG:05142	Chagas disease (American trypanosomiasis)	3.50978E-07	8.74	9.00	[BDKRB2, C3, CCL5, CXCL8, GNAI1, IL6, KNG1, PIK3CA, PIK3R1]
KEGG:04614	Renin-angiotensin system	0.000272724	8.70	2.00	[AGT, AGTR1]
KEGG:04924	Renin secretion	0.000272724	8.70	6.00	[ADORA1, AGT, AGTR1, EDN1, EDNRA, GNAI1]
R-HSA:8963901	Chylomicron remodeling	0.000437865	55.56	5.00	[APOA1, APOA2, APOA5, APOB, APOE]
R-HSA:8963888	Chylomicron assembly	0.000437865	44.44	4.00	[APOA1, APOA2, APOB, APOE]
R-HSA:8964026	Chylomicron clearance	0.000437865	40.00	2.00	[APOB, APOE]
R-HSA:3000471	Scavenging by Class B Receptors	0.000437865	33.33	2.00	[APOA1, APOB]
R-HSA:8964058	HDL remodeling	0.000437865	30.00	3.00	[ALB, APOA1, APOE]
R-HSA:8963898	Plasma lipoprotein assembly	0.000437865	22.22	4.00	[APOA1, APOA2, APOB, APOE]
R-HSA:8963899	Plasma lipoprotein remodeling	0.000437865	20.00	6.00	[ALB, APOA1, APOA2, APOA5, APOB, APOE]
R-HSA:3000480	Scavenging by Class A Receptors	0.000437865	15.79	3.00	[APOA1, APOB, APOE]
R-HSA:2168880	Scavenging of heme from plasma	0.000437865	15.38	2.00	[ALB, APOA1]
R-HSA:8964043	Plasma lipoprotein clearance	0.000437865	12.12	4.00	[APOA1, APOB, APOE, PCSK9]
R-HSA:5686938	Regulation of TLR by endogenous ligand	0.000437865	10.53	2.00	[APOB, FGA]

R-HSA:8964038	LDL clearance	0.000437865	10.53	2.00	<i>[APOB, PCSK9]</i>
R-HSA:174824	Plasma lipoprotein assembly, remodeling, and clearance	0.000437865	10.14	7.00	<i>[ALB, APOA1, APOA2, APOA5, APOB, APOE, PCSK9]</i>
KEGG:04979	Cholesterol metabolism	0.000437865	10.00	5.00	<i>[APOA1, APOA2, APOB, APOE, PCSK9]</i>
R-HSA:2173782	Binding and Uptake of Ligands by Scavenger Receptors	0.000437865	9.52	4.00	<i>[ALB, APOA1, APOB, APOE]</i>
R-HSA:975634	Retinoid metabolism and transport	0.000437865	9.30	4.00	<i>[APOA1, APOA2, APOB, APOE]</i>
R-HSA:6806667	Metabolism of fat-soluble vitamins	0.000437865	8.51	4.00	<i>[APOA1, APOA2, APOB, APOE]</i>
KEGG:04977	Vitamin digestion and absorption	0.000437865	8.33	2.00	<i>[APOA1, APOB]</i>
R-HSA:8851907	MET activates PI3K/AKT signaling	0.004786962	33.33	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:9603381	Activated NTRK3 signals through PI3K	0.004786962	33.33	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:9028335	Activated NTRK2 signals through PI3K	0.004786962	28.57	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:198203	PI3K/AKT activation	0.004786962	22.22	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:1250342	PI3K events in ERBB4 signaling	0.004786962	20.00	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:8853334	Signaling by FGFR3 fusions in cancer	0.004786962	20.00	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5655291	Signaling by FGFR4 in disease	0.004786962	18.18	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5654710	PI-3K cascade:FGFR3	0.004786962	16.67	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:9027276	Erythropoietin activates Phosphoinositide-3-kinase (PI3K)	0.004786962	16.67	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5654720	PI-3K cascade:FGFR4	0.004786962	15.00	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:5654689	PI-3K cascade:FGFR1	0.004786962	14.29	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:5655332	Signaling by FGFR3 in disease	0.004786962	13.64	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>

R-HSA:8853338	Signaling by FGFR3 point mutants in cancer	0.004786962	13.64	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:5637810	Constitutive Signaling by EGFRvIII	0.004786962	13.33	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5637812	Signaling by EGFRvIII in Cancer	0.004786962	13.33	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5654695	PI-3K cascade:FGFR2	0.004786962	13.04	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:1963642	PI3K events in ERBB2 signaling	0.004786962	12.50	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:2730905	Role of LAT2/NTAL/LAB on calcium mobilization	0.004786962	12.50	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5654708	Downstream signaling of activated FGFR3	0.004786962	12.00	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:180292	GAB1 signalosome	0.004786962	11.76	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:9034015	Signaling by NTRK3 (TRKC)	0.004786962	11.76	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:1839117	Signaling by cytosolic FGFR1 fusion mutants	0.004786962	11.11	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:210993	Tie2 Signaling	0.004786962	11.11	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5654716	Downstream signaling of activated FGFR4	0.004786962	11.11	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
KEGG:04923	Regulation of lipolysis in adipocytes	0.004786962	10.91	6.00	<i>[ADORA1, GNAI1, NPY, PIK3CA, PIK3R1, PNPLA2]</i>
R-HSA:1236382	Constitutive Signaling by Ligand-Responsive EGFR Cancer Variants	0.004786962	10.53	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5637815	Signaling by Ligand-Responsive EGFR Variants in Cancer	0.004786962	10.53	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:5654696	Downstream signaling of activated FGFR2	0.004786962	10.00	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:1839124	FGFR1 mutant receptor activation	0.004786962	9.68	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:5654687	Downstream signaling of activated FGFR1	0.004786962	9.68	3.00	<i>[FGF23, PIK3CA, PIK3R1]</i>
R-HSA:389357	CD28 dependent PI3K/Akt signaling	0.004786962	9.09	2.00	<i>[PIK3CA, PIK3R1]</i>

R-HSA:912631	Regulation of signaling by CBL	0.004786962	9.09	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:373753	Nephrin family interactions	0.004786962	8.70	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:1643713	Signaling by EGFR in Cancer	0.004786962	8.00	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:2029485	Role of phospholipids in phagocytosis	0.004786962	8.00	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:9006115	Signaling by NTRK2 (TRKB)	0.004786962	8.00	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:9006335	Signaling by Erythropoietin	0.004786962	8.00	2.00	<i>[PIK3CA, PIK3R1]</i>
R-HSA:9615017	FOXO-mediated transcription of oxidative stress, metabolic and neuronal genes	0.005339022	10.34	3.00	<i>[IGFBP1, NPY, POMC]</i>
R-HSA:202040	G-protein activation	0.005773145	10.71	3.00	<i>[GNAI1, OPRM1, POMC]</i>
KEGG:05143	African trypanosomiasis	0.006542366	8.11	3.00	<i>[APOA1, IL6, KNG1]</i>
R-HSA:380994	ATF4 activates genes	0.013149546	8.00	2.00	<i>[CXCL8, IGFBP1]</i>
R-HSA:381771	Synthesis, secretion, and inactivation of Glucagon-like Peptide-1 (GLP-1)	0.022380594	10.00	2.00	<i>[GCG, GRP]</i>
R-HSA:400508	Incretin synthesis, secretion, and inactivation	0.022380594	8.70	2.00	<i>[GCG, GRP]</i>

Supplementary Table 3. Involved GO terms from ClueGo enrichment analysis for cluster 2 genes.

GO ID	GO Term	Term p-Value Corrected with Bonferroni step down	% Associated Genes	Nr. Genes	Associated Genes Found
R-HSA:114608	Platelet degranulation	3.48546E-20	11.63	15.00	<i>[A2M, CLU, F13A1, FGB, HGF, IGF1, IGF2, PROS1, SERPINE1, SERPINF2, SPARC, TGFB1, THBS1, VEGFA, VWF]</i>

R-HSA:76005	Response to elevated platelet cytosolic Ca ²⁺	5.87143E-20	11.19	15.00	[<i>A2M, CLU, F13A1, FGB, HGF, IGF1, IGF2, PROS1, SERPINE1, SERPINF2, SPARC, TGFB1, THBS1, VEGFA, VWF</i>]
R-HSA:373080	Class B/2 (Secretin family receptors)	9.2479E-13	10.53	10.00	[<i>ADM, CALCA, CRH, GHRH, GIP, GLP1R, GNAS, LAPP, PTH, RAMP1</i>]
KEGG:04610	Complement and coagulation cascades	4.78905E-10	10.13	8.00	[<i>A2M, CLU, F13A1, FGB, PROS1, SERPINE1, SERPINF2, VWF</i>]
KEGG:04923	Regulation of lipolysis in adipocytes	9.30048E-08	10.91	6.00	[<i>ADRB1, ADRB2, ADRB3, CGA, GNAS, TSHR</i>]
R-HSA:419812	Calcitonin-like ligand receptors	1.06302E-07	40.00	4.00	[<i>ADM, CALCA, LAPP, RAMP1</i>]
R-HSA:140877	Formation of Fibrin Clot (Clotting Cascade)	6.20737E-07	12.82	5.00	[<i>A2M, F13A1, FGB, PROS1, VWF</i>]
R-HSA:390696	Adrenoceptors	1.26179E-05	33.33	3.00	[<i>ADRB1, ADRB2, ADRB3</i>]
R-HSA:420092	Glucagon-type ligand receptors	1.31787E-05	12.12	4.00	[<i>GHRH, GIP, GLP1R, GNAS</i>]
R-HSA:140875	Common Pathway of Fibrin Clot Formation	0.000161063	13.64	3.00	[<i>F13A1, FGB, PROS1</i>]
R-HSA:8866910	TFAP2 (AP-2) family regulates transcription of growth factors and their receptors	0.00082292	13.33	2.00	[<i>CGA, VEGFA</i>]
R-HSA:354194	GRB2:SOS provides linkage to MAPK signaling for Integrins	0.00082292	13.33	2.00	[<i>FGB, VWF</i>]
R-HSA:372708	p130Cas linkage to MAPK signaling for integrins	0.00082292	13.33	2.00	[<i>FGB, VWF</i>]
R-HSA:2428933	SHC-related events triggered by IGF1R	0.001140851	22.22	2.00	[<i>IGF1, IGF2</i>]
R-HSA:75205	Dissolution of Fibrin Clot	0.001227039	15.38	2.00	[<i>SERPINE1, SERPINF2</i>]
R-HSA:375281	Hormone ligand-binding receptors	0.001560206	16.67	2.00	[<i>CGA, TSHR</i>]

Supplementary Table 4. Involved GO terms from ClueGo enrichment analysis for cluster 3 genes.

GO ID	GO Term	Term p-Value Corrected with Bonferroni step down	% Associated Genes	Nr. Genes	Associated Genes Found
R-HSA:74749	Signal attenuation	1.00541E-07	40.00	4.00	[<i>INS, INSR, IRS1, SHC1</i>]
R-HSA:74749	Signal attenuation	1.00541E-07	40.00	4.00	[<i>INS, INSR, IRS1, SHC1</i>]

KEGG:04910	Insulin signaling pathway	2.53779E-07	5.11	7.00	[<i>INPPL1, INS, INSR, IRS1, PRKCZ, PTPN1, SHC1</i>]
R-HSA:8856825	Cargo recognition for clathrin-mediated endocytosis	1.85804E-06	5.66	6.00	[<i>IGF2R, LDLR, RPS27A, SH3GL2, TFRC, WNT5A</i>]
R-HSA:74713	IRS activation	2.49046E-06	60.00	3.00	[<i>INS, INSR, IRS1</i>]
R-HSA:432722	Golgi Associated Vesicle Biogenesis	2.59797E-06	8.93	5.00	[<i>FTH1, IGF2R, PIK3C2A, SH3GL2, TFRC</i>]
R-HSA:199992	trans-Golgi Network Vesicle Budding	9.03152E-06	6.94	5.00	[<i>FTH1, IGF2R, PIK3C2A, SH3GL2, TFRC</i>]
R-HSA:421837	Clathrin derived vesicle budding	9.03152E-06	6.94	5.00	[<i>FTH1, IGF2R, PIK3C2A, SH3GL2, TFRC</i>]
KEGG:04930	Type II diabetes mellitus	6.23421E-05	8.70	4.00	[<i>INS, INSR, IRS1, PRKCZ</i>]
R-HSA:512988	Interleukin-3, Interleukin-5 and GM-CSF signaling	7.17434E-05	8.33	4.00	[<i>IL5, INPPL1, RPS27A, SHC1</i>]
KEGG:04913	Ovarian steroidogenesis	7.54143E-05	8.16	4.00	[<i>IGF1R, INS, INSR, LDLR</i>]
R-HSA:74751	Insulin receptor signalling cascade	0.00010795	7.41	4.00	[<i>INS, INSR, IRS1, SHC1</i>]
R-HSA:74751	Insulin receptor signalling cascade	0.00010795	7.41	4.00	[<i>INS, INSR, IRS1, SHC1</i>]
KEGG:04213	Longevity regulating pathway	0.000181635	6.45	4.00	[<i>IGF1R, INS, INSR, IRS1</i>]
R-HSA:6807004	Negative regulation of MET activity	0.00024795	14.29	3.00	[<i>PTPN1, RPS27A, SH3GL2</i>]
R-HSA:74752	Signaling by Insulin receptor	0.000420816	5.13	4.00	[<i>INS, INSR, IRS1, SHC1</i>]
R-HSA:74752	Signaling by Insulin receptor	0.000420816	5.13	4.00	[<i>INS, INSR, IRS1, SHC1</i>]
R-HSA:6806834	Signaling by MET	0.000424953	5.06	4.00	[<i>PTPN1, RPS27A, SH3GL2, SHC1</i>]
R-HSA:912526	Interleukin receptor SHC signaling	0.000478543	11.11	3.00	[<i>IL5, INPPL1, SHC1</i>]
R-HSA:1592389	Activation of Matrix Metalloproteinases	0.000847019	9.09	3.00	[<i>MMP8, MMP9, TIMP2</i>]
KEGG:04960	Aldosterone-regulated sodium reabsorption	0.001145307	8.11	3.00	[<i>INS, INSR, IRS1</i>]
R-HSA:451927	Interleukin-2 family signaling	0.001841966	6.82	3.00	[<i>IL5, INPPL1, SHC1</i>]
R-HSA:177929	Signaling by EGFR	0.002418122	6.12	3.00	[<i>RPS27A, SH3GL2, SHC1</i>]
R-HSA:2428933	SHC-related events triggered by IGF1R	0.002535729	22.22	2.00	[<i>IGF1R, SHC1</i>]
R-HSA:2428933	SHC-related events triggered by IGF1R	0.002535729	22.22	2.00	[<i>IGF1R, SHC1</i>]
KEGG:04923	Regulation of lipolysis in adipocytes	0.002696766	5.45	3.00	[<i>INS, INSR, IRS1</i>]
R-HSA:2404192	Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)	0.002723271	5.56	3.00	[<i>IGF1R, IRS1, SHC1</i>]

R-HSA:2404192	Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R)	0.002723271	5.56	3.00	<i>[IGF1R, IRS1, SHC1]</i>
R-HSA:2428924	IGF1R signaling cascade	0.002736368	5.66	3.00	<i>[IGF1R, IRS1, SHC1]</i>
R-HSA:2428924	IGF1R signaling cascade	0.002736368	5.66	3.00	<i>[IGF1R, IRS1, SHC1]</i>
R-HSA:1236977	Endosomal/Vacuolar pathway	0.002790979	18.18	2.00	<i>[B2M, CTSS]</i>
KEGG:04216	Ferroptosis	0.002937287	5.00	2.00	<i>[FTH1, TFRC]</i>
R-HSA:5654741	Signaling by FGFR3	0.002937287	5.00	2.00	<i>[RPS27A, SHC1]</i>
R-HSA:917937	Iron uptake and transport	0.002948518	5.17	3.00	<i>[FTH1, RPS27A, TFRC]</i>
R-HSA:182971	EGFR downregulation	0.005312053	6.45	2.00	<i>[RPS27A, SH3GL2]</i>
R-HSA:2173791	TGF-beta receptor signaling in EMT (epithelial to mesenchymal transition)	0.005586252	12.50	2.00	<i>[PRKCZ, RPS27A]</i>
R-HSA:8875360	InlB-mediated entry of Listeria monocytogenes into host cell	0.005586252	12.50	2.00	<i>[RPS27A, SH3GL2]</i>
R-HSA:76009	Platelet Aggregation (Plug Formation)	0.005587752	5.13	2.00	<i>[PTPN1, SHC1]</i>
R-HSA:9034015	Signaling by NTRK3 (TRKC)	0.005796306	11.76	2.00	<i>[IRS1, SHC1]</i>
R-HSA:9034015	Signaling by NTRK3 (TRKC)	0.005796306	11.76	2.00	<i>[IRS1, SHC1]</i>
R-HSA:1236382	Constitutive Signaling by Ligand-Responsive EGFR Cancer Variants	0.006609053	10.53	2.00	<i>[RPS27A, SHC1]</i>
R-HSA:5637815	Signaling by Ligand-Responsive EGFR Variants in Cancer	0.006609053	10.53	2.00	<i>[RPS27A, SHC1]</i>
R-HSA:2424491	DAP12 signaling	0.006633994	6.67	2.00	<i>[B2M, SHC1]</i>
R-HSA:354192	Integrin alphaIIb beta3 signaling	0.006716084	7.41	2.00	<i>[PTPN1, SHC1]</i>
R-HSA:9006921	Integrin signaling	0.006716084	7.41	2.00	<i>[PTPN1, SHC1]</i>
R-HSA:77387	Insulin receptor recycling	0.007471563	7.69	2.00	<i>[INS, INSR]</i>
R-HSA:8876384	Listeria monocytogenes entry into host cells	0.008005403	9.09	2.00	<i>[RPS27A, SH3GL2]</i>
R-HSA:1643713	Signaling by EGFR in Cancer	0.008056271	8.00	2.00	<i>[RPS27A, SHC1]</i>
R-HSA:982772	Growth hormone receptor signaling	0.008481092	8.33	2.00	<i>[IRS1, PTPN1]</i>