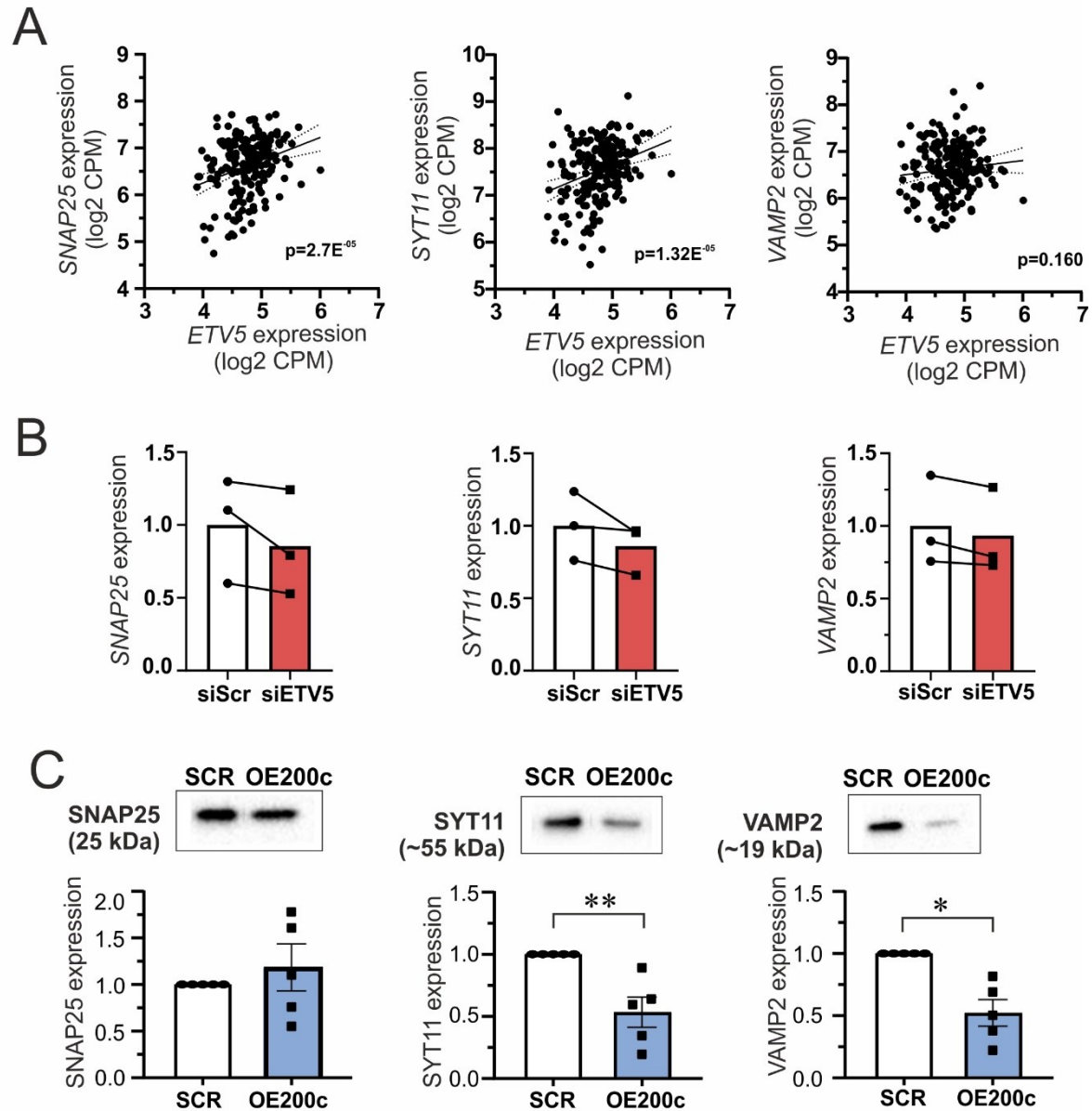


Supplementary information

Title: Human islet microRNA-200c is elevated in type 2 diabetes and targets the transcription factor ETV5 to reduce insulin secretion

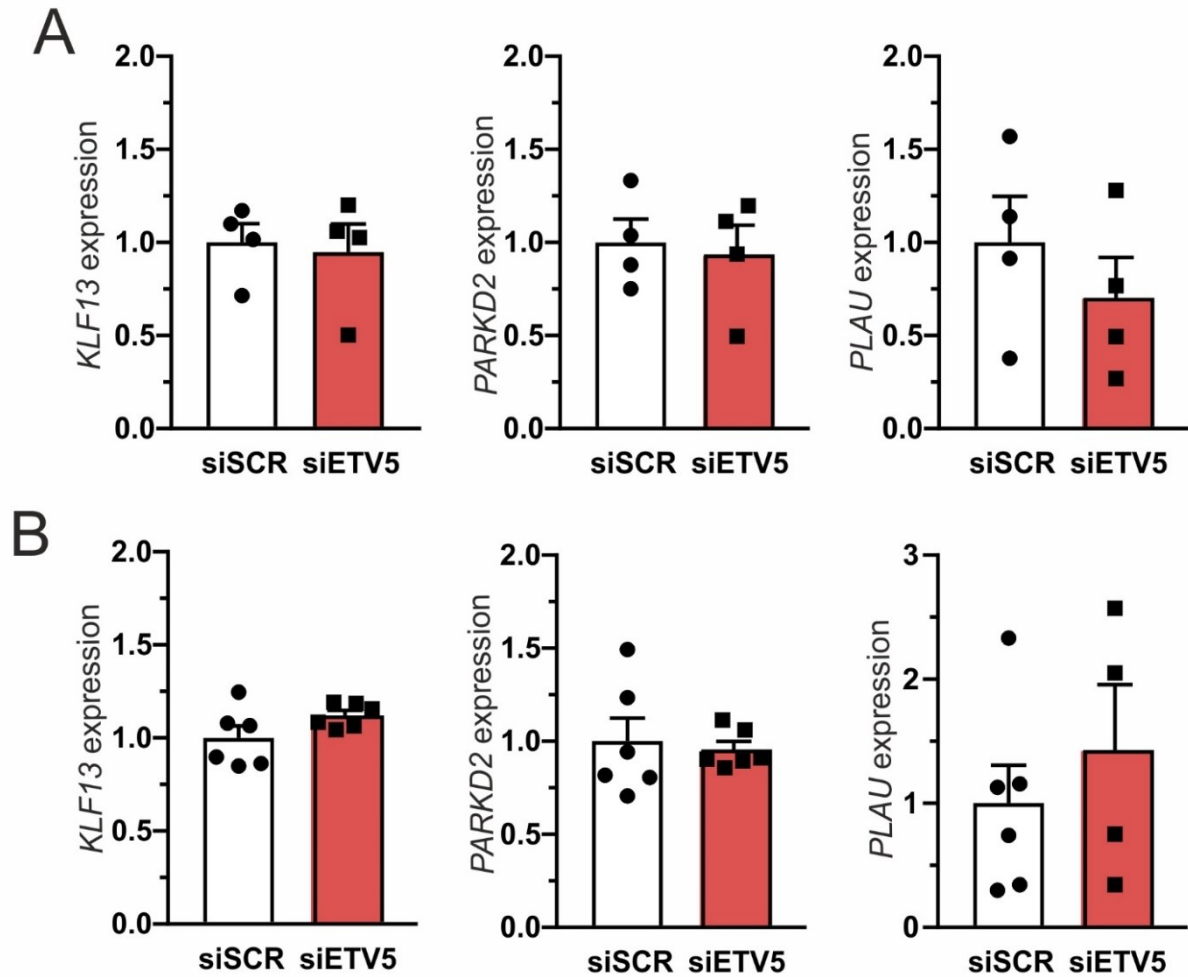
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Supplementary Figures



Supplementary Figure 1. Potential regulation of *SNAP25*, *SYT11* and *VAMP2* by *ETV5* and miR-200c.

A. Pearson correlation between *ETV5* expression and expression of *SNAP25*, *SYT11* and *VAMP2* in human islets (N=185). P-values are given in the figure. **B.** Expression of *SNAP25*, *SYT11* and *VAMP2* in human islets after knock-down of *ETV5* (siETV5) compared to control. (N=3) **C.** Western blot analysis of *SNAP25*, *SYT11* and *VAMP2* in SCR control OE200 in EndoC- β H1. Data are presented as mean of N = 5 biological replicates presented as mean \pm SEM, * $p < 0.05$, ** $p < 0.01$ using Student's t-test.



Supplementary Figure 2. Expression of genes potentially regulated by ETV5.

Expression of *KLF13*, *PARKD2* and *PLAU* measured by qPCR after knock-down of ETV5 (siETV5) in **A**. human islets (N=4) and **B**. EndoC-βH1 beta cells (N=6). Data are presented as mean ± SEM.

Supplementary Tables

Supplementary Table 1. Donor characteristics for experiments with human pancreatic islets.

ND-non-diabetes (HbA1c<6.0), IGT-impaired glucose tolerance (HbA1c between 6% and 6.5%), T2D-type 2 diabetes (diagnosed T2D and HbA1c>6.5) , nD-T2D (undiagnosed and HbA1c>6.5). * Data are from REF# 18; The original data-set contained in total 195 donors, and here we have filtered the data and removed those without condition yielding in total 185 donors in the analyses performed.

Group	n	Gender (Male / Female)	Age (years old)	BMI (kg/m ²)	HbA1c (%, mmol/mol)	Figure
Figure 1A, Figure 5C and ESM Table 2						
ND	25	15 / 10	56.4± 2.0	26.1 ± 0.6	5.43±0.08, 35.9±0.9 (n=20)	Fig 1A, Fig 5C, ESM Table 2
IGT	8	2/6	58.0±2.3	26.4±1.5	6.08±0.03, 42.8±0.3	Fig 5C, ESM Table 2
T2D	9	4/ 5	56.8 ± 2.7	28.5 ± 1.3	6.55 ± 0.16, 48.6±1.8 (n=8)	Fig 1A, Fig 5C, ESM Table 2
nD-T2D	5	2/3	62.8± 3.7	27.4 ± 0.7	7.24±0.37, 56.4±3.5	Fig 5C, ESM Table 2
*Fig 2B-C, ESM Table 3 and ESM Fig 1A						
ND	120	74/46	57.86 ± 0.96	25.97 ± 0.33	5.5 ± 0.03, 37 ± 0.3 (n=101)	Fig 2B-C and ESM Table 3
IGT	33	21/12	60.36 ± 1.11	26.56 ± 0.69	6.1 ± 0.02 43 ± 0.2	ESM Table 3

T2D	32	21/11	61 ± 1.79	27.9 ± 0.78	6.8 ± 0.15 51±0.7 (n=31)	Fig 2B-C and ESM Table 3
Figure 4A-B, Figure 5A, ESM Figure 1B, ESM Figure 2A and ESM Table 4						
ND	4	3 / 1	57.7 ± 7.5	29.4 ± 1.4	5.47 ± 0.34, 36.2 ± 3.6	Figure 4A-B, Figure 5A, ESM Figure 1B, ESM Figure 2A
Figure 6						
T2D	3	2 / 1	73.0 ± 5.0	26.8 ± 0.5	5.80 ± 0.12, 40.0 ± 1.2	Figure 6A-B

Supplementary Table 2 Pearson correlation analysis of potential miR-200c targets.

Pearson correlation analysis between hsa-miR-200c and RNA-seq expression data of potential miR-200c from Target scan. The table only shows genes with negative correlation with has-miR-200c. P<0.05 was regarded as significant. R=Pearson correlation coefficient. P=p-value.

No	Target	hsa-miR-200c	
		R	P
1	<i>ETV5</i>	-0,470322217	0,001113555
2	<i>TMEFF2</i>	-0,441209012	0,002415227
3	<i>FUBP1</i>	-0,40510533	0,005771305
4	<i>FUBP3</i>	-0,395768631	0,007122931
5	<i>KHDRBS1</i>	-0,395401657	0,00718123
6	<i>ZNF362</i>	-0,383514058	0,009306834
7	<i>DCAF16</i>	-0,382995985	0,009410636
8	<i>PALM2</i>	-0,379179803	0,010206393
9	<i>GATSL2</i>	-0,378874754	0,010272425
10	<i>SNX30</i>	-0,368343524	0,012788153
11	<i>PTDSS1</i>	-0,361195282	0,01478055
12	<i>KLF9</i>	-0,360484414	0,014992378
13	<i>ARHGAP20</i>	-0,359297891	0,015351688
14	<i>ZEB2</i>	-0,355872753	0,016430182
15	<i>HSPA9</i>	-0,350151716	0,01837467
16	<i>WASF3</i>	-0,347942836	0,019175722
17	<i>BAG5</i>	-0,347487479	0,019344466
18	<i>NUAK1</i>	-0,346847313	0,019583811
19	<i>FBXO33</i>	-0,34584062	0,019965235
20	<i>ETS1</i>	-0,34379944	0,020757835
21	<i>RND3</i>	-0,342038518	0,021462706
22	<i>C5orf51</i>	-0,341407243	0,021720242
23	<i>ARL5A</i>	-0,339510298	0,022509779
24	<i>TCF4</i>	-0,336575974	0,023778402

25	<i>PLEKHM3</i>	-0,336404819	0,023854208
26	<i>ETF1</i>	-0,331203975	0,026256006
27	<i>TMX4</i>	-0,330028011	0,026826135
28	<i>PI4KB</i>	-0,326176362	0,028766144
29	<i>TTC13</i>	-0,325364636	0,029189515
30	<i>RTF1</i>	-0,324635711	0,029574094
31	<i>GATAD2B</i>	-0,323348795	0,030263326
32	<i>LRIG1</i>	-0,322923782	0,030493853
33	<i>SOCS6</i>	-0,322289614	0,030840528
34	<i>ATXN1L</i>	-0,320094379	0,032065874
35	<i>PPP6C</i>	-0,318751527	0,032835075
36	<i>DNAJB5</i>	-0,316824989	0,033965174
37	<i>PPP2R5C</i>	-0,313363849	0,036075978
38	<i>ADAMTS3</i>	-0,312754381	0,036458606
39	<i>DACT1</i>	-0,311799423	0,037064836
40	<i>CDH11</i>	-0,311367261	0,037341891
41	<i>MIEF1</i>	-0,307190282	0,04010834
42	<i>MARCH8</i>	-0,30707131	0,040189526
43	<i>RANBP9</i>	-0,307065874	0,040193239
44	<i>HNRNPK</i>	-0,306152636	0,040820969
45	<i>CHRD1</i>	-0,305047885	0,041591025
46	<i>PRKAR1A</i>	-0,299812709	0,045403082
47	<i>BHLHE41</i>	-0,299476681	0,045657155
48	<i>NEGR1</i>	-0,297620634	0,047081417
49	<i>ERG</i>	-0,296769312	0,04774664
50	<i>CDYL</i>	-0,29413883	0,049850382
51	<i>FAM168B</i>	-0,292666693	0,05106006
52	<i>POU6F1</i>	-0,289517148	0,05372774
53	<i>FRS2</i>	-0,288882127	0,054278964
54	<i>SLC23A2</i>	-0,287801221	0,055227695
55	<i>CDK12</i>	-0,286780128	0,056136128
56	<i>SCAMP5</i>	-0,285770048	0,057046532
57	<i>SEPHS1</i>	-0,28469957	0,058024264
58	<i>SESN3</i>	-0,28241524	0,060155595
59	<i>HS2ST1</i>	-0,280860958	0,06164123
60	<i>KCNB1</i>	-0,280712392	0,061784755
61	<i>GLI3</i>	-0,27954537	0,062921477
62	<i>PFN2</i>	-0,279064527	0,063394659
63	<i>RAC1</i>	-0,277617241	0,06483602
64	<i>ASTN1</i>	-0,276813974	0,065647181
65	<i>ACTR1A</i>	-0,276493306	0,065973245
66	<i>PARM1</i>	-0,276309639	0,066160581
67	<i>SERINC1</i>	-0,275819229	0,066662861
68	<i>ZFPM2</i>	-0,275727012	0,066757648
69	<i>SLITRK1</i>	-0,2746452	0,067877614

70	<i>KIF13A</i>	-0,274263217	0,068276611
71	<i>DEK</i>	-0,274095626	0,068452253
72	<i>GNAQ</i>	-0,273438175	0,069144748
73	<i>FAM217B</i>	-0,270595226	0,072203357
74	<i>CDK17</i>	-0,268521795	0,074500714
75	<i>UBQLN1</i>	-0,267329083	0,075848102
76	<i>ZNF711</i>	-0,26396865	0,079747621
77	<i>ATP6V0A2</i>	-0,262059062	0,082032573
78	<i>ANKRD28</i>	-0,259009061	0,08578796
79	<i>ARCN1</i>	-0,25733447	0,087906077
80	<i>PTPN11</i>	-0,256843932	0,088534178
81	<i>FLI1</i>	-0,255010001	0,090913351
82	<i>FBXW11</i>	-0,253454583	0,092969819
83	<i>E2F3</i>	-0,25218752	0,094671507
84	<i>COMMD3-BMI1</i>	-0,25139875	0,095742935
85	<i>COPS8</i>	-0,250501908	0,096972511
86	<i>PAM</i>	-0,247787904	0,100767695
87	<i>CNOT7</i>	-0,246736824	0,102267781
88	<i>TBK1</i>	-0,246466732	0,102656008
89	<i>DENND5B</i>	-0,245461493	0,104110863
90	<i>XIAP</i>	-0,244845167	0,105010635
91	<i>XKR4</i>	-0,24480238	0,10507332
92	<i>ERI3</i>	-0,244355875	0,105729181
93	<i>GRAP2</i>	-0,241624507	0,109809622
94	<i>CRTAP</i>	-0,239919488	0,112416964
95	<i>CDC40</i>	-0,239750542	0,112677862
96	<i>ZCCHC24</i>	-0,239073393	0,113728178
97	<i>DCUN1D1</i>	-0,238151391	0,115170218
98	<i>SURF4</i>	-0,237497577	0,116201179
99	<i>KCMF1</i>	-0,236309936	0,118091773
100	<i>GABBR2</i>	-0,236089584	0,118445096
101	<i>UBE2D1</i>	-0,235450762	0,119473927
102	<i>YME1L1</i>	-0,235299349	0,119718766
103	<i>SMIM5</i>	-0,233870314	0,122048271
104	<i>DYRK2</i>	-0,233291119	0,123002103
105	<i>NAA50</i>	-0,232845235	0,123740212
106	<i>PJA2</i>	-0,232813608	0,123792692
107	<i>SLIT2</i>	-0,232135298	0,124922304
108	<i>ARIH2</i>	-0,231374609	0,126198305
109	<i>RPS6KA3</i>	-0,231279765	0,126358083
110	<i>LHFP</i>	-0,230868694	0,127052345
111	<i>PPP6R3</i>	-0,230524021	0,127636672
112	<i>COPS2</i>	-0,230449936	0,127762531
113	<i>SECISBP2L</i>	-0,230447821	0,127766125

114	<i>ATXN1</i>	-0,230096119	0,128364899
115	<i>FRMD6</i>	-0,230002582	0,1285245
116	<i>ZNF148</i>	-0,228971932	0,130292941
117	<i>USP6NL</i>	-0,228618995	0,130902695
118	<i>FSTL1</i>	-0,228020278	0,131941952
119	<i>USP46</i>	-0,22796163	0,132044085
120	<i>PVRL1</i>	-0,227934313	0,132091675
121	<i>BAZ2B</i>	-0,227180829	0,13340944
122	<i>RASSF8</i>	-0,226809072	0,134063208
123	<i>AMFR</i>	-0,224883059	0,137488589
124	<i>RNF38</i>	-0,223512302	0,139965813
125	<i>SRSF2</i>	-0,223055271	0,140799077
126	<i>PTGDR</i>	-0,223016511	0,140869913
127	<i>MR1</i>	-0,22277152	0,141318261
128	<i>TWISTNB</i>	-0,222322739	0,142142299
129	<i>ASAP1</i>	-0,222140872	0,14247725
130	<i>BASP1</i>	-0,221966234	0,142799437
131	<i>NKAP</i>	-0,22151731	0,143630122
132	<i>SCD</i>	-0,220770283	0,145020332
133	<i>FOSB</i>	-0,218906001	0,148533069
134	<i>PRDM1</i>	-0,217370981	0,15147213
135	<i>REV1</i>	-0,216856183	0,152467304
136	<i>KCNA2</i>	-0,21669038	0,152788843
137	<i>SLC6A6</i>	-0,215784674	0,154554051
138	<i>ZDHHC20</i>	-0,215617325	0,154881842
139	<i>ZBTB20</i>	-0,214042687	0,157991092
140	<i>NRIP1</i>	-0,213682426	0,158708821
141	<i>CADM1</i>	-0,213612434	0,15884854
142	<i>GMFB</i>	-0,213227781	0,159617983
143	<i>SLC30A4</i>	-0,212442798	0,161196657
144	<i>YIPF5</i>	-0,212344776	0,161394584
145	<i>CHSY1</i>	-0,211410136	0,163290721
146	<i>KDR</i>	-0,210565963	0,165017204
147	<i>EIF4E3</i>	-0,209987444	0,166208005
148	<i>CDC73</i>	-0,209790143	0,166615545
149	<i>EIF4E</i>	-0,209405581	0,167411966
150	<i>FXR1</i>	-0,20929857	0,167634075
151	<i>STYX</i>	-0,209213694	0,167810391
152	<i>FYN</i>	-0,208974704	0,168307578
153	<i>PIGA</i>	-0,208488292	0,169322786
154	<i>ZEB1</i>	-0,208406995	0,169492896
155	<i>SPRYD7</i>	-0,206396256	0,173739665
156	<i>SIAH1</i>	-0,204434518	0,177956328
157	<i>SMARCD1</i>	-0,203357882	0,180301491
158	<i>BNIP3L</i>	-0,202778302	0,181573082

159	<i>PALM2-AKAP2</i>	-0,202043967	0,183193406
160	<i>RIMS3</i>	-0,201533193	0,184326513
161	<i>SETD7</i>	-0,200136217	0,187451127
162	<i>ZDHHHC17</i>	-0,199301893	0,189335152
163	<i>VTI1A</i>	-0,196306145	0,196210851
164	<i>EFNA5</i>	-0,195879126	0,197205109
165	<i>RFX7</i>	-0,194182561	0,20119047
166	<i>KLF12</i>	-0,193597716	0,202577358
167	<i>STX12</i>	-0,193453007	0,202921551
168	<i>ATP2A2</i>	-0,191953024	0,206513521
169	<i>DNAJC3</i>	-0,191008868	0,20879717
170	<i>TCEB1</i>	-0,190773169	0,209370002
171	<i>CALU</i>	-0,190118853	0,210965976
172	<i>C16orf72</i>	-0,190003882	0,211247282
173	<i>RHOA</i>	-0,188981693	0,213759829
174	<i>FOXK1</i>	-0,186196322	0,220711597
175	<i>THRA</i>	-0,185565793	0,222306739
176	<i>CTNND2</i>	-0,185190829	0,223259107
177	<i>PPP4R2</i>	-0,183195442	0,22837452
178	<i>ERRFI1</i>	-0,182736038	0,229563568
179	<i>CDHR1</i>	-0,182418859	0,230386978
180	<i>JAZF1</i>	-0,182232807	0,230870917
181	<i>TMEM200C</i>	-0,181450221	0,232914132
182	<i>BACH2</i>	-0,180604361	0,235136416
183	<i>NAPB</i>	-0,178425983	0,240926071
184	<i>SHC1</i>	-0,177880137	0,242391855
185	<i>NR3C1</i>	-0,177523563	0,243352637
186	<i>JAKMIP2</i>	-0,175152815	0,249806193
187	<i>BBX</i>	-0,175087084	0,249986749
188	<i>MXD3</i>	-0,17484111	0,250663202
189	<i>KATNAL1</i>	-0,174418197	0,251829129
190	<i>FBXO30</i>	-0,174370461	0,251960961
191	<i>DCAF5</i>	-0,174329126	0,252075155
192	<i>SYNCRIP</i>	-0,174203771	0,252421671
193	<i>PPP2CA</i>	-0,173956795	0,253105324
194	<i>CELF2</i>	-0,173906971	0,25324339
195	<i>AVL9</i>	-0,173230794	0,255122156
196	<i>ZNF597</i>	-0,17322593	0,255135705
197	<i>DAG1</i>	-0,17257531	0,256952327
198	<i>FBXO42</i>	-0,171577673	0,259754655
199	<i>PDIK1L</i>	-0,171571713	0,259771456
200	<i>DENND2C</i>	-0,171420981	0,260196645
201	<i>MMGT1</i>	-0,171380263	0,260311581
202	<i>CFL2</i>	-0,171266367	0,260633265
203	<i>DACH1</i>	-0,170232588	0,263565148

204	<i>NRP2</i>	-0,169503483	0,265646099
205	<i>OTUD4</i>	-0,169032583	0,266995887
206	<i>PHF12</i>	-0,168826355	0,267588452
207	<i>WNK1</i>	-0,168696352	0,267962439
208	<i>IL6ST</i>	-0,167174863	0,272365182
209	<i>OSBPL11</i>	-0,166520882	0,274272201
210	<i>CSNK1G3</i>	-0,166470065	0,274420753
211	<i>OSR1</i>	-0,165522199	0,277201315
212	<i>NR2C2</i>	-0,165249976	0,278003288
213	<i>PSME4</i>	-0,165057884	0,278570114
214	<i>CYP1B1</i>	-0,163461122	0,283311172
215	<i>TMEM170B</i>	-0,163353052	0,283633943
216	<i>QKI</i>	-0,16283369	0,285188467
217	<i>SLC6A17</i>	-0,162277071	0,286860663
218	<i>SLC16A2</i>	-0,159557202	0,295123367
219	<i>ZFHX4</i>	-0,156794239	0,303672866
220	<i>SYDE1</i>	-0,155639096	0,307293828
221	<i>NCOA2</i>	-0,155270606	0,308454688
222	<i>RECK</i>	-0,154777005	0,310014066
223	<i>LATS2</i>	-0,153200921	0,31502676
224	<i>SEC23A</i>	-0,151446519	0,320666662
225	<i>WAPAL</i>	-0,151148506	0,321630974
226	<i>SMIM13</i>	-0,150181978	0,324771017
227	<i>NRXN1</i>	-0,146296624	0,337587056
228	<i>FBXL17</i>	-0,14495647	0,342079325
229	<i>CBX5</i>	-0,144874029	0,342356869
230	<i>TUBB3</i>	-0,144577015	0,343357947
231	<i>RIMKLB</i>	-0,144488921	0,343655213
232	<i>WIPF1</i>	-0,144401047	0,343951892
233	<i>RAP2C</i>	-0,144290543	0,344325198
234	<i>DNAJB14</i>	-0,144110365	0,344934415
235	<i>CAMK2D</i>	-0,143845378	0,345831594
236	<i>CHD2</i>	-0,142606463	0,350045236
237	<i>PCDH8</i>	-0,141914531	0,352412158
238	<i>NEK10</i>	-0,140917855	0,355838662
239	<i>UBE2W</i>	-0,139855668	0,359512614
240	<i>HNRNPD</i>	-0,139304941	0,361426514
241	<i>PDS5B</i>	-0,138666028	0,363654582
242	<i>MYBL1</i>	-0,137703979	0,367025112
243	<i>MYT1</i>	-0,137582815	0,367450937
244	<i>DDX3Y</i>	-0,135783501	0,37380942
245	<i>GOLGA7</i>	-0,134452523	0,378554858
246	<i>XRN1</i>	-0,133108758	0,38338199
247	<i>TSC22D1</i>	-0,131683239	0,388542345
248	<i>EVI5</i>	-0,131228901	0,390195576

249	<i>CEBPA</i>	-0,131016646	0,390969333
250	<i>MAP4K3</i>	-0,129003926	0,3983511
251	<i>PIK3CB</i>	-0,12886189	0,398875068
252	<i>FAM107B</i>	-0,128676498	0,399559571
253	<i>ZNF697</i>	-0,128029702	0,401953009
254	<i>DOCK4</i>	-0,127434259	0,404163731
255	<i>CHST2</i>	-0,127267022	0,404785901
256	<i>CDYL2</i>	-0,126666957	0,407022846
257	<i>GABPA</i>	-0,124616961	0,414718365
258	<i>RUSC2</i>	-0,123564953	0,418699506
259	<i>MAP4K4</i>	-0,123132034	0,420344095
260	<i>MYLK</i>	-0,122765622	0,421738888
261	<i>MIER3</i>	-0,122168345	0,424018097
262	<i>FOXN2</i>	-0,121378233	0,427043815
263	<i>AGO2</i>	-0,120034366	0,432217903
264	<i>CLIP1</i>	-0,119642905	0,433731646
265	<i>RNF2</i>	-0,118827194	0,436895399
266	<i>ARL14EPL</i>	-0,11873296	0,437261711
267	<i>SFXN1</i>	-0,118710053	0,437350784
268	<i>MSN</i>	-0,11783109	0,440776139
269	<i>GREB1L</i>	-0,117477555	0,442158052
270	<i>SPTSSA</i>	-0,117408565	0,442427999
271	<i>INHBA</i>	-0,117150877	0,443437106
272	<i>PCSK2</i>	-0,117140382	0,443478231
273	<i>KDM3B</i>	-0,116477859	0,446078617
274	<i>GPC6</i>	-0,114727661	0,452988225
275	<i>PPP2R5E</i>	-0,110896063	0,468316458
276	<i>HAS2</i>	-0,110428914	0,470204033
277	<i>GJC1</i>	-0,110269034	0,470850976
278	<i>SCN1A</i>	-0,10880311	0,476804776
279	<i>TP53INP1</i>	-0,107296658	0,482964359
280	<i>FMR1</i>	-0,10661348	0,485771415
281	<i>KIAA0087</i>	-0,105888836	0,488758126
282	<i>CEP41</i>	-0,1054455	0,490590086
283	<i>ZBTB16</i>	-0,104670887	0,49379948
284	<i>ZC3H6</i>	-0,103767033	0,497558006
285	<i>DPYSL2</i>	-0,103487218	0,498724537
286	<i>TRIM33</i>	-0,101808902	0,505750672
287	<i>TRERF1</i>	-0,101749538	0,506000113
288	<i>NUP153</i>	-0,100914996	0,509513339
289	<i>SCAMP1</i>	-0,098757477	0,518652743
290	<i>GATA2</i>	-0,097984568	0,521946601
291	<i>CREBBP</i>	-0,096077172	0,530119374
292	<i>MED1</i>	-0,09376519	0,540109047
293	<i>FAM60A</i>	-0,093270133	0,54225985

294	<i>NALCN</i>	-0,092575315	0,545285453
295	<i>NUDT4</i>	-0,092108814	0,54732137
296	<i>HIPK1</i>	-0,0893032	0,559641633
297	<i>BRWD1</i>	-0,088799581	0,561866828
298	<i>AFF1</i>	-0,08545589	0,576744218
299	<i>GAD2</i>	-0,085364262	0,577154417
300	<i>CGGBP1</i>	-0,08444694	0,581268348
301	<i>GRIN2A</i>	-0,084401026	0,581474606
302	<i>CSNK1G1</i>	-0,08434164	0,581741431
303	<i>NCS1</i>	-0,083828862	0,584047692
304	<i>SERPINC1</i>	-0,083373336	0,586099888
305	<i>UBE2I</i>	-0,083345771	0,586224177
306	<i>GNAI3</i>	-0,082586267	0,589653313
307	<i>ZFAND5</i>	-0,082046004	0,592097995
308	<i>SH3GL1</i>	-0,081617163	0,594041688
309	<i>FOXP1</i>	-0,080558473	0,598852125
310	<i>CLIC4</i>	-0,079740936	0,602578441
311	<i>ANKRD40</i>	-0,079730484	0,602626145
312	<i>DENND5A</i>	-0,077573982	0,612503711
313	<i>MPRIIP</i>	-0,076969558	0,615284527
314	<i>FBXL16</i>	-0,075939263	0,620036975
315	<i>PRKACB</i>	-0,075507398	0,622033617
316	<i>TMEM164</i>	-0,075126558	0,623796582
317	<i>DNAJC5</i>	-0,074649971	0,626005709
318	<i>MXD4</i>	-0,074261214	0,627810121
319	<i>PLCL1</i>	-0,073501484	0,631342588
320	<i>SESN1</i>	-0,073311154	0,632228834
321	<i>REEP1</i>	-0,072424055	0,636366191
322	<i>CSRNP3</i>	-0,072401549	0,636471301
323	<i>MAP2</i>	-0,071800924	0,639278989
324	<i>AMBRA1</i>	-0,070725252	0,644319795
325	<i>LCOR</i>	-0,06930451	0,651001891
326	<i>CKAP4</i>	-0,06924842	0,651266256
327	<i>FOXG1</i>	-0,069002414	0,652426242
328	<i>SPATS2L</i>	-0,068787548	0,653440055
329	<i>PTBP1</i>	-0,068105041	0,65666445
330	<i>ELAVL4</i>	-0,06706533	0,661588265
331	<i>MBOAT2</i>	-0,06702696	0,661770248
332	<i>LHX5</i>	-0,06544345	0,669297289
333	<i>BMI1</i>	-0,062272192	0,68446764
334	<i>KIF26B</i>	-0,061696298	0,687235981
335	<i>ZNF131</i>	-0,061085136	0,690178291
336	<i>ABAT</i>	-0,061037696	0,690406871
337	<i>C16orf52</i>	-0,060462458	0,693180695
338	<i>WASF1</i>	-0,059057568	0,699971773

339	<i>NPTX1</i>	-0,057512995	0,707464842
340	<i>PHTF2</i>	-0,056539185	0,712203155
341	<i>ETS2</i>	-0,05592795	0,715182763
342	<i>LHX9</i>	-0,055695134	0,716318786
343	<i>MED13</i>	-0,055182976	0,718819982
344	<i>SIX1</i>	-0,054749053	0,720941385
345	<i>PHACTR3</i>	-0,054711331	0,721125902
346	<i>CNOT6</i>	-0,054422806	0,722537737
347	<i>PKIA</i>	-0,054188307	0,723685881
348	<i>AGFG1</i>	-0,054182794	0,723712878
349	<i>EGR3</i>	-0,053109197	0,728977065
350	<i>SCHIP1</i>	-0,052990241	0,729561106
351	<i>RBFOX2</i>	-0,052825524	0,730370073
352	<i>VCPIP1</i>	-0,052385867	0,73253076
353	<i>CNEP1R1</i>	-0,052297657	0,732964512
354	<i>FEM1C</i>	-0,051261858	0,738063945
355	<i>PPP1R18</i>	-0,050812443	0,740279978
356	<i>PFDN4</i>	-0,048887987	0,749792661
357	<i>NPC1</i>	-0,048536394	0,751534624
358	<i>SLC6A15</i>	-0,048181163	0,753295851
359	<i>IQCJ-SCHIP1</i>	-0,048112281	0,753637512
360	<i>CASR</i>	-0,048031173	0,754039873
361	<i>XPR1</i>	-0,047945747	0,754463726
362	<i>RIMS2</i>	-0,047714099	0,75561343
363	<i>PAPD5</i>	-0,047664474	0,755859798
364	<i>AFF4</i>	-0,046007279	0,764100613
365	<i>LRP1B</i>	-0,040867206	0,789821534
366	<i>CNOT4</i>	-0,040732592	0,790498252
367	<i>SULF1</i>	-0,040154138	0,793407922
368	<i>PTCD1</i>	-0,040132863	0,793514993
369	<i>APOO</i>	-0,039062741	0,79890527
370	<i>SCN2A</i>	-0,038681076	0,800829996
371	<i>RSRC2</i>	-0,038558554	0,80144812
372	<i>SMAD7</i>	-0,035722057	0,815791014
373	<i>FIGN</i>	-0,035697482	0,815915547
374	<i>TMEM135</i>	-0,03530021	0,817929322
375	<i>NXPH1</i>	-0,035125173	0,818816955
376	<i>KLF10</i>	-0,034138549	0,823824403
377	<i>ADAMTS8</i>	-0,034061657	0,824214949
378	<i>CLASP1</i>	-0,032748188	0,83089266
379	<i>ADCY2</i>	-0,031218345	0,838685273
380	<i>KRAS</i>	-0,029947255	0,845171523
381	<i>PLXNA4</i>	-0,029691017	0,84648032
382	<i>BAP1</i>	-0,029620801	0,846839036
383	<i>FGD1</i>	-0,028419889	0,852978901

384	<i>YPEL2</i>	-0,027254777	0,858943956
385	<i>MDFIC</i>	-0,026627288	0,86215977
386	<i>ARIH1</i>	-0,026111169	0,864806482
387	<i>TUBB</i>	-0,025723137	0,866797312
388	<i>DLC1</i>	-0,025493178	0,867977522
389	<i>SMARCAD1</i>	-0,025103029	0,869980521
390	<i>SPAG9</i>	-0,024946193	0,870785931
391	<i>ZC3HAV1L</i>	-0,024714049	0,871978314
392	<i>RLF</i>	-0,023835615	0,876492822
393	<i>MMD</i>	-0,023123746	0,880154161
394	<i>IAH1</i>	-0,022690083	0,882385823
395	<i>LCA5</i>	-0,022287209	0,884459855
396	<i>SCN5A</i>	-0,020342121	0,894483838
397	<i>CRKL</i>	-0,019200907	0,900372744
398	<i>RBM20</i>	-0,018066842	0,906230009
399	<i>HIVEP3</i>	-0,017261357	0,910393218
400	<i>SLC24A4</i>	-0,016690402	0,913345684
401	<i>NDN</i>	-0,015375215	0,92015098
402	<i>AKT2</i>	-0,013890183	0,927841879
403	<i>MFHAS1</i>	-0,013743257	0,928603167
404	<i>FBXW7</i>	-0,013375707	0,930507876
405	<i>ST6GALNAC5</i>	-0,01306682	0,932108883
406	<i>TBC1D22B</i>	-0,012244754	0,936371042
407	<i>ZBTB38</i>	-0,012107148	0,937084659
408	<i>CNTN4</i>	-0,011602294	0,939703231
409	<i>CACNA1C</i>	-0,011391519	0,940796661
410	<i>ZC3H15</i>	-0,011214429	0,94171543
411	<i>YWHAB</i>	-0,011113665	0,94223824
412	<i>GIT2</i>	-0,010663971	0,944571755
413	<i>PIP4K2B</i>	-0,010424122	0,945816551
414	<i>KLF4</i>	-0,009569089	0,950255113
415	<i>MAFG</i>	-0,009433992	0,950956553
416	<i>GPR173</i>	-0,009097981	0,952701323
417	<i>AMOTL2</i>	-0,007740085	0,959754482
418	<i>ELF2</i>	-0,00772278	0,959844388
419	<i>KMT2C</i>	-0,004934761	0,974334872
420	<i>PTHLH</i>	-0,004006812	0,979159849
421	<i>JUN</i>	-0,00376711	0,980406335
422	<i>DUSP1</i>	-0,003093807	0,983907839
423	<i>ARHGDIA</i>	-0,001411984	0,992655312
424	<i>SUV420H1</i>	-0,001391473	0,992761999
425	<i>HSPE1-MOB4</i>	-0,000510947	0,997342187
426	<i>RAB13</i>	-0,000293638	0,998472568

Supplementary Table 3. Regression model details.

JAZF1 ~ Gender + Age + Condition					
	Estimate	Std. Error	t value	P-value	
(Intercept)	5.319506	0.195810	27.167	<2e-16	***
GenderMale	0.047694	0.065996	0.723	0.4708	
Age	0.002702	0.003241	0.834	0.4056	
ConditionIGT	-0.135953	0.085678	-1.587	0.1143	
ConditionT2D	-0.162535	0.086958	-1.869	0.0632	. (Fig 2B - 1)

ETV5 ~ Gender + Age + Condition					
	Estimate	Std. Error	t value	P-value	
(Intercept)	4.295774	0.156751	27.405	< 2e-16	***
GenderMale	0.224886	0.052831	4.257	3.33e-05	*** (Fig 2C)
Age	0.006322	0.002595	2.437	0.0158	*
ConditionIGT	-0.079105	0.068588	-1.153	0.2503	
ConditionT2D	-0.170082	0.069613	-2.443	0.0155	* (Fig 2B - 3)

SNX30 ~ Gender + Age + Condition					
	Estimate	Std. Error	t value	P-value	
(Intercept)	4.704908	0.201796	23.315	< 2e-16	***
GenderMale	0.098597	0.068013	1.450	0.14889	
Age	0.007156	0.003340	2.142	0.03352	*
ConditionIGT	-0.157020	0.088298	-1.778	0.07704	.
ConditionT2D	-0.272311	0.089617	-3.039	0.00273	** (Fig 2B - 2)

Supplementary Table 4. Analysis of differentially expressed genes after ETV5 knockdown (siETV5) in human islets (N=4 donors).

Genes are sorted based on the adjusted p-value in ascending order.

Ensembl Gene ID	Gene Name	log2FoldChange	padj	Gene Description
ENSG00000165272	AQP3	-0,84407012	2,28577E-15	aquaporin 3 (Gill blood group) [Source:HGNC Symbol;Acc:HGNC:636]
ENSG00000170345	FOS	-0,547036135	4,08947E-05	Fos proto-oncogene AP-1 transcription factor subunit [Source:HGNC Symbol;Acc:HGNC:3796]
ENSG00000116237	ICMT	-0,381761384	0,000315982	isoprenylcysteine carboxyl methyltransferase [Source:HGNC Symbol;Acc:HGNC:5350]
ENSG00000117899	MESD	-0,421109924	0,0013311	mesoderm development LRP chaperone [Source:HGNC Symbol;Acc:HGNC:13520]
ENSG00000067955	CBFB	-0,415422058	0,0013311	core-binding factor subunit beta [Source:HGNC Symbol;Acc:HGNC:1539]
ENSG00000150961	SEC24D	-0,299761373	0,0013311	SEC24 homolog D COPII coat complex component [Source:HGNC Symbol;Acc:HGNC:10706]
ENSG00000105220	GPI	0,35127152	0,001476019	glucose-6-phosphate isomerase [Source:HGNC Symbol;Acc:HGNC:4458]
ENSG00000166265	CYYR1	-0,611651067	0,002416749	cysteine and tyrosine rich 1 [Source:HGNC Symbol;Acc:HGNC:16274]

ENSG00000138029	HADHB	-0,30360527	0,002432679	hydroxyacyl-CoA dehydrogenase trifunctional multienzyme complex subunit beta [Source:HGNC Symbol;Acc:HGNC:4803]
ENSG00000183458	AC138932.1	0,574908789	0,003268826	polycystic kidney disease 1 (autosomal dominant) (PKD1) pseudogene
ENSG00000159388	BTG2	-0,383945882	0,003268826	BTG anti-proliferation factor 2 [Source:HGNC Symbol;Acc:HGNC:1131]
ENSG00000198682	PAPSS2	-0,251746375	0,003268826	3'-phosphoadenosine 5'-phosphosulfate synthase 2 [Source:HGNC Symbol;Acc:HGNC:8604]
ENSG00000184203	PPP1R2	-0,292700186	0,004201327	protein phosphatase 1 regulatory inhibitor subunit 2 [Source:HGNC Symbol;Acc:HGNC:9288]
ENSG00000169926	KLF13	0,39934699	0,004797034	Kruppel like factor 13 [Source:HGNC Symbol;Acc:HGNC:13672]
ENSG00000164023	SGMS2	-0,350325503	0,005087572	sphingomyelin synthase 2 [Source:HGNC Symbol;Acc:HGNC:28395]
ENSG00000140992	PDPK1	0,350890529	0,005710493	3-phosphoinositide dependent protein kinase 1 [Source:HGNC Symbol;Acc:HGNC:8816]
ENSG00000105287	PRKD2	0,700392965	0,006655541	protein kinase D2 [Source:HGNC Symbol;Acc:HGNC:17293]
ENSG00000114315	HES1	-0,416884025	0,006655541	hes family bHLH transcription factor 1 [Source:HGNC Symbol;Acc:HGNC:5192]
ENSG00000144597	EAF1	-0,340560973	0,006655541	ELL associated factor 1 [Source:HGNC Symbol;Acc:HGNC:20907]
ENSG00000149654	CDH22	0,521304474	0,015717833	cadherin 22 [Source:HGNC Symbol;Acc:HGNC:13251]
ENSG00000135250	SRPK2	0,381506004	0,015717833	SRSF protein kinase 2 [Source:HGNC Symbol;Acc:HGNC:11306]
ENSG00000151135	TMEM263	-0,315333595	0,018759369	transmembrane protein 263 [Source:HGNC Symbol;Acc:HGNC:28281]
ENSG00000171564	FGB	-0,488200147	0,02446076	fibrinogen beta chain [Source:HGNC Symbol;Acc:HGNC:3662]
ENSG00000162873	KLHDC8A	-0,4739101	0,026582486	kelch domain containing 8A [Source:HGNC Symbol;Acc:HGNC:25573]
ENSG00000110060	PUS3	-0,478281016	0,026997331	pseudouridine synthase 3 [Source:HGNC Symbol;Acc:HGNC:25461]
ENSG00000137942	FNBP1L	-0,273767052	0,034127156	formin binding protein 1 like [Source:HGNC Symbol;Acc:HGNC:20851]
ENSG00000244405	ETV5	-0,513534064	0,044566135	ETS variant transcription factor 5 [Source:HGNC Symbol;Acc:HGNC:3494]
ENSG00000072506	HSD17B10	-0,408186665	0,044566135	hydroxysteroid 17-beta dehydrogenase 10 [Source:HGNC Symbol;Acc:HGNC:4800]
ENSG00000139438	FAM222A	0,308562037	0,044566135	family with sequence similarity 222 member A [Source:HGNC Symbol;Acc:HGNC:25915]
ENSG00000140612	SEC11A	-0,258233101	0,044566135	SEC11 homolog A signal peptidase complex subunit [Source:HGNC Symbol;Acc:HGNC:17718]
ENSG00000074370	ATP2A3	0,211540898	0,052301212	ATPase sarcoplasmic/endoplasmic reticulum Ca2+ transporting 3 [Source:HGNC Symbol;Acc:HGNC:813]
ENSG00000105357	MYH14	0,249544585	0,052718566	myosin heavy chain 14 [Source:HGNC Symbol;Acc:HGNC:23212]
ENSG00000182952	HMGN4	-0,373296955	0,058973762	high mobility group nucleosomal binding domain 4 [Source:HGNC Symbol;Acc:HGNC:4989]
ENSG00000143952	VPS54	-0,259556258	0,058973762	VPS54 subunit of GARP complex [Source:HGNC Symbol;Acc:HGNC:18652]

ENSG00000139364	TMEM132B	0,531795304	0,084864881	transmembrane protein 132B [Source:HGNC Symbol;Acc:HGNC:29397]
ENSG00000266714	MYO15B	0,479109302	0,084864881	myosin XVB [Source:HGNC Symbol;Acc:HGNC:14083]
ENSG00000198535	C2CD4A	-0,386871132	0,084864881	C2 calcium dependent domain containing 4A [Source:HGNC Symbol;Acc:HGNC:33627]
ENSG00000149527	PLCH2	0,36166687	0,084864881	phospholipase C eta 2 [Source:HGNC Symbol;Acc:HGNC:29037]
ENSG00000039068	CDH1	-0,18670402	0,084864881	cadherin 1 [Source:HGNC Symbol;Acc:HGNC:1748]
ENSG00000125968	ID1	-0,284429389	0,087784112	inhibitor of DNA binding 1 HLH protein [Source:HGNC Symbol;Acc:HGNC:5360]
ENSG00000104419	NDRG1	0,381104626	0,089197771	N-myc downstream regulated 1 [Source:HGNC Symbol;Acc:HGNC:7679]
ENSG00000111799	COL12A1	-0,358905607	0,089197771	collagen type XII alpha 1 chain [Source:HGNC Symbol;Acc:HGNC:2188]
ENSG00000128050	PAICS	0,305022253	0,089197771	phosphoribosylaminoimidazole carboxylase and phosphoribosylaminoimidazolesuccinocarboxamide synthase [Source:HGNC Symbol;Acc:HGNC:8587]
ENSG00000134333	LDHA	0,340549744	0,091148856	lactate dehydrogenase A [Source:HGNC Symbol;Acc:HGNC:6535]
ENSG00000169710	FASN	-0,560872292	0,091350417	fatty acid synthase [Source:HGNC Symbol;Acc:HGNC:3594]
ENSG00000160360	GPSM1	0,415137817	0,094469082	G protein signaling modulator 1 [Source:HGNC Symbol;Acc:HGNC:17858]
ENSG00000176840	MIR7-3HG	-0,311248048	0,094469082	MIR7-3 host gene [Source:HGNC Symbol;Acc:HGNC:30049]
ENSG00000108828	VAT1	0,278611812	0,094469082	vesicle amine transport 1 [Source:HGNC Symbol;Acc:HGNC:16919]
ENSG00000072803	FBXW11	-0,247590533	0,094469082	F-box and WD repeat domain containing 11 [Source:HGNC Symbol;Acc:HGNC:13607]
ENSG00000112715	VEGFA	0,237853282	0,094469082	vascular endothelial growth factor A [Source:HGNC Symbol;Acc:HGNC:12680]
ENSG00000077264	PAK3	-0,230811732	0,094469082	p21 (RAC1) activated kinase 3 [Source:HGNC Symbol;Acc:HGNC:8592]
ENSG00000236824	BCYRN1	-0,442926612	0,0947316	brain cytoplasmic RNA 1 [Source:HGNC Symbol;Acc:HGNC:1022]
ENSG00000139641	ESYT1	-0,213017417	0,095040485	extended synaptotagmin 1 [Source:HGNC Symbol;Acc:HGNC:29534]
ENSG00000122861	PLAU	-0,421782205	0,099735564	plasminogen activator urokinase [Source:HGNC Symbol;Acc:HGNC:9052]
ENSG00000145888	GLRA1	0,414226429	0,099735564	glycine receptor alpha 1 [Source:HGNC Symbol;Acc:HGNC:4326]
ENSG00000129757	CDKN1C	0,367258612	0,099735564	cyclin dependent kinase inhibitor 1C [Source:HGNC Symbol;Acc:HGNC:1786]
ENSG00000172466	ZNF24	-0,207173696	0,099735564	zinc finger protein 24 [Source:HGNC Symbol;Acc:HGNC:13032]