

Single-cell transcriptomics of East-Asian pancreatic islets cells

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Supplementary Tables

Supplementary Table 1: Details of human islets utilized in study. Glucose Stimulated Insulin Secretion (GSIS) data is shown as area under the curve, which reflects amount of insulin secreted per 10 minutes.

Subject	Age	Ethnicity	Sex	HbA1c (%)	Days in Culture	Islet-Glucose Stimulated Insulin Secretion		Cells captured on Fluidigm C1		
						Low Glucose	High Glucose	Total cells	β -cells passed QC	α -cells passed QC
1	65	Chinese	Male	5.9	3	48.2	299.9	138	32	33
2	49	Chinese	Female	5.8	3	64.9	1187.3	84	33	15
3	49	Chinese	Female	5.1	3	87.9	732.2	226	40	70

Supplementary table 2: Identification of top 5 upstream transcriptional regulators from significant gene showing high expression in β -cells and α -cells.

Upstream transcription factors	P-value	Target molecules in dataset
14 genes highly expressed in β-cells		
FOXA2	9.04E-07	<i>G6PC2,HADH,MAP1B,SCD</i>
MAFA	9.10E-06	<i>G6PC2,INS</i>
XBP1	7.59E-05	<i>DNAJC3,INS,SEC11C</i>
MAF	2.17E-04	<i>G6PC2,INS</i>
HNF1A	7.23E-04	<i>G6PC2,INS,PFKFB2</i>
20 genes highly expressed in α-cells		
FOXM1	7.78E-05	<i>GCG,LDHA,STMN1</i>
H2AFX	1.15E-04	<i>CLU,MYL6</i>
FOXA2	3.44E-04	<i>FABP5,GCG,TTR</i>
MYC	7.18E-04	<i>CLU,FABP5,H3F3A/H3F3B,LDHA,STMN1</i>
NKX6-2	7.30E-04	<i>GCG</i>

Supplementary table 3: Significant transcripts and genes from ANOVA analysis of 1) β -cells compared to α -cells and 2) α -cells compared to β -cells in our study. Cells from patient 1 and 2 used in discovery stage and cells from patient 3 used for validation. Highly expressed transcripts were cut-off based on proportion of cells in the smallest islet cell endocrine group in the discovery stage [232 transcripts (314 genes) with RPKM > 50 in at least 42% of cells] and replication stage [202 transcripts (298 genes) with RPKM > 50 in at least 47% of cells]. Discovery stage p-value adjusted for 232 transcripts tested. Validation stage p-value adjusted for 8 and 16 transcripts tested, respectively.

Gene	Transcript	Discovery stage (65 β -cells vs 48 α -cells)		Validation stage (40 β -cells vs 70 α -cells)	
		Adj p-value	Fold Change	Adj p-value	Fold Change
ANOVA β-cells compared to α-cells					
<i>INS</i>	NM_000207	6.94E-36	343.6	1.81E-47	449.61
<i>INS</i>	NM_001185097	1.03E-11	77.18	7.85E-16	351.20
<i>HADH</i>	NM_005327	2.69E-08	31.08	1.13E-10	30.08
<i>PFKFB2</i>	NM_006212	1.29E-07	8.96	7.37E-09	7.31
<i>MAP1B</i>	NM_001324255	6.70E-06	2.40	3.02E-05	2.14
<i>RNR2</i>	NR_137295	1.96E-04	2.35	1.99E-04	2.46
<i>OLMALINC</i>	NR_026762	1.29E-03	5.65	1.52E-12	6.98
<i>DNAJC3</i>	NM_006260	2.04E-03	2.12	5.30E-04	1.92
ANOVA α-cells compared to β-cells					
<i>GCG</i>	NM_002054	1.35E-50	200.93	5.15E-44	320.77
<i>TTR</i>	NM_000371	3.85E-21	20.38	4.64E-18	22.12
<i>ALDH1A1</i>	NM_000689	1.39E-06	7.13	2.05E-15	14.86
<i>CLU</i>	NM_001831	2.23E-11	11.84	5.05E-14	6.59
<i>TMEM176B</i>	NM_001101312	9.58E-10	8.47	7.30E-13	7.36
<i>BEX3</i>	NM_206917	1.40E-02	2.29	1.10E-07	3.77
<i>HIGD1A</i>	NM_014056	6.80E-08	3.76	1.20E-06	3.44
<i>ELL2</i>	NM_012081	1.22E-09	3.36	4.16E-06	7.38
<i>MYL6</i>	NM_079423	1.75E-07	3.75	6.24E-05	4.28
<i>H3F3B</i>	NM_005324	3.11E-05	2.09	5.63E-06	2.42
<i>LDHA</i>	NM_005566	1.16E-03	4.88	6.56E-04	9.27
<i>NAA20</i>	NM_016100	7.75E-03	1.92	1.05E-03	2.32
<i>FABP5</i>	NM_001444	7.56E-06	8.79	5.15E-04	5.43
<i>SH3BGRL3</i>	NM_031286	7.08E-05	4.33	1	1.83
<i>YWHAE</i>	NM_006761	8.12E-03	1.51	1	1.05
<i>PPIA</i>	NM_021130	2.48E-04	2.11	1	1.06

Supplementary table 4: *In silico* replication of unique α -cells upregulated genes and β -cells upregulated genes reported in recent mouse islet single-cell studies [2]. Adjusted P-value corrected for 5 and 7 transcripts tested, respectively.

Gene	Transcript	p-value	Adj p-value	Fold Change
Validation of highly expressed mouse α-cell genes				
GCG	NM_002054	9.92E-99	4.96E-98	223.04
TTR	NM_000371	2.10E-42	1.05E-41	20.22
HIGD1A	NM_014056	3.39E-16	1.69E-15	3.22
GPX3	NM_002084	3.32E-13	1.66E-12	3.15
PDK4	NM_002612	2.72E-06	1.36E-05	6.97
Validation of highly expressed mouse β-cell genes				
INS	NM_000207	5.62E-83	3.93E-82	415.58
INS	NM_001185097	3.24E-30	2.26E-29	132.44
HADH	NM_005327	2.26E-21	1.58E-20	31.35
G6PC2	NM_001081686	3.09E-12	2.16E-11	9.95
RRAGD	NM_021244	1.26E-07	8.81E-07	2.93
IAPP	NM_000415	4.64E-06	3.25E-05	317.52
FAM46A	NM_017633	6.01E-05	4.21E-04	-2.35

Supplementary table 5: Association details of all 624 transcripts with RPKM values > 50 in 25% of cells in ANOVA analysis of 105 β -cells compared 118 α -cells from all 3 non-T2D East-Asian subjects.

Gene Symbol	Transcript	p-value	Fold Change
GCG	NM_002054	9.92E-99	-223.044
INS	NM_000207	5.62E-83	415.576
TTR	NM_000371	2.10E-42	-20.222
GC	NM_001204307	1.48E-30	-47.890
INS	NM_001185097	3.24E-30	132.443
CLU	NM_001831	1.26E-29	-8.729
TMEM176B	NM_001101312	1.14E-25	-8.492
ALDH1A1	NM_000689	4.81E-25	-10.942
HADH	NM_005327	2.26E-21	31.354
PFKFB2	NM_006212	3.93E-19	10.902
HIGD1A	NM_014056	3.39E-16	-3.217
OLMALINC	NR_026762	3.62E-16	6.532
MAP1B	NM_001324255	5.64E-15	2.658
ELL2	NM_012081	1.79E-14	-3.270
H3F3B	NM_005324	3.92E-14	-2.251
BEX3	NM_206917	4.07E-14	-3.279
MYL6	NM_079423	6.07E-14	-3.479
GPX3	NM_002084	3.32E-13	-3.148
TM4SF4	NM_004617	5.94E-13	-46.744
CYSTM1	NM_032412	1.36E-12	-2.186
SEC11C	NM_033280	2.12E-12	2.367
G6PC2	NM_001081686	3.09E-12	9.950
RNR2	NR_137295	3.68E-12	2.480
FABP5	NM_001444	7.48E-12	-6.704
SCD	NM_005063	1.45E-11	3.091
ERO1B	NM_019891	4.49E-10	3.052
LDHA	NM_005566	7.23E-10	-5.592
CHGB	NM_001819	7.97E-10	-2.689
RPL5	NM_000969	1.68E-09	1.763
UCHL1	NM_004181	2.42E-09	2.640
NAA20	NM_016100	3.37E-09	-2.042
STMN1	NM_005563	4.24E-09	-3.527
RPS6	NM_001010	4.67E-09	1.445
CRYBA2	NM_057094	6.86E-09	-30.647
RPS3A	NM_001006	7.93E-09	1.515
RPL3	NM_000967	8.93E-09	1.696
EIF4A2	NM_001967	1.84E-08	1.687
CD63	NM_001780	2.38E-08	-1.821

SCG2	NM_003469	2.84E-08	-1.963
RPL34	NM_001319236	4.30E-08	1.658
SERPINA1	NM_000295	4.83E-08	-16.314
ROMO1	NM_080748	1.09E-07	-2.150
RRAGD	NM_021244	1.26E-07	2.929
SH3BGRL3	NM_031286	1.65E-07	-2.562
NDUFA13	NM_015965	1.72E-07	-2.016
HMGN2	NM_005517	3.01E-07	-1.698
COX8A	NM_004074	3.11E-07	-1.831
RPS4X	NM_001007	3.23E-07	1.661
HNRNPC	NM_004500	5.52E-07	1.771
PCBD1	NM_000281	6.17E-07	-2.238
TPT1	NM_003295	1.22E-06	1.515
RPS13	NM_001017	1.33E-06	1.516
NDUFB2	NM_004546	1.44E-06	-1.593
COX17	NM_005694	1.86E-06	-1.525
STMN1	NM_203399	2.54E-06	-2.758
MALAT1	NR_002819	2.57E-06	1.421
PDK4	NM_002612	2.72E-06	-6.971
CTTN	NM_138565	3.69E-06	-2.123
DNAJC3	NM_006260	4.39E-06	1.845
IAPP	NM_000415	4.64E-06	317.515
HIST1H4C	NM_003542	7.49E-06	1.635
HLA-E	NM_005516	7.51E-06	-2.656
COX6A1	NM_004373	8.01E-06	-1.524
RBX1	NM_014248	9.25E-06	-1.851
CANX	NM_001024649	1.02E-05	1.856
ERGIC3	NM_015966	1.13E-05	-2.730
DNAJB9	NM_012328	1.29E-05	3.037
NDUFB8	NM_005004	1.32E-05	-1.801
UBB	NM_018955	1.42E-05	-1.797
ARHGAP1	NM_004308	1.55E-05	-1.993
RPS3	NM_001256802	1.98E-05	1.416
PARK7	NM_001123377	2.55E-05	-1.573
HNRNPA2B1	NM_002137	2.96E-05	-1.709
MARCKS	NM_002356	3.05E-05	-1.513
MIR7-3HG	NR_027148	3.10E-05	-2.142
ATP5E	NM_006886	3.87E-05	-1.535
UBE2B	NM_003337	4.17E-05	1.925
ALDOA	NM_184043	4.28E-05	1.954
TSC22D1	NM_006022	4.48E-05	2.995

FAM162A	NM_014367	4.78E-05	2.083
SCG3	NM_013243	4.89E-05	1.595
RAB11A	NM_004663	4.98E-05	-1.778
ATP6V1G1	NM_004888	5.39E-05	1.480
FAM46A	NM_017633	6.01E-05	-2.351
CPE	NM_001873	6.87E-05	1.551
RPL7	NM_000971	7.90E-05	1.422
PPP1CB	NM_206876	8.04E-05	1.473
CD164	NM_006016	8.57E-05	-1.943
OSTC	NM_021227	9.19E-05	2.288
BRK1	NM_018462	1.13E-04	-1.568
PJA2	NM_014819	1.22E-04	2.015
SNRPG	NM_003096	1.38E-04	-1.486
HSP90B1	NM_003299	1.39E-04	1.895
ACAT1	NM_000019	1.40E-04	2.165
C4orf3	NM_001001701	1.40E-04	1.764
PSME2	NM_002818	1.56E-04	-1.854
SRSF6	NM_006275	1.58E-04	-1.523
RPL24	NM_000986	1.61E-04	1.371
PALLD	NM_001166110	1.98E-04	-2.066
TVP23B	NM_001316920	2.04E-04	1.775
RPS25	NM_001028	2.09E-04	1.382
RNR1	NR_137294	2.12E-04	2.113
NPC2	NM_006432	2.17E-04	-1.579
RPL14	NM_003973	2.28E-04	1.416
PRDX2	NM_005809	2.39E-04	-1.491
GSTP1	NM_000852	2.41E-04	-1.778
ENO1	NM_001428	2.66E-04	1.569
RPS15	NM_001018	2.78E-04	-1.508
BNIP3L	NM_004331	2.90E-04	1.766
COX7A2	NM_001865	2.94E-04	-1.321
TMEM167A	NM_174909	3.47E-04	2.007
RPS27	NM_001030	3.61E-04	1.290
ATP5B	NM_001686	4.01E-04	-1.563
C10orf10	NM_007021	4.40E-04	2.399
ARF4	NM_001660	4.49E-04	1.665
CLIC1	NM_001287594	5.14E-04	-1.678
RPL31	NM_000993	5.21E-04	1.323
ATP6V0D1	NM_004691	6.57E-04	-2.118
PPP1CB	NM_002709	6.62E-04	1.325
SAT1	NM_002970	6.84E-04	-2.121

PRDX1	NM_181697	7.96E-04	1.692
CALM2	NM_001743	8.01E-04	-1.271
C14orf2	NM_004894	8.08E-04	-1.486
LAPTM4A	NM_014713	8.25E-04	1.397
RTN4	NR_135830	8.45E-04	1.729
SERINC1	NM_020755	8.55E-04	1.692
WSB2	NM_001278558	9.38E-04	1.481
ERGIC2	NM_016570	9.75E-04	1.807
GNAS	NM_001309840	9.76E-04	1.363
RPL4	NM_000968	9.78E-04	1.456
FAU	NM_001997	9.90E-04	-1.468
SSR3	NM_007107	9.99E-04	1.628
HSPE1	NM_002157	1.00E-03	-1.481
RPS12	NM_001016	1.03E-03	1.319
NDUFB1	NM_004545	1.09E-03	-1.483
RTN4	NR_135829	1.09E-03	1.715
ATP6V1A	NM_001690	1.15E-03	1.590
RPL6	NM_000970	1.20E-03	1.398
NDUFA1	NM_004541	1.21E-03	-1.336
OAZ1	NM_004152	1.26E-03	-1.456
CNBP	NM_001127196	1.30E-03	1.674
ERO1A	NM_014584	1.32E-03	2.259
ZFAND6	NM_001242915	1.37E-03	2.308
RHOA	NM_001664	1.44E-03	-1.579
RPL12	NM_000976	1.60E-03	1.314
CCNI	NM_006835	1.72E-03	1.699
EIF3E	NM_001568	1.84E-03	1.574
PFDN5	NM_002624	1.85E-03	1.365
EIF3L	NM_016091	2.03E-03	1.850
ARL6IP1	NM_015161	2.13E-03	1.586
RNASEK	NM_001004333	2.25E-03	-1.355
LINC01420	NR_015367	2.27E-03	-1.698
OTUD6B-AS1	NR_110439	2.41E-03	1.756
RPL13A	NM_012423	2.54E-03	1.509
CNBP	NM_003418	2.62E-03	1.665
ALDOA	NM_184041	2.67E-03	1.532
HINT1	NM_005340	2.78E-03	-1.265
GHITM	NM_014394	2.82E-03	1.450
COA3	NM_001040431	2.96E-03	-1.599
EEF1B2	NM_021121	3.01E-03	1.775
TAF7	NM_005642	3.11E-03	1.622

ENPP2	NR_045555	3.19E-03	-1.962
TMBIM6	NM_003217	3.29E-03	-1.262
CDC42	NM_001791	3.30E-03	-1.368
KRTCAP2	NM_173852	3.45E-03	-1.506
RPS27A	NM_001177413	3.50E-03	1.304
NDUFA9	NM_005002	3.51E-03	-1.783
TLK1	NM_001136555	3.51E-03	1.538
TTC3	NM_001001894	3.56E-03	1.736
MT1X	NM_005952	3.57E-03	3.482
SCGB2A1	NM_002407	3.63E-03	-1.581
SLC25A5	NM_001152	3.71E-03	-1.387
SLC25A3	NM_002635	3.78E-03	-1.746
QPCT	NM_012413	4.16E-03	-1.571
DYNLRB1	NM_014183	4.24E-03	-1.620
COX6B1	NM_001863	4.36E-03	-1.419
RPS14	NM_005617	4.38E-03	1.240
SH3BGRL	NM_003022	4.50E-03	2.012
EEF1G	NM_001404	4.69E-03	1.338
NOP10	NM_018648	4.92E-03	-1.419
PDIA6	NM_005742	4.93E-03	1.501
NEDD8	NM_006156	5.18E-03	-1.389
PSMB3	NM_002795	5.35E-03	-1.429
GTF3C6	NM_138408	5.38E-03	-1.711
GNG5	NM_005274	5.55E-03	-1.659
MORF4L1	NM_001265605	5.84E-03	1.261
PON2	NM_000305	5.89E-03	1.769
RPS15A	NM_001030009	5.94E-03	1.295
SRPRB	NM_021203	6.51E-03	1.499
RPL15	NM_001253383	6.88E-03	1.325
CHURC1	NM_001204063	7.36E-03	1.485
RPL11	NM_000975	7.53E-03	1.316
PGK1	NM_000291	7.53E-03	1.476
ITGB1	NM_133376	8.13E-03	-1.580
ATP5A1	NM_004046	8.22E-03	-1.550
H2AFZ	NM_002106	8.36E-03	1.394
PLP2	NM_002668	8.77E-03	-1.426
UFC1	NM_016406	9.02E-03	-1.459
PTMA	NM_002823	9.39E-03	1.298
RPL30	NM_000989	9.47E-03	1.249
EIF1B	NM_005875	9.94E-03	1.661
DAD1	NM_001344	1.01E-02	1.286

TXNL1	NM_004786	1.01E-02	1.648
FTH1	NM_002032	1.03E-02	1.554
NORAD	NR_027451	1.03E-02	1.374
RPL41	NM_021104	1.06E-02	1.161
BEX1	NM_018476	1.11E-02	-1.330
PSMB6	NM_002798	1.13E-02	-1.649
WTAP	NM_001270531	1.14E-02	1.467
ATP6V1E1	NM_001696	1.17E-02	1.564
SLC30A8	NM_173851	1.20E-02	1.556
CDV3	NM_001282764	1.23E-02	1.619
RPL26	NM_000987	1.26E-02	1.322
PPIA	NM_021130	1.32E-02	-1.358
PSMB1	NM_002793	1.37E-02	1.357
DYNLT3	NM_006520	1.45E-02	1.412
SSR4	NM_006280	1.49E-02	-1.233
USMG5	NM_001206426	1.61E-02	-1.272
NACA	NM_001113202	1.63E-02	1.321
MT2A	NM_005953	1.64E-02	3.492
RACK1	NM_006098	1.67E-02	1.317
ARRDC3	NM_020801	1.77E-02	1.495
PAIP2	NM_016480	1.86E-02	1.448
EEF1B2	NM_001037663	1.87E-02	1.491
MORN2	NM_001145450	1.90E-02	-1.791
PSME1	NM_006263	1.91E-02	-1.409
ATP6AP2	NM_005765	2.03E-02	-1.362
HNRNPDL	NM_031372	2.05E-02	-1.416
ACTG1	NM_001614	2.05E-02	1.504
RPL15	NM_001253382	2.25E-02	1.359
HAX1	NM_006118	2.29E-02	1.482
SRP54	NM_003136	2.36E-02	1.807
RAN	NM_006325	2.41E-02	-1.346
TMEM60	NM_032936	2.49E-02	1.893
TMEM33	NM_018126	2.56E-02	1.283
RPL23	NM_000978	2.58E-02	1.165
EAF1	NM_033083	2.58E-02	1.397
OST4	NM_001134693	2.59E-02	-1.224
RPS5	NM_001009	2.73E-02	1.263
PSMB5	NM_002797	2.77E-02	-1.367
ISL1	NM_002202	2.82E-02	-1.482
YWHAE	NM_006761	2.84E-02	-1.218
NDUFV2	NM_021074	2.89E-02	-1.306

HSP90AA1	NM_005348	2.94E-02	1.563
RGS2	NM_002923	3.11E-02	2.144
POLR2K	NM_005034	3.17E-02	1.373
TMA7	NM_015933	3.19E-02	-1.259
CLK1	NR_027855	3.26E-02	1.670
SARAF	NM_001284239	3.45E-02	1.507
ATP5I	NM_007100	3.47E-02	-1.221
TERF2IP	NM_018975	3.47E-02	1.395
NDUFS4	NM_002495	3.52E-02	-1.466
SDHB	NM_003000	3.62E-02	-1.453
ATP5G1	NM_001002027	3.70E-02	-1.338
GNAS	NM_001309861	3.71E-02	1.261
ARPC2	NM_005731	3.71E-02	-1.368
GAPDH	NM_002046	3.75E-02	-1.256
RPL35A	NM_000996	3.79E-02	1.203
EIF4G2	NM_001042559	3.83E-02	1.353
TMBIM4	NM_016056	3.87E-02	-1.296
S100A11	NM_005620	4.00E-02	-1.669
YWHAG	NM_012479	4.11E-02	1.354
COMMD3	NM_012071	4.16E-02	1.507
ANXA5	NM_001154	4.30E-02	1.428
PDIA3	NM_005313	4.32E-02	-1.378
TAF9	NM_003187	4.38E-02	1.456
RPS20	NM_001023	4.74E-02	1.167
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EIF1	NM_005801	4.80E-02	1.192
NDUFB3	NM_002491	4.81E-02	-1.226
CHMP5	NM_016410	5.19E-02	1.442
PSMD6	NM_001271781	5.25E-02	-1.509
TBCA	NM_004607	5.30E-02	1.192
RPL27	NM_000988	5.36E-02	-1.152
METTL5	NM_001293187	5.42E-02	1.436
RPS18	NM_022551	5.59E-02	1.141
ARL6IP5	NM_006407	5.79E-02	1.292
RIN2	NM_018993	5.84E-02	1.419
PPT1	NM_001142604	5.91E-02	1.447
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EIF2S3	NM_001415	6.10E-02	1.292
VPS35	NM_018206	6.16E-02	1.308
PRDX3	NM_006793	6.48E-02	-1.303
ATP5H	NM_006356	6.79E-02	-1.289

PSMB5	NM_001130725	6.80E-02	-1.254
MYL12B	NM_033546	6.85E-02	-1.180
ARL1	NM_001177	6.95E-02	1.306
SPCS2	NM_014752	6.98E-02	1.279
PNRC2	NM_017761	7.21E-02	1.380
POMP	NM_015932	7.21E-02	1.226
SELK	NM_021237	7.23E-02	1.236
CD63	NM_001257400	7.41E-02	-1.276
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SHFM1	NM_006304	7.56E-02	-1.212
PPA2	NM_176869	7.58E-02	-1.569
PRDX4	NM_006406	7.63E-02	-1.308
SDCBP	NM_005625	7.74E-02	1.362
DPYSL2	NM_001244604	7.81E-02	1.256
SCG5	NM_003020	7.87E-02	-1.144
SCG5	NM_001144757	8.16E-02	-1.139
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DBI	NM_001079862	8.43E-02	1.210
FKBP2	NM_004470	8.50E-02	-1.391
C18orf32	NM_001199346	8.74E-02	1.291
SDCBP	NM_001007069	8.91E-02	1.421
EIF3H	NM_003756	9.05E-02	1.318
C3orf14	NM_001291941	9.12E-02	1.265
FKBP3	NM_002013	9.23E-02	-1.339
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IRF2BP2	NM_182972	1.02E-01	1.310
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NAP1L1	NM_001307924	1.05E-01	1.353
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RPL8	NM_000973	1.07E-01	-1.156
CHP1	NM_007236	1.11E-01	-1.203
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COX7C	NM_001867	1.12E-01	-1.139
IRF2BP2	NM_001077397	1.12E-01	1.312
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SKP1	NM_170679	1.25E-01	1.130
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VDAC3	NM_005662	1.26E-01	1.418
PPIG	NM_004792	1.26E-01	-1.330
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SOD1	NM_000454	1.35E-01	-1.139
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SELT	NM_016275	2.00E-01	1.197
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YWHAQ	NM_006826	2.10E-01	1.172
ATP6V1D	NM_015994	2.14E-01	1.178
UBC	NM_021009	2.16E-01	1.140
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SYPL1	NM_182715	2.25E-01	1.298
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FOS	NM_005252	2.25E-01	-1.257
C14orf166	NM_016039	2.26E-01	1.210
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EEF1E1	NM_004280	2.53E-01	1.303
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ATP5F1	NM_001688	2.55E-01	-1.166
COPB2	NM_004766	2.59E-01	1.227
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EEF1A1	NM_001402	2.63E-01	1.065
SSR1	NM_003144	2.65E-01	1.165
RUFY3	NM_001291993	2.65E-01	-1.203
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PFN2	NM_053024	2.75E-01	-1.278
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ETNK1	NM_018638	2.82E-01	-1.135
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ARRDC3	NM_001329672	3.42E-01	1.146
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COX4I1	NM_001861	3.98E-01	-1.091
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CFAP36	NM_080667	4.09E-01	1.170
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COPB1	NM_001144062	4.17E-01	-1.167
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CAPZA1	NM_006135	6.18E-01	-1.057
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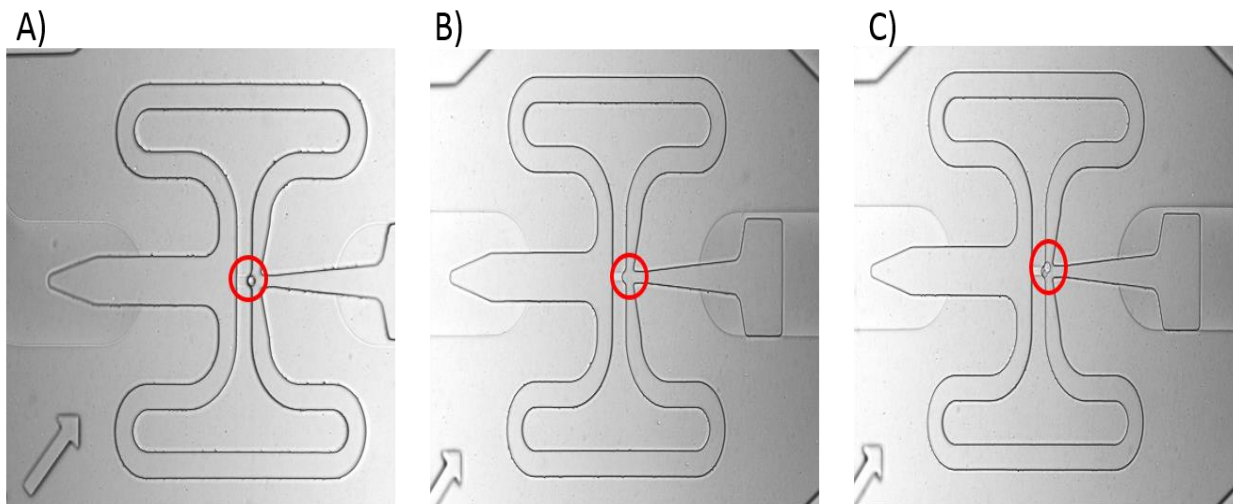
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MAPRE1	NM_012325	8.70E-01	-1.025
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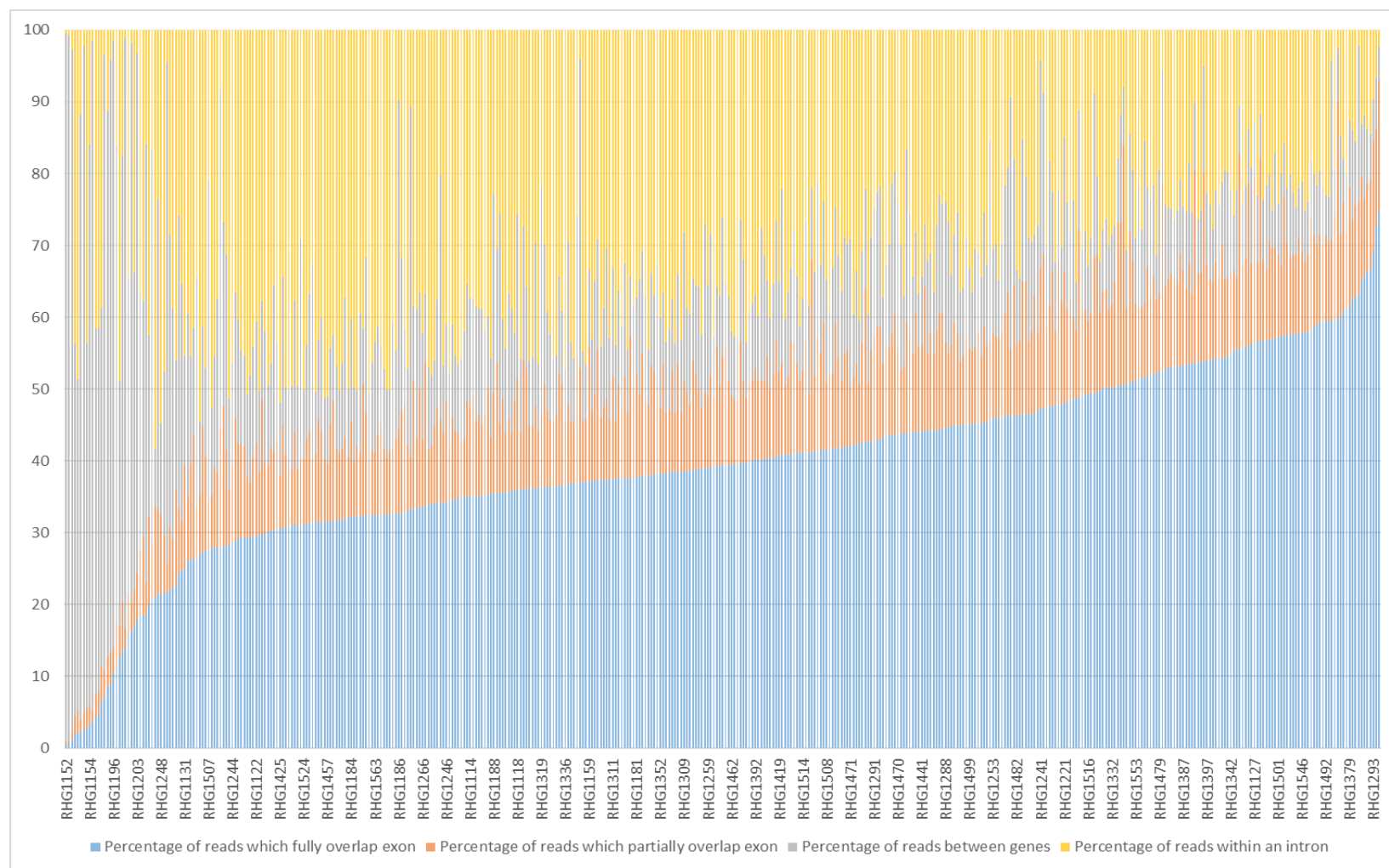
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LAMTOR5	NM_006402	9.80E-01	1.003
PAFAH1B2	NR_110282	9.81E-01	1.003
HNRNPH1	NM_001257293	9.93E-01	-1.001
PIGF	NM_002643	9.98E-01	1.001
EID1	NM_014335	1.00E+00	-1.000

Supplementary Figures

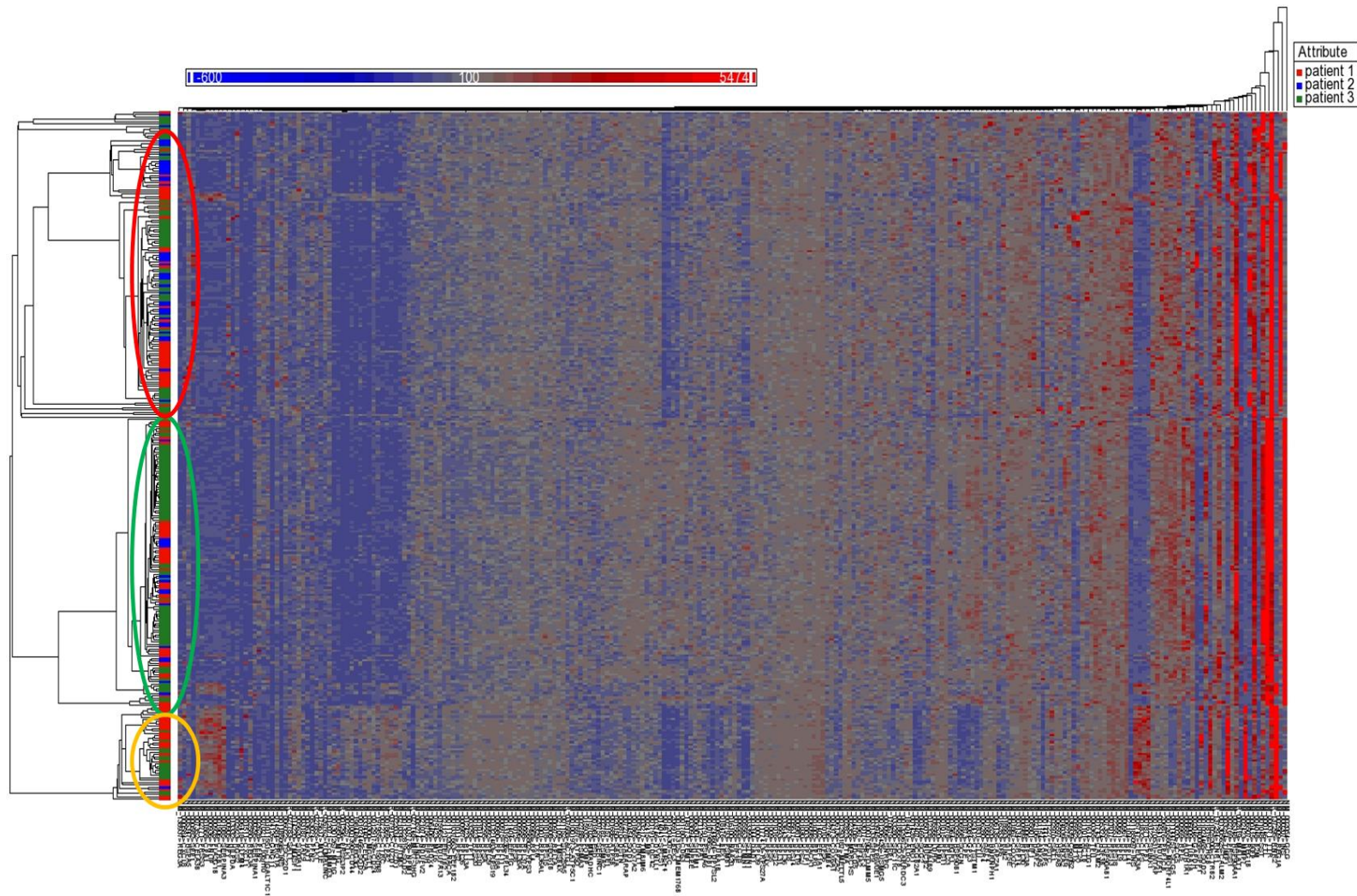
Supplementary figure 1: Diagrams of C1 wells in the study with A) 1 single cell captured, B) no cell captured and C) more than 1 cell captured. All wells without any cells or with multiple cells captured were excluded from further analysis.



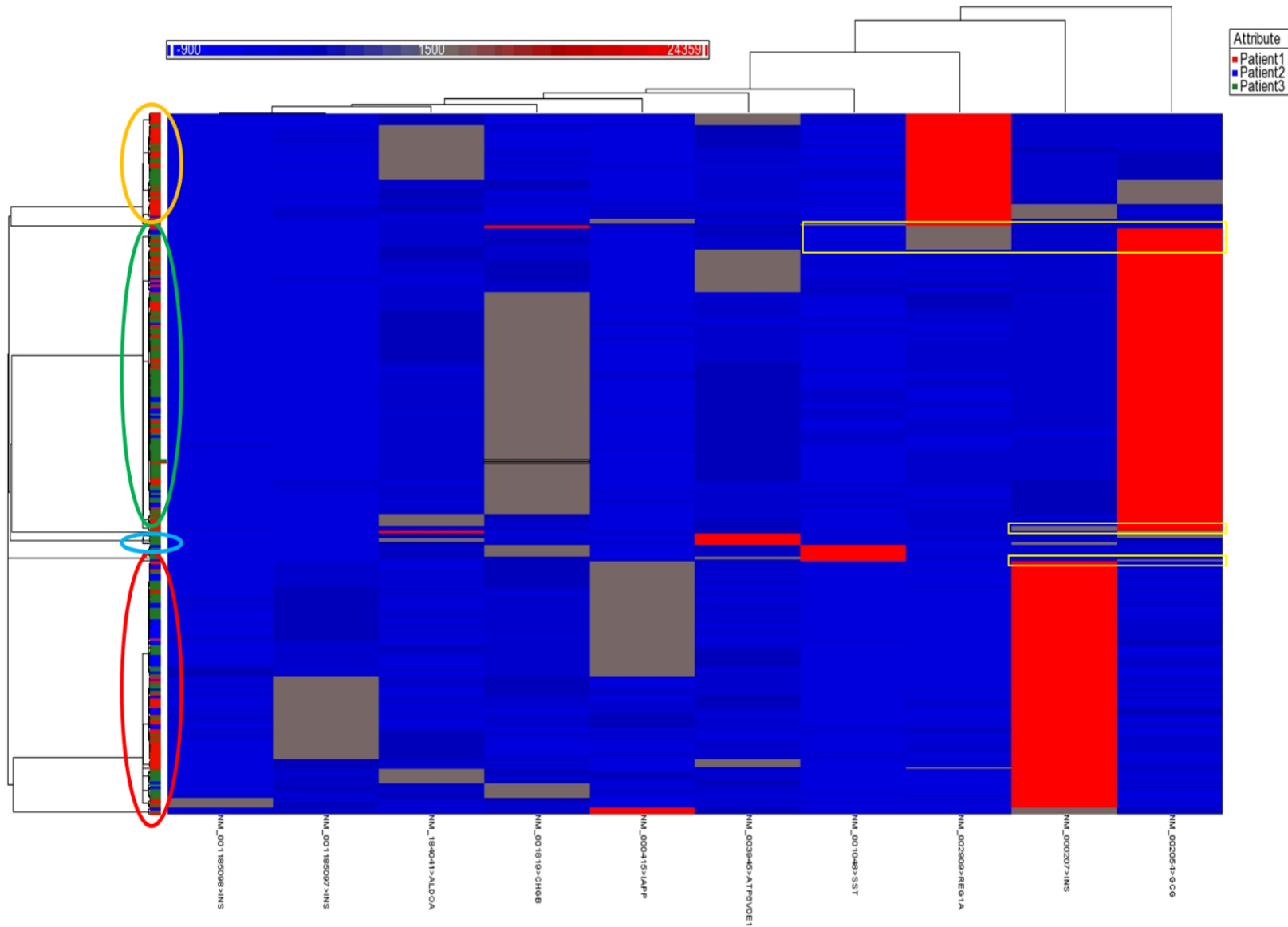
Supplementary Figure 2: Mapping of sequence read to exonic, intergenic and intronic regions among 442 single cells captured in the study. 47 cells with < 30% mapping to exonic regions were excluded.



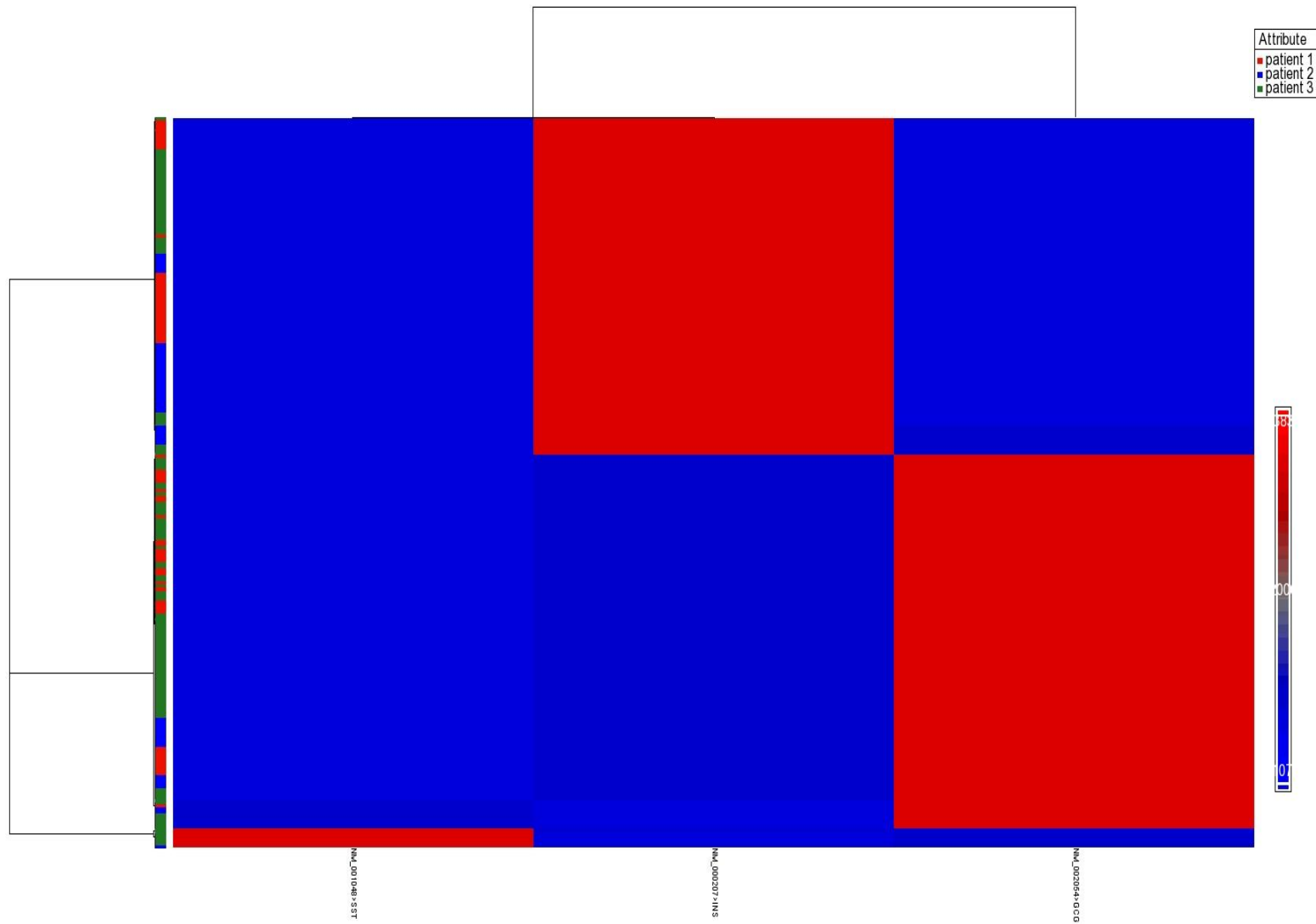
Supplementary Figure 3: Clustering of 294 single islet cells based on all 252 transcripts (146 genes) with RPKM values ≥ 500 in $\geq 2\%$ of cells revealed 3 main cluster of cells. These were based on *GCG* (green oval), *INS* (red oval) and *REG1A* (yellow oval). Scale indicates quantile-normalized expression levels.



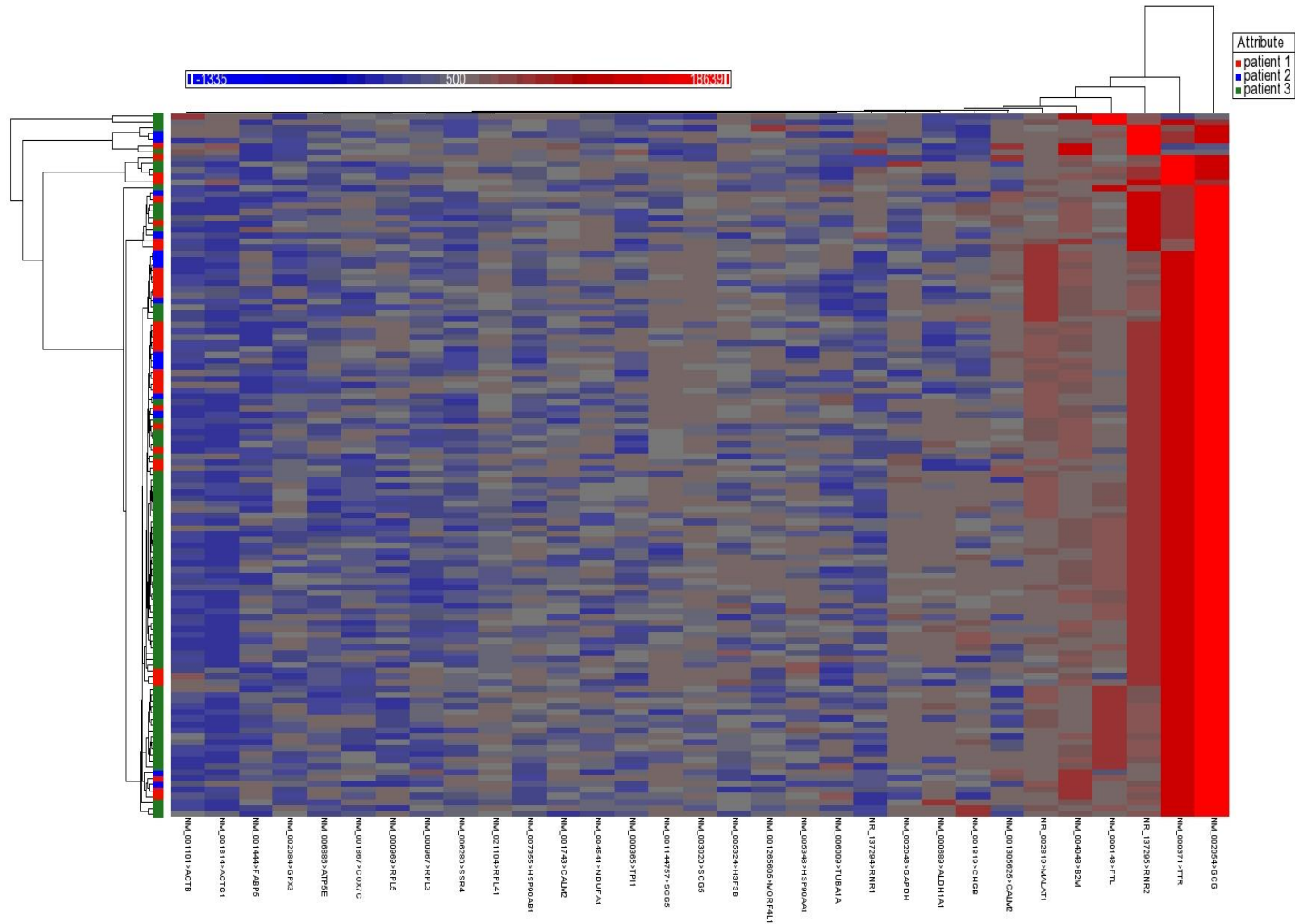
Supplementary Figure 4: Hierarchical clustering of 294 single islet cells based on pancreatic cell lineage gene transcripts and *REG1A*. 10 transcripts (from 10 genes) with RPKM values > 500 in 25% of cells were utilized for clustering and data was quantile normalized. 18 doublet cells indicated in yellow boxes. Red oval: cluster in INS expressing cells; blue oval: cluster of SST expressing cells; green oval: cluster of GCG expressing cells; orange oval: cluster of *REG1A* expressing cells. Scale indicates quantile-normalized expression levels.



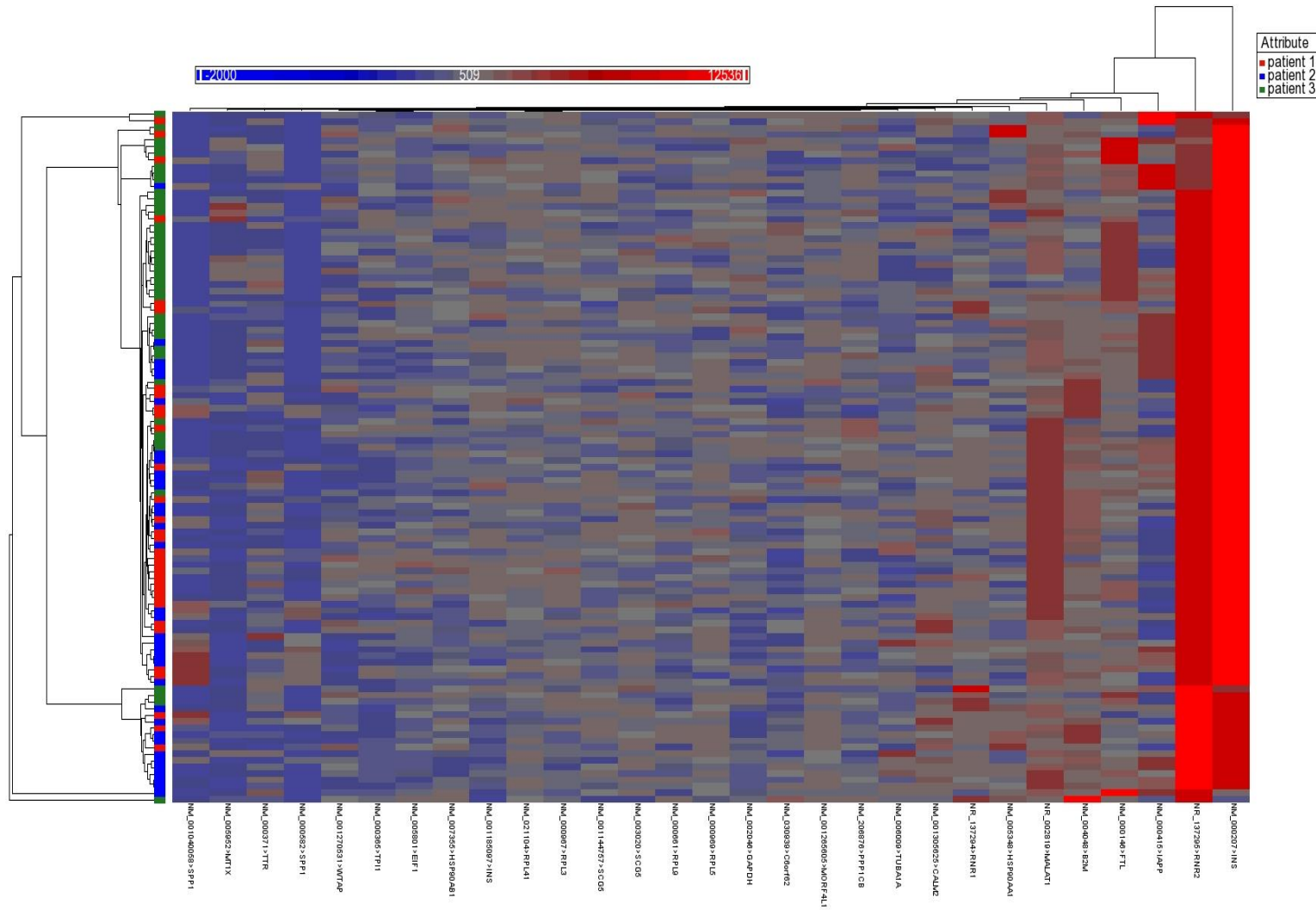
Supplementary Figure 5: Hierarchical clustering 226 predominantly mono-hormonal cells among our based on *INS*, *GCG* and *SST* expression levels. Scale indicates quantile-normalized expression levels.



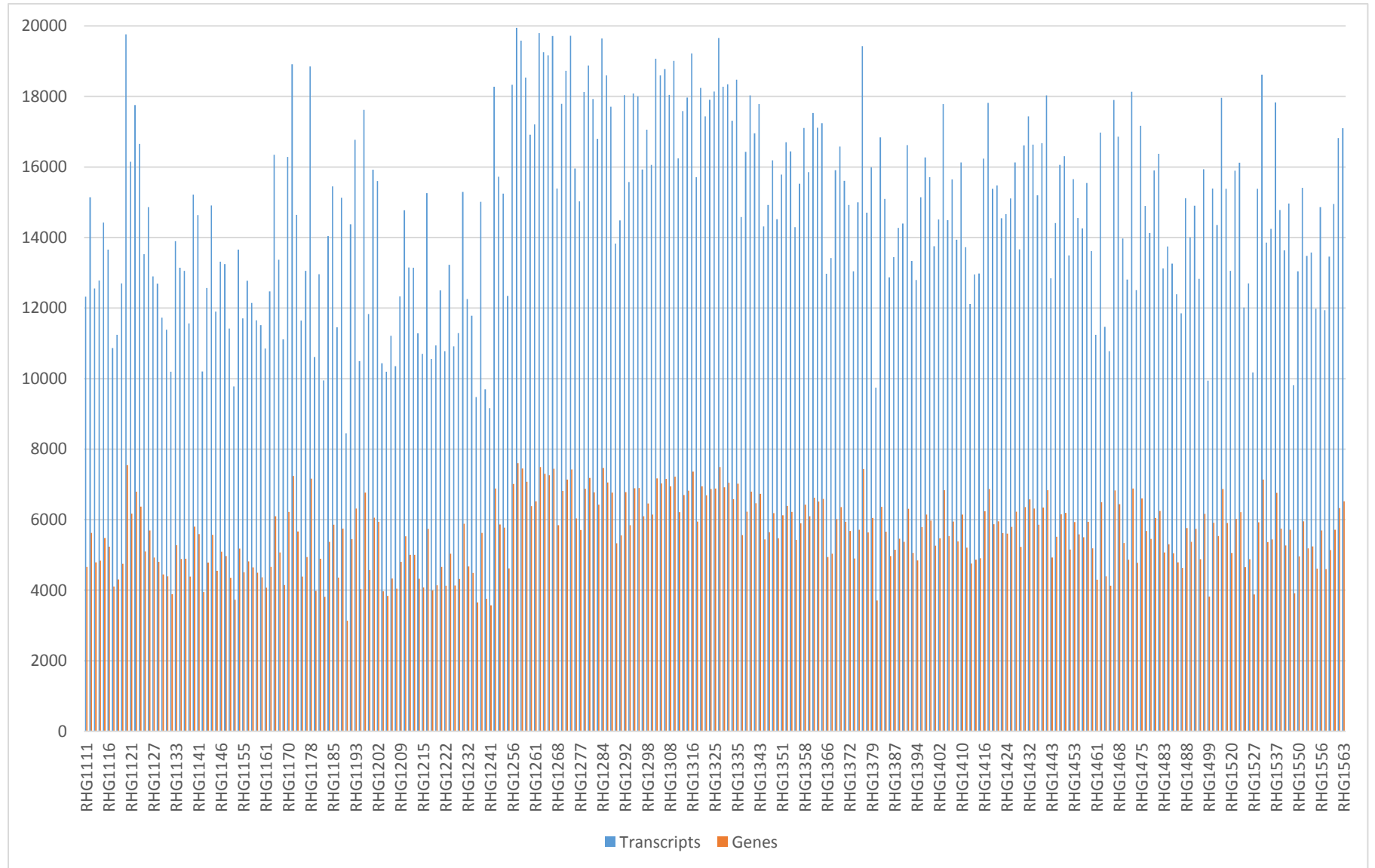
Supplementary figure 6: Hierarchical clustering of 118 *GCG* expressing cells using transcripts with RPKM values ≥ 500 in $\geq 2\%$ of cells. We however did not identify distinct sub-clustering of these *GCG* and *INS* cells, although some cells were separated based on relative expression on *TTR*. Repeating these analyses using less stringent transcript RPKM cut-off (RPKM values ≥ 50 in $\geq 2\%$ of cells) did not change main findings (data not shown)



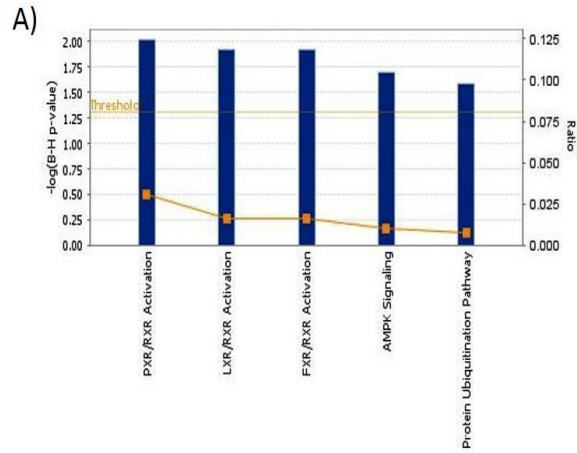
Supplementary figure 7: Hierarchical clustering of 105 *INS* expressing cells using transcripts with RPKM values ≥ 500 in $\geq 2\%$ of cells. We however did not identify distinct sub-clustering of these *GCG* and *INS* cells, although some cells were separated based on relative expression on *RNR2*. Repeating these analyses using less stringent transcript RPKM cut-off (RPKM values ≥ 50 in $\geq 2\%$ of cells) did not change main findings (data not shown)



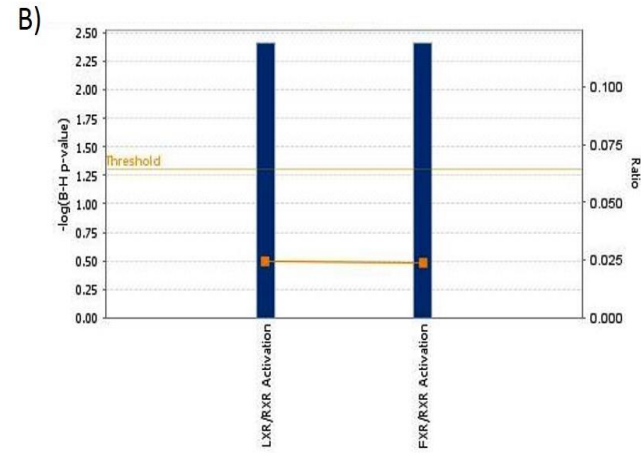
Supplementary figure 8: Number of transcripts and genes detected at each of the 276 cells that passed QC.



Supplementary figure 9: A) 5 significant canonical pathways identified from 11 significant β -cell genes. B) 2 significant canonical pathways identified from 17 significant α -cell genes. Threshold line represent p-value cut-off for significant pathways after Benjamini-Hochberg correction. Ratio represent proportion of input genes in canonical pathway.

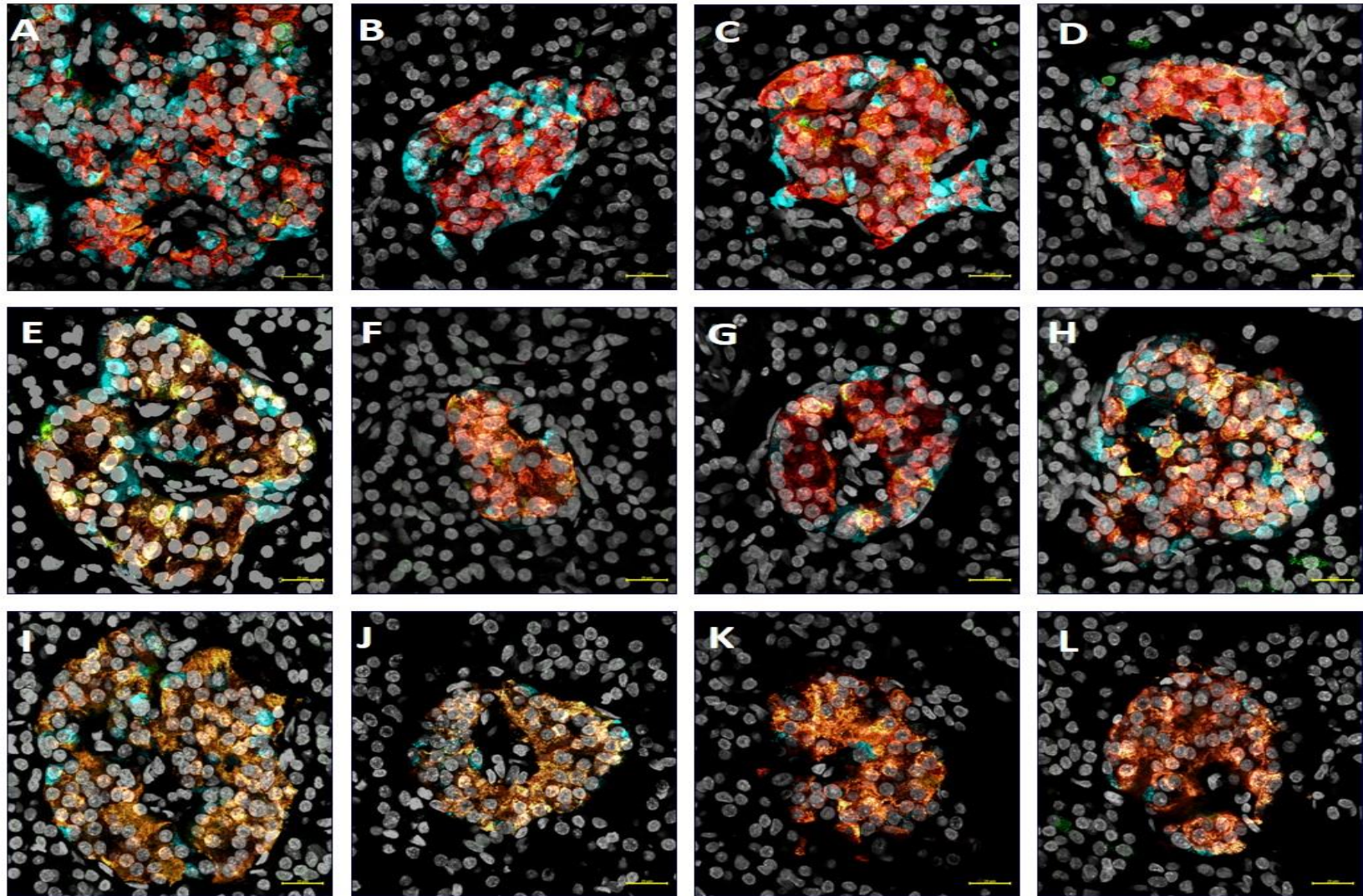


Ingenuity Canonical Pathways	$-\log(\text{B-H p-value})$	Molecules
PXR/RXR Activation	2.02	SCD,INS
LXR/RXR Activation	1.92	SCD,HADH
FXR/RXR Activation	1.92	G6PC2,INS
AMPK Signaling	1.70	INS,PFKFB2
Protein Ubiquitination Pathway	1.59	UCL1,DNAJC3

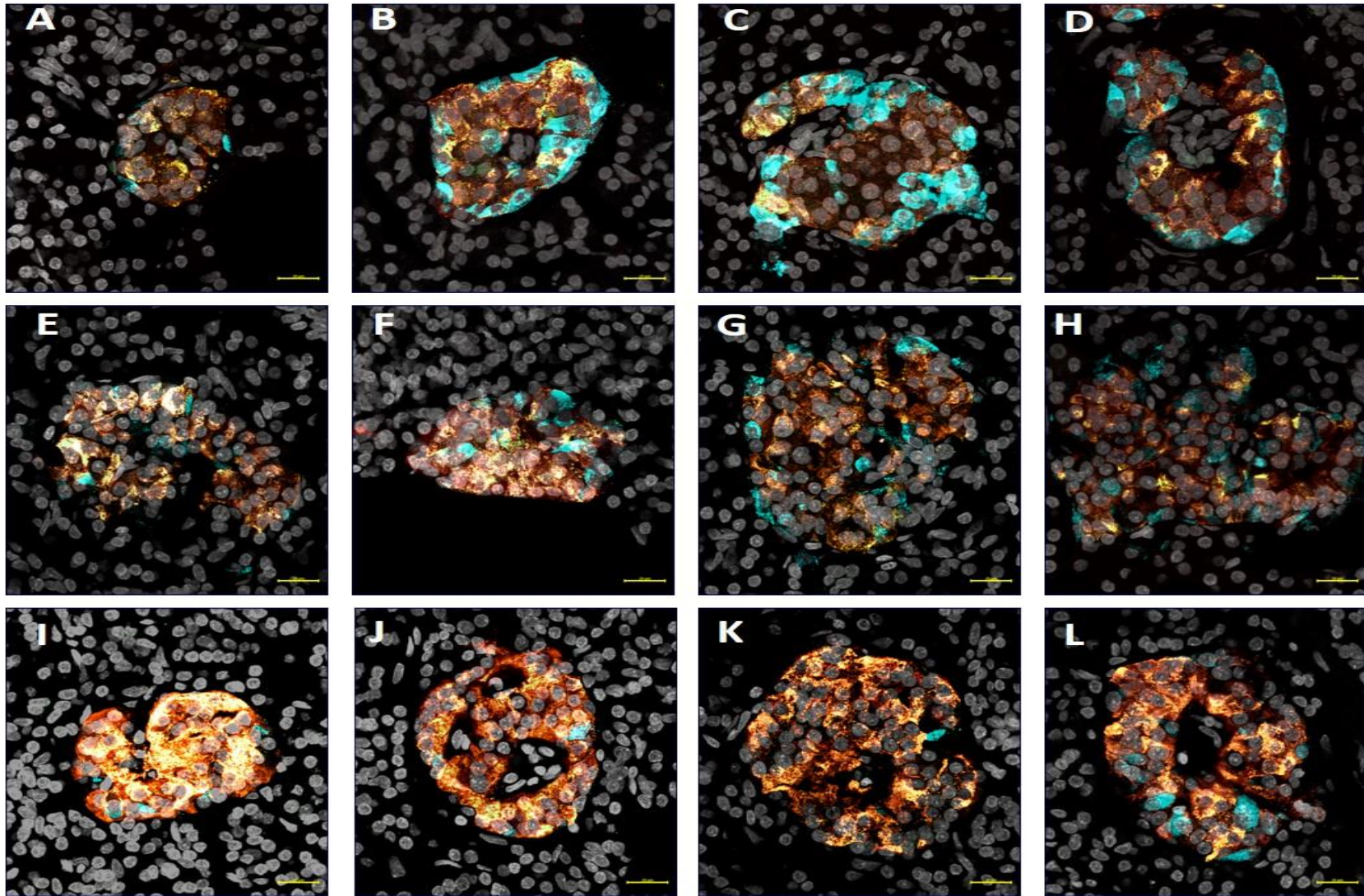


Ingenuity Canonical Pathways	$-\log(\text{B-H p-value})$	Molecules
LXR/RXR Activation	2.41	TTR,GC,CLU
FXR/RXR Activation	2.41	TTR,GC,CLU

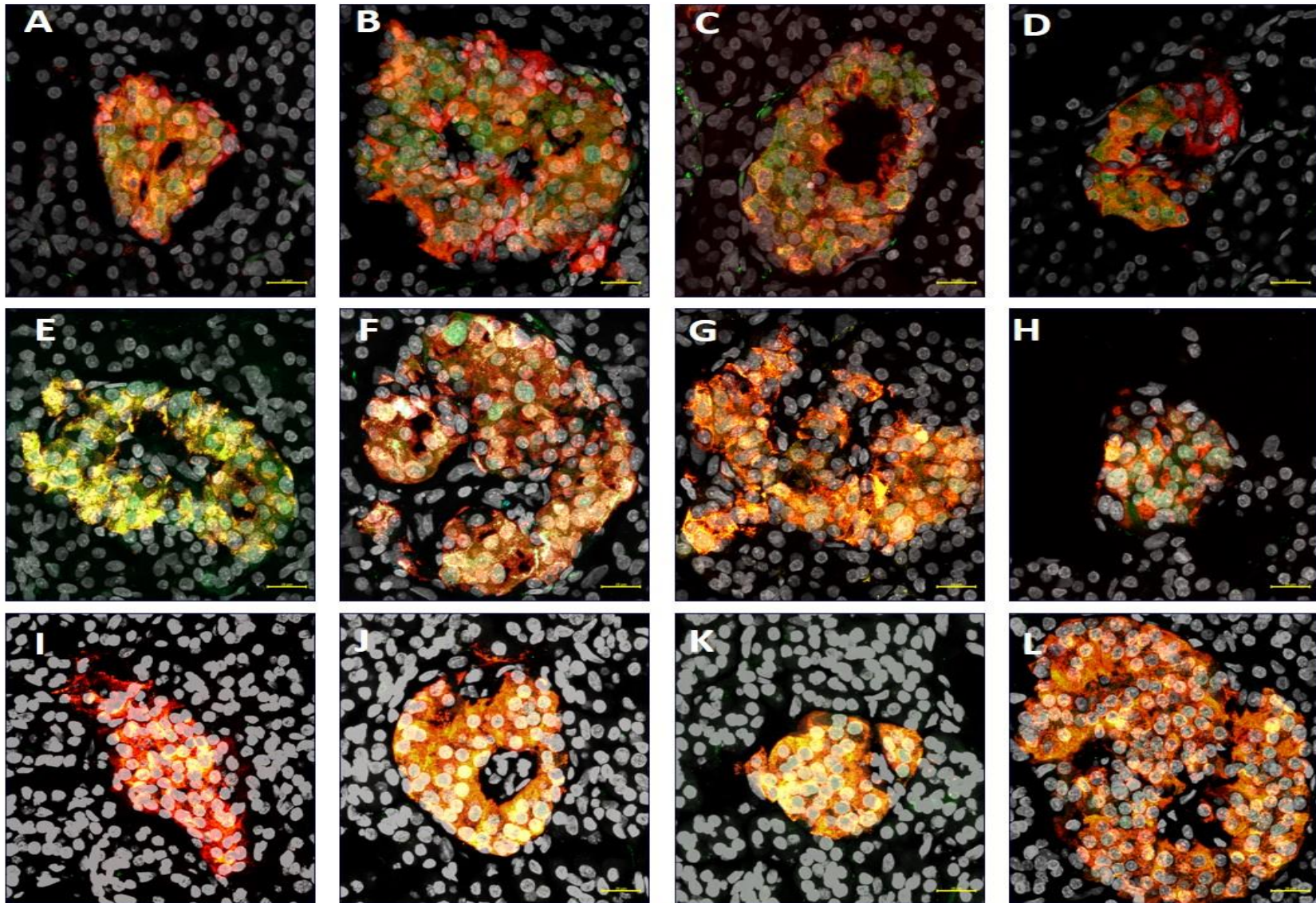
Supplementary 10: Additional immunofluorescence sections showing co-localization of DNAJC3 with INS+ cells from pancreas of three different subjects. Subject 1 (1A-D), subject 2 (1E-H) and subject 3 (1I-L). DNAJC3 (green), INS (red), GCG (blue) and nucleus (grey) stains. Cell co-expressing INS and DNAJC indicated in yellow. Scale bar represents 20µm.



Supplementary 11: Additional immunofluorescence sections showing co-localization of PFKB2 with INS+ cells from pancreas of three different subjects. Subject 1 (1A-D), subject 2 (1E-H) and subject 3 (1I-L). PFKB2 (green), INS (red), GCG (blue) and nucleus (grey) stains. Cell co-expressing INS and PFKB2 indicated in yellow. Scale bar represents 20 μ m.

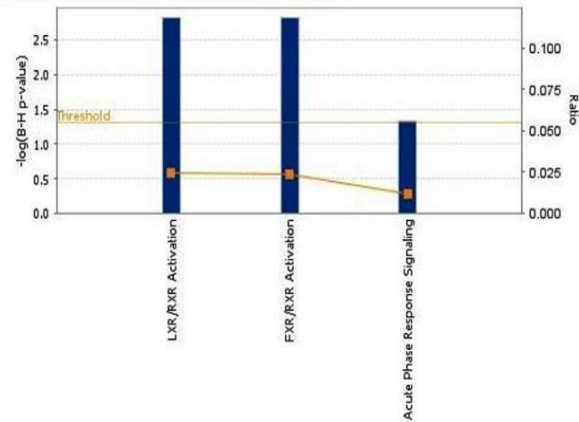


Supplementary 12: Additional immunofluorescence sections showing co-localization of UCHL1 with INS⁺ cells from pancreas of three different subjects. Subject 1 (1A-D), subject 2 (1E-H) and subject 3 (1I-L). UCHL1 (green), INS (red) and nucleus (grey) stains. Cell co-expressing INS and UCHL1 indicated in yellow. Scale bar represents 20μm.



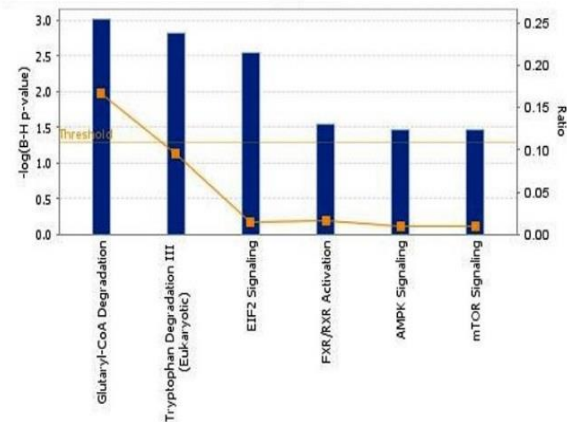
Supplementary figure 13: A) 3 significant canonical pathways identified from 16 common α -cell genes. B) 6 significant canonical pathways identified from 14 common β -cell genes. Threshold line represent p-value cut-off for significant pathways after Benjamini-Hochberg correction. Ratio represent proportion of input genes in canonical pathway.

A)



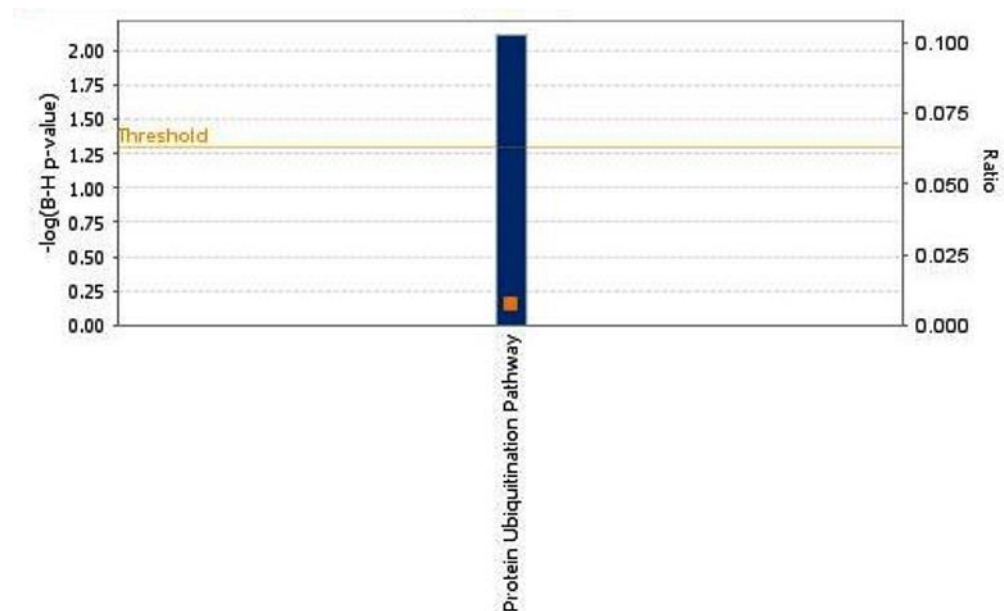
Ingenuity Canonical Pathways	$-\log(\text{B-H p-value})$	Molecules
LXR/RXR Activation	2.83	TTR, SERPINA1, GC
FXR/RXR Activation	2.83	TTR, SERPINA1, GC
Acute Phase Response Signaling	1.32	TTR, SERPINA1

B)



Ingenuity Canonical Pathways	$-\log(\text{B-H p-value})$	Molecules
Glutaryl-CoA Degradation	3.01	ACAT1, HADH
Tryptophan Degradation III (Eukaryotic)	2.81	ACAT1, HADH
EIF2 Signaling	2.54	RPL3, INS, EIF4A2
FXR/RXR Activation	1.56	G6PC2, INS
AMPK Signaling	1.47	INS, PFKFB2
mTOR Signaling	1.47	INS, EIF4A2

Supplementary figure 14: Canonical pathways detected from Ingenuity pathway analysis of unique β -cell genes (significantly high in only our study). No pathways remained significant after p-value corrections from unique α -cell gene list. Threshold line represent p-value cut-off for significant pathways after Benjamini-Hochberg correction. Ratio represent proportion of input genes in canonical pathway.



Ingenuity Canonical Pathways	$-\log(\text{B-H p-value})$	Molecules
Protein Ubiquitination Pathway	2.11	UCHL1,DNAJC3

Supplementary figure 15: Protein ubiquitination pathway identified to be significantly associated in East-Asian β -cells. Gene highlighted in green: UCHL1. Gene highlighted in orange: DNAJC3. Canonical pathway analysis performed using Ingenuity Pathway Analysis (version 1-07). Mean (SD) RPKM of UCHL1 in β -cells = 66.8 (66.9), Mean (SD) RPKM of UCHL1 in α -cells = 25.6 (41.6), Mean (SD) RPKM of DNAJC3 in β -cells = 134.3 (136.7) and Mean (SD) RPKM of DNAJC3 in α -cells = 70.6 (73.9).

