

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Organ Donor		
HPAP-126 (Figure 4F)	Human Pancreas Analysis Program	RRID:SAMN30486796
Islets (Figure 4A-E)	IIDP	RRID: SAMN41789873
Animals		
NSG	The Jackson Laboratory	RRID:IMSR_JAX:005557
CRISPR reagents		
Alt-R S.p. Cas9 D10A Nickase V3	IDT	CAT# 1081062
Alt-R CRISPR-Cas9 tracrRNA, 20 nmol	IDT	CAT# 1072533
Alt-R CRISPR-Cas9 crRNA, 2 nmol (5'- TTCGGTCCCCAGAGTCGCTG -3')	IDT	N/A; Custom
Alt-R CRISPR-Cas9 crRNA, 2 nmol (5'- CTTAACATCCTGAGCACTCT -3')	IDT	N/A; Custom
5'- ATTCCCCCAGGACCCTCAGTGA CTTCC CTCCCTAATACCGCCCGCAGCGACTCT GGGGACTGAAGGCAGATCCTTAACATC CTGAGCACTCTGGGCCTTCGACCCTCT GTCGCCGACTGCG -3'	IDT	N/A; Custom
Primers and TaqMan probes		
Gck_F7: 5' – GGCATTGTCATCCTCACGAC – 3'	IDT	N/A; Custom
Gck_R7 5' – CCAGGGAGAATCAAGCAGGA – 3'	IDT	N/A; Custom
TaqMan probe ANU644V	Thermo Fisher Scientific	CAT# 4332075
Glucose monitoring, hormone detection and insulin		
AlphtaTRAK2 automatic glucometer	Zortis	N/A

AlphaTRAK2 test strips	Zortis	N/A
Human insulin ELISA kit (Figure 5)	Mercodia	CAT# 10-1132-01
Human insulin ELISA kit (Figure 4)	Crystal Chem	CAT# 90095
Mouse insulin ELISA kit	Crystal Chem	CAT# 90080
Mouse glucagon ELISA kit	Crystal Chem	CAT# 81518
Lantus Insulin U100	Midwest Vet Supply	CAT# 191.49250.3
Software		
GraphPad Prism (v9.4.1)	GraphPad Software	https://www.graphpad.com/ ; RRID:SCR_002798
Fiji	Schindelin et al., 2012	https://imagej.net/Fiji/ ; RRID:SCR_002285
Ilastik 1.3.3	Stuart et al., 2019	https://www.ilastik.org/ ; RRID:SCR_015246
Cellprofiler 3.1.9	Carpenter et al., 2006	https://cellprofiler.org/ ; RRID:SCR_007358
Antibodies		
Rabbit anti-insulin	Proteintech	CAT# 15848-1-AP; RRID:AB_10597100
Mouse anti-glucagon	Santa Cruz Biotechnology	CAT# sc-514592; RRID:AB_2629431
IMC Antibodies		
141Pr-HLA-ABC (Clone EMR8-5)	BD Biosciences	Cat#565292
142Nd-CD57 (Clone HCD57)	Fluidigm	Cat#3142007B
143Nd-CD31 (Clone C31.3+C31.7+C31.10)	LifeSpan BioSciences	Cat#LS-C390863-100
144Nd- CD14 (Clone EPR3653)	Fluidigm	Cat#3144025D
145Nd-C- peptide (Clone 3A1)	Thermo	Cat#MA1-22710; RRID: AB_558517
146Nd-Nestin (Clone 196908)	Fluidigm	Cat#3146015B

147Sm-Glucagon (Clone C-11)	Santa Cruz	Cat#sc-514592; RRID: AB_2629431
148Nd-Pan-Keratin (Clone C11)	Fluidigm	Cat#3148020D
149Sm-CD11b (Clone EPR1344)	Fluidigm	Cat#3149028D
150Nd-CD44 (Clone IM7)	Fluidigm	Cat#3150018B
151Eu-PDX1	R&D systems	Cat#AF2419; RRID: AB_355257
152Sm-CD45 (Clone 2B11)	Fluidigm	Cat#3152016D
153Eu-CD56	Proteintech	Cat#14255-1-AP; RRID: AB_2149421
154Sm-Beta-actin (Clone 2F1-1)	Fluidigm	Cat#3154021D
155Gd-FoxP3 (Clone 236A/E7)	Fluidigm	Cat#3155016D
156Gd-CD4 (Clone EPR6855)	Fluidigm	Cat#3156033D
158Gd-NKX6.1	Sigma	Cat#HPA036774; RRID: AB_10673664
159Tb-CD68 (Clone KP1)	Fluidigm	Cat#3159035D
160Gd-Somatostatin (G-10)	Santa Cruz	Cat#sc-13099; RRID: AB_2195930
161Dy-CD20 (Clone H1)	Fluidigm	Cat#3161029D
162Dy-CD8 (Clone C8/144B)	Fluidigm	Cat#3162034D
164Dy-CD99	R&D systems	Cat#AF3968; RRID: AB_2076301
165Ho-CA2	Rockland	Cat#200-401-136S; RRID: AB_2612117
166Er-NF- κ B (Clone K10895.12.50)	Fluidigm	Cat#3166006A
167Er-Granzyme B (Clone EPR20129-217)	Fluidigm	Cat#3167021D
168Er-Ki67 (Clone B56)	Fluidigm	Cat#3168022D
169Tm-Collagen Type 1	Fluidigm	Cat#3169023D
170Er-CD3	Fluidigm	Cat#3170019D
171Yb-p16 (Clone 2D9A12)	Abcam	Cat#ab54210

172Yb-pS6 (Clone N7-548)	Fluidigm	Cat#3172008A
173Yb-CD45RO (UCHL1)	Fluidigm	Cat#3173016D
174Yb-HLA-DR (Clone TAL 1B5)	Abcam	Cat#ab20181; RRID: AB_445401
175Lu-Pancreatic Polypeptide	Abcam	Cat#ab77192; RRID: AB_1524152
176Yb-Ghrelin	Santa Cruz	Cat#sc-10368; RRID: AB_2232479
1X Trace Element B	BD Biosciences	Cat# 25-022-CI
Penicillin-Streptomycin	Thermo Fisher Scientific	Cat# 15140122
SC-islet maintenance and differentiation		
ROCK Inhibitor Y-27632	Stem Cell Technologies	Cat# 72307
mTeSR1	Stem Cell Technologies	Cat# 85850
DMEM/F12	VWR	Cat# 45000-346
MCDB 131	Thermo Fisher Scientific	Cat# 10372-019
Bovine Serum Albumin (BSA) Fraction V	Life Technologies	Cat# 15260-037
Matrigel	BD Biosciences	Cat# 356231
Nonessential Amino Acids (100x)	Thermo Fisher Scientific	Cat# 00-4555-56
Accutase	Thermo Fisher Scientific	Cat# 00-4555-56
Recombinant Mouse Wnt3A	R&D Systems	Cat# 1324-WN/CF
Activin A	R&D Systems	Cat# 338-AC/CF
ALK5 inhibitor II (ALK5i II)	Enzo Life Sciences	Cat# ALX-270-445
	Cayman Chemicals	Cat# 14794
L-Ascorbic Acid (Vitamin C)	Sigma-Aldrich	Cat# A4544
BSA	Proliant	Cat# 68700
CHIR99021	SelleckChem	Cat# S294
γ -secretase inhibitor XX	Calbiochem,	Cat# 565789

D-Glucose	Thermo Fisher Scientific	Cat# D161
GlutaMAX	Thermo Fisher Scientific	Cat# 35050061
Heparin	Sigma-Aldrich	Cat# H3149
Insulin-Transferrin-Selenium- Ethanolamine (ITS-X)	Thermo Fisher Scientific	Cat# 51500056
Recombinant KGF/FGF-7	R&D Systems	Cat# 251-KG/CF
LDN193189	Stemgent	Cat# 04-0074
N-Acetyl-L-cysteine	Sigma-Aldrich	Cat# A9165
Retinoic Acid (RA)	Sigma-Aldrich	Cat# R2625
SANT-1	Sigma-Aldrich	Cat# S4572
Sodium bicarbonate (NaHCO ₃)	Sigma-Aldrich	Cat# S6297
3,3',5-Triiodo-L-thyronine sodium salt (T3)	Sigma-Aldrich	Cat# T6397
TPB	Calbiochem	Cat# 565740
Zinc sulfate heptahydrate (ZnSO ₄)	Sigma-Aldrich	Cat# Z0251
MEM nonessential amino acid	Thermo Fisher Scientific	Cat# 11140076
1X Trace Element A	BD Biosciences	Cat# 25-021-CI
1X Trace Element B	BD Biosciences	Cat# 25-022-CI
Penicillin-Streptomycin	Thermo Fisher Scientific	Cat# 15140122