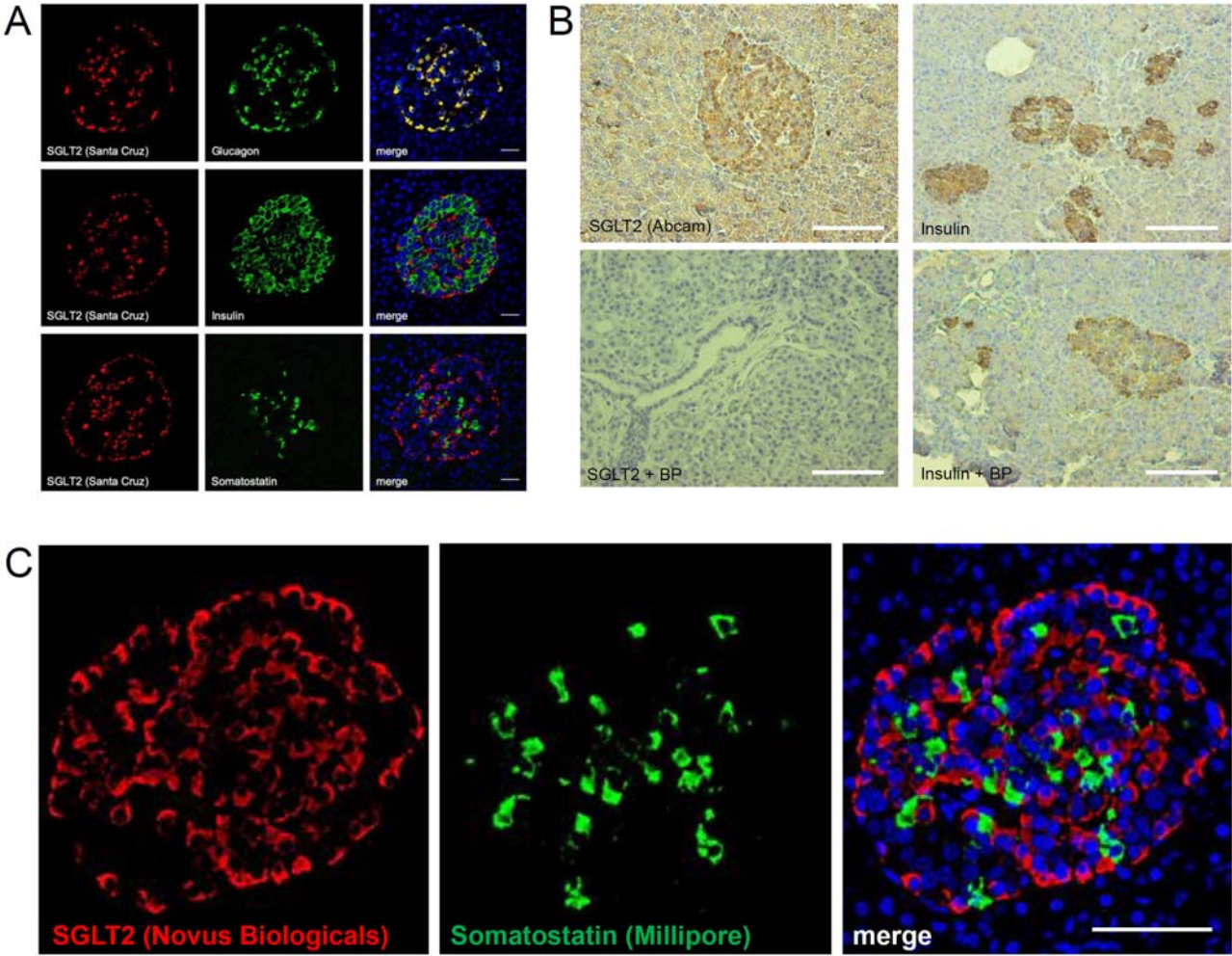


SUPPLEMENTARY DATA

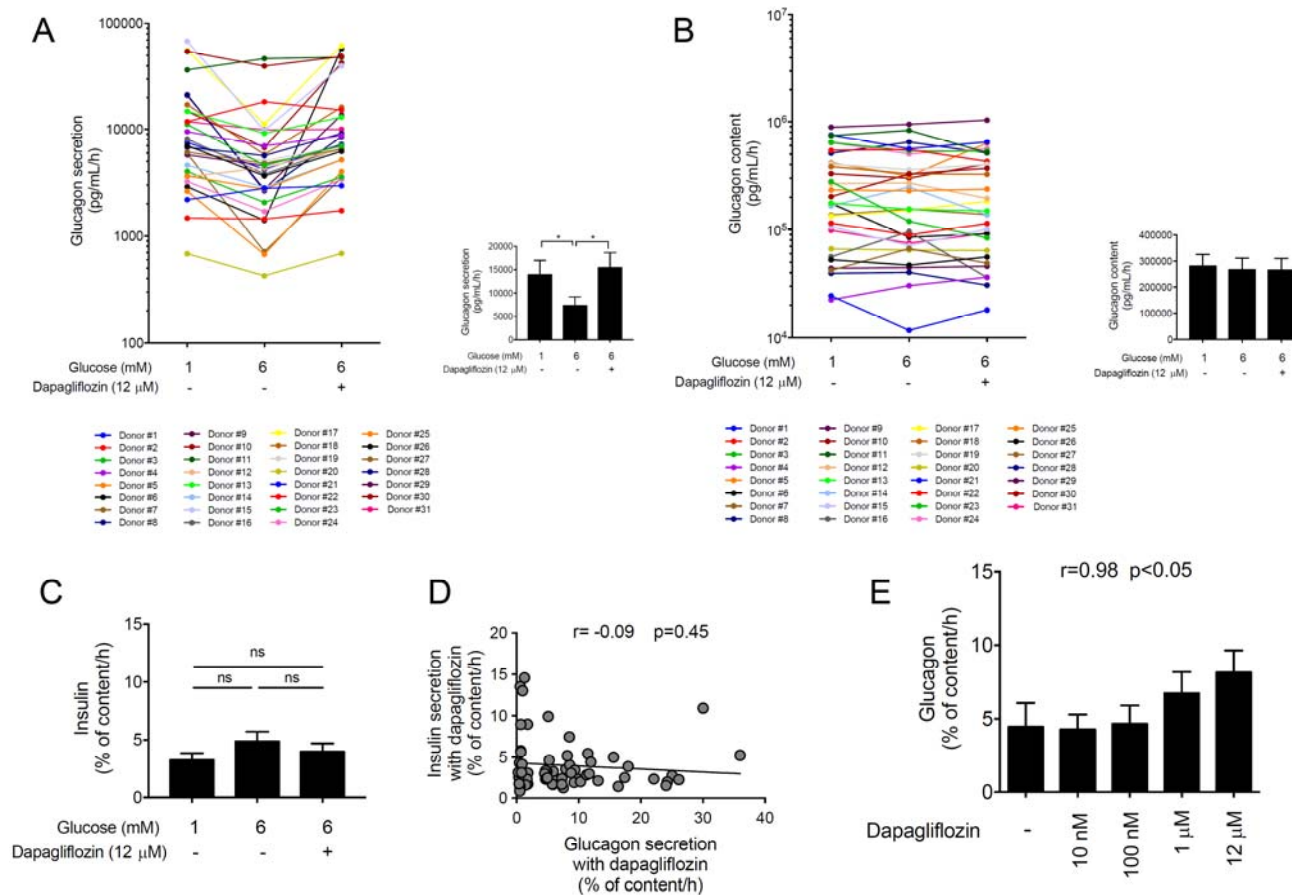
Supplementary Figure 1. Immunofluorescence and immunohistochemistry with different anti-SGLT2 antibodies confirm SGLT2 protein expression in human pancreatic islets. (A) Representative images of immunofluorescence staining for SGLT2 (Santa Cruz) (red), glucagon (Abcam) (green), insulin (Abcam) (green) and somatostatin (Dako) (green) performed on formalin-fixed paraffin-embedded tissue sections from human pancreas (donor H1043). DAPI, blue. Scale bars, 20 μm . (B) Representative images of immunohistochemical staining for SGLT2 (Abcam) and insulin (Dako) performed on formalin-fixed paraffin-embedded tissue sections (donor H1043), alone or in combination with the specific blocking peptide for SGLT2 (Abcam). Scale bars, 200 μm . (C) Representative images of immunofluorescence staining for SGLT2 (Novus Biologicals) (red) and somatostatin (Merck Millipore) (green) performed on formalin-fixed paraffin-embedded tissue sections from human pancreas (donor H1043). DAPI, blue. Scale bars, 20 μm .

SUPPLEMENTARY DATA



SUPPLEMENTARY DATA

Supplementary Figure 2. Glucagon and insulin secretion from $n = 31$ donor islet preparations. (A) Glucagon secretion (pg/mL/h) and (B) intracellular content (pg/mL/h) of islets incubated at 1 mM and at 6 mM glucose with or without dapagliflozin (12 μ M). Data are expressed on a logarithmic scale. (C) Insulin secretion (normalized to insulin content per hour) at 1 mM and 6 mM glucose with or without dapagliflozin (12 μ M) ($n = 16$ human islet preparations). Data are expressed as median \pm SEM; two-way analysis of variance (ANOVA) and Tukey's multiple comparison test were used. (D) Linear regression between glucagon secretion and insulin secretion at 6 mM glucose with dapagliflozin ($r=-0.09$; $p=0.45$). (E) Glucagon secretion (normalized to glucagon content per hour) at 6 mM glucose with or without several concentrations of dapagliflozin (10 nM, 100 nM, 1 μ M and 12 μ M) ($n = 6$ human islet preparations).



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Supplementary Table 1. Gene ID, median expression as Transcripts per Million (TPM) and coefficient of variation of selected genes analyzed from TIGER database.

Ensembl ID	Short ID	Median expression (TPM)	Coefficient of variation	Gene name
ENSG00000172987	HPA2	0.072	0.81	heparanase 2 (inactive)
ENSG00000140675	SLC5A2	1.255	1.24	solute carrier family 5 member 2
ENSG00000004848	ARX	3.753	1.02	aristaless related homeobox
ENSG00000106633	GCK	11.111	0.66	glucokinase
ENSG00000152804	HHEX	20.472	0.52	hematopoietically expressed homeobox
ENSG00000139515	PDX1	20.381	1.05	pancreatic and duodenal homeobox 1
ENSG00000130816	DNMT1	20.518	0.85	DNA methyltransferase 1
ENSG00000163623	NKX6.1	24.138	0.63	NK6 homeobox 1
ENSG00000117394	SLC2A1	29.395	1.05	solute carrier family 2 member 1
ENSG00000163581	SLC2A2	4.637	1.03	solute carrier family 2 member 2
ENSG00000115263	SLC5A1	8.219	0.71	solute carrier family 5 member 1
ENSG00000115263	GCG	8909.600	1.42	glucagon
ENSG00000254647	INS	38105.000	1.69	insulin
ENSG00000157005	SST	2943.400	0.66	somatostatin
ENSG00000100604	CHGA	588.470	1.09	chromogranin A
ENSG00000121351	IAPP	930.170	0.75	islet amyloid polypeptide

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Supplementary Table 2. Checklist for Reporting Human Islet Preparations Used in Research

Adapted from Hart NJ, Powers AC (2018) Progress, challenges, and suggestions for using human islets to understand islet biology and human diabetes. Diabetologia <https://doi.org/10.1007/s00125-018-4772-2>.

Manuscript DOI: https://doi.org/10.2337/[insert manuscript submission number] (Example, https://doi.org/10.2337/db18-1234)								
Title: Inter-Individual Heterogeneity of SGLT2 Expression and Function in Human								
Author list: Chiara Saponaro, Markus Mühlemann, Ana Acosta-Montalvo, Anthony Piron, Valery Gmyr, Nathalie Delalleau, Ericka Moerman, Julien Thévenet, Gianni Pasquetti, Anais Coddeville, Miriam Cnop, Julie Kerr-Conte, Bart Staels, François Pattou & Caroline Bonner								
Corresponding author: Caroline Bonner					Email address: caroline.bonner@univ-lille.fr			
Islet preparation	1	2	3	4	5	6	7	8
MANDATORY INFORMATION								
Unique identifier	H596	H638	H717	H730	H738	H774	H777	H818
Donor age (years)	48	55	45	57	44	67	48	23
Donor sex (M/F)	M	F	M	M	M	M	F	M
Donor BMI (kg/m ²)	30.2	22.4	30.9	22.6	22.8	27.8	35.2	24.9
Donor HbA _{1c} or other measure of blood glucose control	5.6	7.7	6.0	5.5	5.4	6.2	5.6	5.4
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	No	No	No	Yes	No	No
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	-	-	0	0	0	-	0	0
Glucose-lowering therapy at time of death ^c	Metformin	No	No	No	No	Velmetia & Glucor	No	No
RECOMMENDED INFORMATION								
Donor cause of death	Traumatic	Stroke	Cerebral Haemorrhage	Traumatic	Brain Hematoma	Brain Hematoma	Stroke	Traumatic
Warm ischaemia time (h)	0	0	0	0	0	0	0	0
Cold ischaemia time (h)	5.58	3.05	8.92	5.02	6.62	6.93	4.30	9.85
Estimated purity (%)	70	N/A	45	70	90	85	65	80
Estimated viability (%)	95.8	89	97.7	98.5	97.8	97.4	94	95.2
Total culture time (h) ^d	12	16	20	21	18	18	46	20
Glucose-stimulated insulin secretion or other functional measurement ^e	GSIS: 1,82	N/A	GSIS: 1,98	GSIS: 3,85	GSIS: 1,44	GSIS: 2,32	GSIS: 1,13	GSIS: 0,96
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No	No	No	No	No

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Additional notes	Used for immunostaining	Used for immunostaining	Used for immunostaining	Used for immunostaining	Used for immunostaining	Used for immunostaining	Used for immunostaining	Used for static incubation
Islet preparation	9	10	11	12	13	14	15	16
MANDATORY INFORMATION								
Unique identifier	H819	H823	H836	H840	H845	H846	H847	H848
Donor age (years)	53	40	44	68	66	48	52	58
Donor sex (M/F)	F	F	F	F	F	M	M	M
Donor BMI (kg/m ²)	18.3	25.6	17.1	33.5	22.6	25	41.3	33.8
Donor HbA _{1c} or other measure of blood glucose control	5.9	4.7	6.0	5.8	5.6	5.6	5.6	6.6
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190
Donor history of diabetes? Please select yes/no from drop down list	No	No	No	No	No	No	No	No
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0	0	0	0	0	0	0	0
Glucose-lowering therapy at time of death ^c	No	No	No	No	No	No	No	No
RECOMMENDED INFORMATION								
Donor cause of death	Cerebral Haemorrhage	Cerebral Haemorrhage	Anoxia	Stroke	Stroke	Cerebral Haemorrhage	Cerebral Haemorrhage	Cerebral Haemorrhage
Warm ischaemia time (h)	0	0	0	0	0	0	0	0
Cold ischaemia time (h)	4.50	7.30	6.07	7.27	6.13	4.38	3.50	8.98
Estimated purity (%)	65	95	80	50	75	80	50	70
Estimated viability (%)	94.5	96.2	95.5	97.4	95.7	95.2	98.8	91.9
Total culture time (h) ^d	18	18	18	61	20	41	18	18
Glucose-stimulated insulin secretion or other functional measurement ^e	N/A	GSIS: 0,43	GSIS: 0,59	GSIS: 1,39	GSIS: 2,47	GSIS: 1,25	GSIS: 6,93	GSIS: 2,18
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No	No	No	No	No
Additional notes	Used for static incubation	Used for static incubation	Used for static incubation	Used for immunostaining	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation
Islet preparation	17	18	19	20	21	22	23	24
MANDATORY INFORMATION								
Unique identifier	H850	H904	H905	H909	H912	H913	H920	H925
Donor age (years)	24	51	65	58	65	56	63	32
Donor sex (M/F)	M	M	F	F	F	F	F	F
Donor BMI (kg/m ²)	24.9	28.6	28.7	33.7	27	34.5	21.3	23.4
Donor HbA _{1c} or other measure of blood glucose control	4.9	4.8	6.5	5.7	6.1	7.9	5.8	5.2
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190

SUPPLEMENTARY DATA

Donor history of diabetes? Please select yes/no from drop down list	No	No	No	No	No	Yes	No	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0	0	0	0	0	-	0	9
Glucose-lowering therapy at time of death ^c	No	No	No	No	No	-	No	Insulin
RECOMMENDED INFORMATION								
Donor cause of death	Traumatic	Stroke	Stroke	Stroke	Traumatic	Stroke	Ruptured Aneurysm	Stroke
Warm ischaemia time (h)	0	0	0	0	0	0	0	0
Cold ischaemia time (h)	3.87	5.37	6.28	5.08	7.60	5.07	6.33	4.67
Estimated purity (%)	90	80	80	80	85	70	90	70
Estimated viability (%)	93.2	88.9	95.4	94.3	96.5	98.4	98.8	93.6
Total culture time (h) ^d	39	15	15	18	36	18	44	20
Glucose-stimulated insulin secretion or other functional measurement ^e	GSIS: 0,92	GSIS: 7,05	GSIS: 2,17	GSIS: 1,13	GSIS: 1,59	GSIS: 1,15	GSIS: 0,55	GSIS: 1,1
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No	No	No	No	No
Additional notes	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation
Islet preparation	25	26	27	28	29	30	31	32
MANDATORY INFORMATION								
Unique identifier	H927	H940	H943	H950	H951	H957	H961	H962
Donor age (years)	36	53	48	58	51	56	51	64
Donor sex (M/F)	F	M	F	F	H	H	F	F
Donor BMI (kg/m ²)	30.9	32.8	22	19,2	23,1	26	17,3	21,4
Donor HbA _{1c} or other measure of blood glucose control	5.1	6.2	5,7	-	-	-	5,4	6
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190
Donor history of diabetes? Please select yes/no from drop down list	No	No	No	No	No	No	No	No
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0	0	0	0	0	0	0	0
Glucose-lowering therapy at time of death ^c	No	No	No	No	No	No	No	No
RECOMMENDED INFORMATION								
Donor cause of death	Stroke	Cerebral Haemorrhage	Autolysis	Cardio vascular accident	Traumatic	Cardio vascular accident	Brain Hematoma	Cerebral Haemorrhage
Warm ischaemia time (h)	0	0	0	0	0	0	0	0
Cold ischaemia time (h)	4.37	6.20	4,15	3,87	2,77	4,13	4,9	9,55

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Estimated purity (%)	70	80	60	90	90	90	90	90
Estimated viability (%)	93.1	93.7	95,3	98,5	96,2	94,9	97,3	95
Total culture time (h) ^d	56	18	18	16	18	54	30	21
Glucose-stimulated insulin secretion or other functional measurement ^e	GSIS: 1,16	GSIS: 3,67	GSIS: 2,67	GSIS: 1,37	GSIS: 1,09	GSIS: 1,02	GSIS: 1,38	GSIS: 0,92
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No	No	No	No	No
Additional notes	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation	Used for static incubation
Islet preparation	33	34	35	36	37	38	39	40
MANDATORY INFORMATION								
Unique identifier	H964	H970	H971	H974	H986	H993	H1011	H1012
Donor age (years)	54	64	66	22	52	63	42	55
Donor sex (M/F)	H	H	H	H	H	H	H	H
Donor BMI (kg/m ²)	40,6	37,2	28,4	21,6	22,9	25,9	34,7	23,5
Donor HbA _{1c} or other measure of blood glucose control	6	5,8	9,5 DTII :OUI	5,5	5,9	5,3	5,3	5
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190
Donor history of diabetes? Please select yes/no from drop down list	No	No	Yes	No	No	No	No	No
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0	0	-	0	0	0	0	0
Glucose-lowering therapy at time of death ^c	No	No	-	No	No	No	No	No
RECOMMENDED INFORMATION								
Donor cause of death	Cardio vascular accident	Traumatic	Cardio vascular accident	Cardio vascular accident	Cardio vascular accident	Cardio vascular accident	Traumatic	Cardio vascular accident
Warm ischaemia time (h)	0	0	0	0	0	0	0	0
Cold ischaemia time (h)	3,9	5,7	5,95	4,5	5,97	7,23	6,57	2,22
Estimated purity (%)	70	80	0	80	80	80	30	90
Estimated viability (%)	97,1	93,9	0	98,3	96,3	98,7	94,8	96,9
Total culture time (h) ^d	19	18	0	42	18	18	18	72
Glucose-stimulated insulin secretion or other functional measurement ^e	GSIS: 1,26	GSIS: 1,31	N/A	GSIS: 1,38	GSIS: 11,6	GSIS: 3,8	GSIS: 2,02	GSIS: 3,16
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No	No	No	No	No

SUPPLEMENTARY DATA

Additional notes	Used for static incubation	Used for static incubation	Used for immunostaining	Used for static incubation	Used for static incubation	Used for static incubation	Used for immunostaining	Used for static incubation
Islet preparation	41	42	43	44	45	46	47	48
MANDATORY INFORMATION								
Unique identifier	H1014	H1032	H1034	H1040	H1043	H1051	H1058	H1061
Donor age (years)	54	35	68	40	52	26	47	32
Donor sex (M/F)	F	H	H	H	F	F	F	H
Donor BMI (kg/m ²)	45,3	35,2	37,1	26,5	19,8	38,6	26	24,7
Donor HbA _{1c} or other measure of blood glucose control	5,7	5,4	6,4 DTII: OUI	6,6 DTII :OUI	5,3	5,6	6,1	5,4
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT	ECIT
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190	UMR1190
Donor history of diabetes? Please select yes/no from drop down list	No	No	Yes	Yes	No	No	No	No
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0	0	-	-	0	0	0	0
Glucose-lowering therapy at time of death ^c	No	No	-	-	No	No	No	No
RECOMMENDED INFORMATION								
Donor cause of death	Cardio vascular accident	Cardio vascular accident	Traumatic	Meningitis	Traumatic	Cardiac Arrest	Cardio vascular accident	Traumatic
Warm ischaemia time (h)	0	0	0	0	0	0	0	0
Cold ischaemia time (h)	4,78	4,57	7,15	3,08	4,2	6,68	3,03	8,72
Estimated purity (%)	90	80	70	60	90	70	70	90
Estimated viability (%)	96	95,5	95,7	91,4	94,5	96,2	96,5	90,1
Total culture time (h) ^d	24	18	22	20	48	18	63	14
Glucose-stimulated insulin secretion or other functional measurement ^e	GSIS: 1,13	GSIS: 7,19	GSIS: 5,63	GSIS: 3,92	GSIS: 6,46	GSIS: 4,09	GSIS: 4,26	GSIS: 1,95
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No	No	No	No	No
Additional notes	Used for Western-blot	Used for Western-blot	Used for Western-blot	Used for immunostaining and Western-blot	Used for immunostaining	Used for Western-blot	Used for Western-blot	Used for Western-blot
Islet preparation	49	50	51	52				
MANDATORY INFORMATION								
Unique identifier	H1067	H1069	H1073	H1091				
Donor age (years)	43	42	57	50				
Donor sex (M/F)	H	F	F	M				
Donor BMI (kg/m ²)	24,8	20,2	35,3	25,5				

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Donor HbA _{1c} or other measure of blood glucose control	5,2	5,4	6,4	5,7				
Origin/source of islets ^b	ECIT	ECIT	ECIT	ECIT				
Islet isolation centre	UMR1190	UMR1190	UMR1190	UMR1190				
Donor history of diabetes? Please select yes/no from drop down list	No	No	No	No				
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0	0	0	0				
Glucose-lowering therapy at time of death ^c	No	No	No	No				
RECOMMENDED INFORMATION								
Donor cause of death	Cardio vascular accident	Cardio vascular accident	Stroke	Traumatic				
Warm ischaemia time (h)	0	0	0	0				
Cold ischaemia time (h)	5,07	9,05	6,42	8,65				
Estimated purity (%)	80	90	80	70				
Estimated viability (%)	97,4	97,2	97,4	96,1				
Total culture time (h) ^d	15	20	16	19				
Glucose-stimulated insulin secretion or other functional measurement ^e	N/A	GSIS: 2,83	GSIS: 2,19	GSIS: 6,19				
Handpicked to purity? Please select yes/no from drop down list	No	No	No	No				
Additional notes	Used for Western-blot	Used for Western-blot	Used for Western-blot	Used for static incubation				

^aIf you have used more than eight islet preparations, please complete additional forms as necessary; ^bFor example, IIDP, ECIT, Alberta IsletCore; ^cPlease specify the therapy/therapies; ^dTime of islet culture at the isolation centre, during shipment and at the receiving laboratory; ^ePlease specify the test and the results

SUPPLEMENTARY DATA

Supplementary Table 3. Overview of antibodies and blocking peptides used for histology and Western blot analysis.

N°	Antibody	Manufacturer	Catalogue number	Species	Type	Technique	Dilution	Antigen Retrieval/preincubation
1	anti-SGLT2	Novus Biologicals	NBP1-92384	Rabbit	Polyclonal	Immunofluorescence	1:100	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
						Western Blot	1:1000	N/A
2	anti-insulin	Dako	A0564	Guinea pig	Polyclonal	Immunofluorescence	1:500	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
						Immunohistochemistry	1:200	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
3	anti-glucagon	Gentex	GTX10988	Mouse	Monoclonal	Immunofluorescence	1:1000	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
4	anti-somatostatin	Gentex	GTX71935	Mouse	Monoclonal	Immunofluorescence	1:500	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
5	anti-somatostatin	Merck Millipore	MAB354	Rat	Polyclonal	Immunofluorescence	1:500	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
6	Blocking peptide against NBP1-92384	Novus Biologicals	NBP1-92384PEP	N/A	N/A	Immunohistochemistry	10x molecular excess	1h preincubation with primary antibody
7	anti-SGLT2	Santa Cruz	Sc-393350	Mouse	Monoclonal	Immunofluorescence	1:50	10mM citrate, 1mM EDTA Buffer pH: 6 Waterbath . Time: 30 minutes
8	anti-insulin	Abcam	ab63820	Rabbit	Polyclonal	Immunofluorescence	1:800	10mM citrate, 1mM EDTA Buffer pH: 6 Waterbath . Time: 30 minutes
9	anti-glucagon	Abcam	ab137817	Rabbit	Polyclonal	Immunofluorescence	1:800	10mM citrate, 1mM EDTA Buffer pH: 6 Waterbath . Time: 30 minutes
10	anti-somatostatin	Dako	A0566	Rabbit	Polyclonal	Immunofluorescence	1:500	10mM citrate, 1mM EDTA Buffer pH: 6 Waterbath . Time: 30 minutes
11	anti-SGLT2	Abcam	ab85626	Rabbit	Polyclonal	Immunohistochemistry	1:100	10mM tris-HCl, 1mM EDTA Buffer pH: 8 Microwave 650 W. Time: 9 minutes
						Western Blot	1:1000	N/A
12	Blocking peptide against ab85626	Abcam	ab101414	N/A	N/A	Immunofluorescence	10x molecular excess	1h preincubation with primary antibody
13	anti-SGLT1	Merck Millipore	07-1417	Rabbit	Polyclonal	Western Blot	1:1000	N/A
14	anti-β Actin	Sigma	A5441	Mouse	Monoclonal	Western Blot	1:10000	N/A