

Electronic Supplementary Material (ESM)

ESM Table 1. Supplementary Tables of Reagents: Primary Antibodies (Table 1A) and Accessory Agents (Table 1B)

1A. Primary Antibodies

Primary Antibody	Manufacturer and catalogue No.	Antigen Retrieval	Antibody Dilution	Secondary Antibody Details	Validation
Insulin	Dako C#A0564 Guinea-pig polyclonal (now supplied by Agilent) C#IR00261-2	10mM citrate pH6.0	1/600 for 1h at RT	Dako REAL™ Envision™ Detection System, as per manufacturers instructions	Validated in pancreas tissue with appropriate negative tissue and isotype controls. Used in >540 publications in the literature. The antibody cross-reacts with insulin from several mammalian species. Specificity as determined by radioimmunoassay was 100% for human insulin, 100% for porcine insulin and less than 0.05% for glucagon and human growth hormone. This product has been optimised for use on human tissues. Antibody Registry: AB_10013624 https://antibodyregistry.org/search?q=A0564
Glucagon	Abcam C#ab10988, [K79bB10] Mouse monoclonal	10mM citrate pH6.0	1/2000	Vector AP-ABC kit combined with Vector Red Substrate kit, as	Validated in pancreas tissue with appropriate negative tissue and isotype controls.

				per manufacturers instructions	<p>Cite ab: https://www.citeab.com/antibodies/733352-ab10988-anti-glucagon-antibody-k79bb10</p> <p>Antibody Registry: AB_297642 https://antibodyregistry.org/search.php?q=AB_297642</p>
--	--	--	--	--------------------------------	---

1B. Accessory Agents

Accessory Agents	Company	Catalogue No.	Description	Details
Dako REAL peroxidase blocking system	Dako (now supplied by Agilent)	S2023 (S202386-2)	Blocking agent	Use as per manufacturers instructions
Dako Antibody Diluent	Dako (now supplied by Agilent)	S2022 (S202230-2)	Antibody Diluent	Use as per manufacturers instructions
Normal Goat serum	Vector Laboratories	S1000	Blocking agent	5% NGS in Tris buffered saline
Dako REAL™ Envision-HRP, Detection System	Dako (now supplied by Agilent)	K5007 (K500711-2)	Secondary detection system used for Insulin antibody	Use as per manufacturers instructions
Vector AP-ABC kit (Mouse)	Vector Laboratories	AK-5002	Secondary detection system used for glucagon antibody	Use as per manufacturers instructions
Vector Red Substrate kit	Vector Laboratories	SK-5100	Secondary detection system used for glucagon antibody	Use as per manufacturers instructions
Dako Haematoxylin	Dako (now supplied by Agilent)	S2020	Counterstain	Use as per manufacturers instructions

ESM Table 2. Characteristics of donors in the study (n=110), and comparison by residual ICI%

	All	Residual ICI<5% N=80	Residual ICI≥5% N=30	p-value
% residual ICI: Mean (SD) (range)	9.8 (21.5) (0.0, 92.2)	0.2 (0.5) (0, 2.2)	35.6 (28.3) (6.4, 92.2)	<0.001
Age, attained (years): Mean (SD) (range)	27.9 (13.4) (4.4, 78.0)	30 (14.3) (4.4, 78.0)	22.2 (8.8) (11.0, 45.0)	0.007
Age at T1D onset (years): Mean (SD) (range)	12.2 (7.9) (0-36)	11.1 (8) (0.0,36.0)	15.3 (6.9) (3.0,35.0)	0.013
Age at T1D onset category:				0.007
<7 years	32 (29.1%)	30 (37.5%)	2 (6.7%)	

7-12 years	31 (28.2%)	20 (25.0%)	11 (36.7%)	
≥13 years	47 (42.7%)	30 (37.5%)	17 (56.7%)	
T1D duration (years): Mean (SD) (range)	15.3 (13.7) (0-74)	18.5 (14.3) (0.0,74.0)	7.0 (7.4) (0.0,32.5)	<0.001
BMI: Mean (SD) (range)	24.5 (4.6) (12.9-42.5)	24.7 (4.1) (15.9,37.1)	24.1 (5.8) (12.9,42.5)	0.610
BMI percentile*: Mean (SD) (range)	67.0 (26.3) (2.0, 98.1)	68.2 (24.2) (2.0,98.1)	63.9 (31.5) (2.0,98.1)	0.445
BMI Z-score*: Mean (SD) (range)	0.6 (1.0) (-3.4, 3.9)	0.6 (0.9) (-2.1,3.9)	0.4 (1.2) (-3.4,2.2)	0.316
BMI Category				0.455
Underweight	8 (7.3%)	4 (5%)	4 (13.3%)	

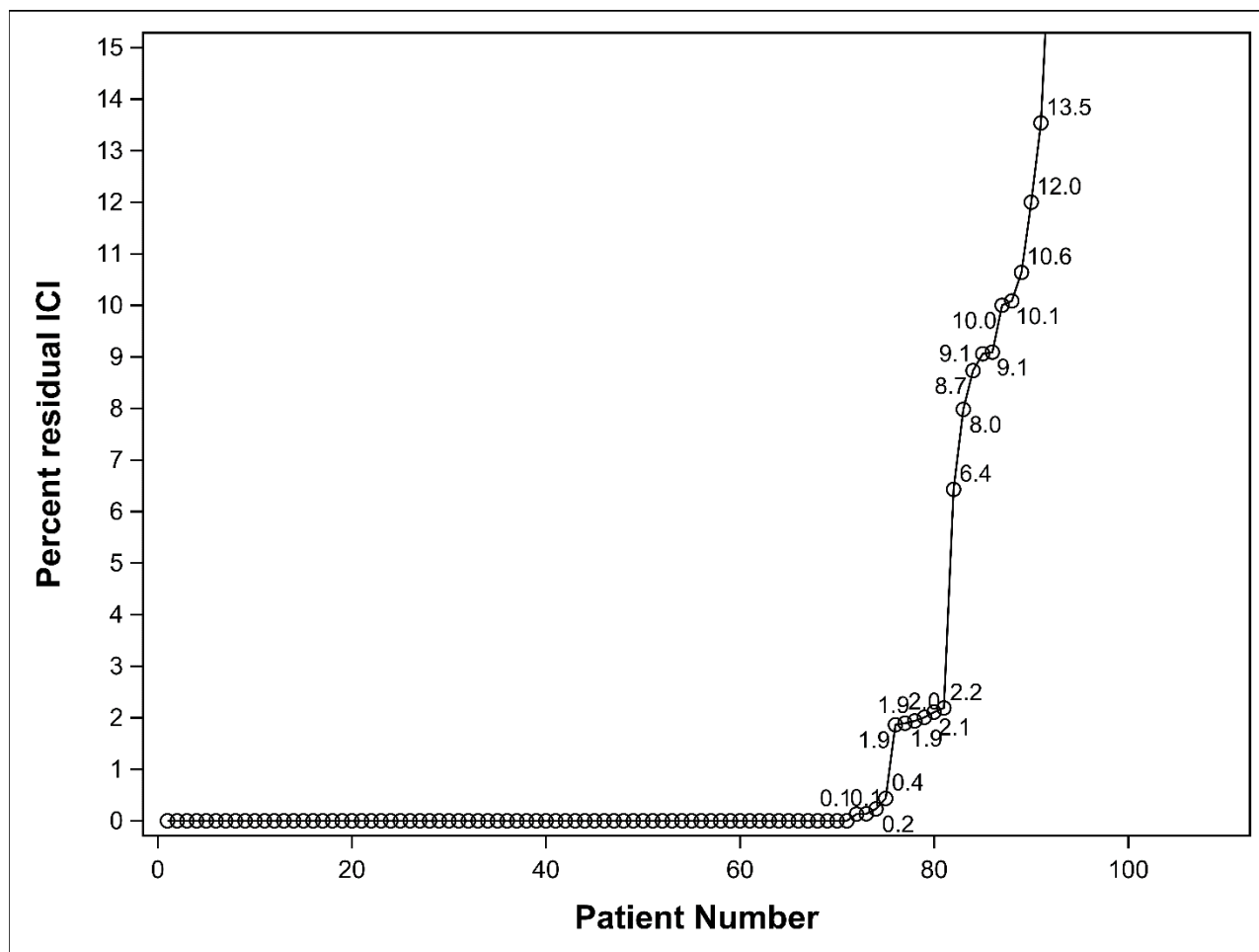
Normal	53 (48.2%)	39 (48.8%)	14 (46.7%)	
Overweight	32 (29.1%)	25 (31.3%)	7 (23.3%)	
Obese	17 (15.5%)	12 (15%)	5 (16.7%)	
Gender				0.227
Female	52 (47.3%)	35 (43.8%)	17 (56.7%)	
Male	58 (52.7%)	45 (56.3%)	13 (43.3%)	
Race/ethnicity				0.083
Non-Hispanic White	88 (80%)	68 (85%)	20 (66.7%)	
African American	14 (12.7%)	7 (8.8%)	7 (23.3%)	
Hispanic/Latino	8 (7.3%)	5 (6.3%)	3 (10%)	
African American race				0.0410

African American	14 (12.7%)	7 (8.8%)	7 (23.3%)	
Other	96 ((87.3%)	73 (91.3%)	23 (76.7%)	
Ancestry score: Mean (SD) (range)				
AFR	0.1 (0.3) (0.0,0.9)	0.1 (0.2) (0.0,0.9)	0.2 (0.3) (0.0,0.9)	0.043
AMR	0.0 (0.1) (0.0,0.8)	0.0 (0.1) (0.0,0.8)	0.1 (0.2) (0.0,0.6)	0.395
EAS	0.0 (0.0) (0.0,0.0)	0.0 (0.0) (0.0,0.0)	0.0 (0.0) (0.0,0.0)	0.149
EUR	0.8 (0.3) (0.1,1.0)	0.9 (0.3) (0.1,1.0)	0.7 (0.3) (0.1,1.0)	0.023
SAS	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.663

	(0.0,0.1)	(0.0,0.1)	(0.0,0.1)	
<i>TCF7L2</i> rs7903146 (Major allele: C)				
CC	60 (54.5%)	47 (58.8%)	13 (43.3%)	0.322
TC	46 (41.8%)	30 (37.5%)	16 (53.3%)	
TT	4 (3.6%)	3 (3.8%)	1 (3.3%)	

*BMI percentile and Z-score for adults were obtained by assigning the age of 20 years old.

ESM Figure 1. Distribution of ICI% in the study sample



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>

(1) Authors' note: Please note that our study examined tissue sections and not isolated islets and thus, "origin/source of islets" and "isolation centre" do not apply.

Islet preparation	1	2	3	4	5	6	7	8 ^a
MANDATORY INFORMATION								
Unique identifier	6025	6026	6031	6032	6035	6036	6038	6039
Donor age (years)	23.8	22.4	39	33.8	32.1	49.2	37.2	28.7
Donor sex (M/F)	Male	Male	Male	Male	Male	Female	Female	Female
Donor BMI (kg/m ²)	26.6	24.1	24.5	29.4	27.1	25.5	30.9	23.4
Donor HbA _{1c} or other measure of blood glucose control	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	19.00	9.00	35.00	0.00	28.00	34.00	20.00	12.00
Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: Humalog and Lantus	Yes: insulin	n/a	Yes: humulin N	Yes: insulin	Yes: Humulin 70/30	Yes: insulin
RECOMMENDED INFORMATION								

Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

^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

Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Islet preparation	17	18	19	20	21	22	23	24
MANDATORY INFORMATION								

Unique identifier	6061	6063	6064	6066	6067	6070	6071	6077
Donor age (years)	28.1	4.4	19.6	78	32.6	22.6	28	32.9
Donor sex (M/F)	Male	Male	Female	Male	Female	Female	Female	Female
Donor BMI (kg/m ²)	22.1	23.8	22.6	30.9	26.8	21.6	19.5	22
Donor HbA _{1c} or other measure of blood glucose control	n/a	n/a	n/a	n/a	n/a	n/a	7.3	12.4
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	23.00	3.00	9.00	74.00	8.00	7.00	17.00	19.00
Glucose-lowering therapy at time of death ^c	Yes: Lantus and Novolog	Yes: Lantus and Novolog	Yes: insulin	Yes: Humalog and Lantus	Yes: insulin	Yes: Lantus (non-compliant)	Yes: Lantus and Novolog	Yes: insulin
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								

Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Islet preparation	25	26	27	28	29	30	31	32
MANDATORY INFORMATION								
Unique identifier	6079	6083	6084	6087	6088	6089	6113	6119
Donor age (years)	11.1	15.2	14.2	17.5	31.2	14.3	13.1	27.8
Donor sex (M/F)	Female	Female	Male	Male	Male	Male	Female	Male

Donor BMI (kg/m ²)	18.6	18.4	26.3	21.9	27	26	24.75	19.4
Donor HbA _{1c} or other measure of blood glucose control	n/a	n/a	n/a	n/a	n/a	10.4	n/a	8.4
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	8.00	11.00	4.00	4.00	5.00	8.00	1.58	14.00
Glucose-lowering therapy at time of death ^c	Yes: Lantus, NPH, Lispro	Yes: Humalog	Yes: insulin	Yes: Humalog and Lantus	Yes: insulin	Yes: Humalog and Lantus	Yes: insulin	Yes: Novolog
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								

Additional notes								
------------------	--	--	--	--	--	--	--	--

Islet preparation	33	34	35	36	37	38	39	40
MANDATORY INFORMATION								
Unique identifier	6128	6141	6143	6145	6148	6150	6152	6155
Donor age (years)	33.8	36.7	32.6	18	17.1	41.2	29.6	50
Donor sex (M/F)	Female	Male	Female	Male	Male	Male	Female	Female
Donor BMI (kg/m ²)	22.2	26	26.1	23.1	23.9	25.5	30.1	26

Donor HbA _{1c} or other measure of blood glucose control	n/a	n/a	n/a	n/a	n/a	n/a	11.3	n/a
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	31.50	28.00	7.00	11.00	7.00	35.00	12.00	43.00
Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: Lantus and Novolog	Yes: Humalog and Lantus	Yes: insulin	Yes: Humalog	Yes: insulin	Yes: Humalog and Lantus	Yes: Novolog and Novolin N
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	44.00	7.00	30.00	15.00	15.00	11.00	5.00	15.00
Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: Humulin R	Yes: insulin	Yes: insulin	Yes: Humalog and Lantus	Yes: Novolog	Yes: insulin	Yes: insulin
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

If Yes, complete the next two lines if this information is available

Diabetes duration (years)	3.00	21.00	33.00	10.00	16.00	0.25	4.00	5.00
Glucose-lowering therapy at time of death ^c	Yes: 70/30	Yes: insulin (non-compliant most of time)	Yes: Lantus and Novolog	Yes: Humalog and Lantus	Yes: insulin	Yes: Humalog and Lantus	Yes: Lantus and Novolog	Insulin: Humalog

RECOMMENDED INFORMATION

Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Islet preparation	57	58	59	60	61	62	63	64
MANDATORY INFORMATION								
Unique identifier	6215	6220	6223	6224	6228	6231	6236	6237
Donor age (years)	34	35	61	21	13	49	25	18
Donor sex (M/F)	Male	Female	Male	Female	Male	Female	Male	Female
Donor BMI (kg/m ²)	26.6	27.4	23.4	22.8	17.36	25.4	20.1	26
Donor HbA _{1c} or other measure of blood glucose control	8	n/a	n/a	n/a	13.3	10.4	11.6	n/a
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	15.00	11.00	52.00	1.50	0.00	20.00	11.00	12.00

Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: insulin	Yes: insulin	Yes: Humulin and Novolog	No	Yes: Lantus and Novolog	Yes: Humalog and Lantus	Yes: insulin
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								
Additional notes								

Islet preparation	89	90	91	92	93	94	95	96
MANDATORY INFORMATION								
Unique identifier	6322	6323	6325	6327	6328	6330	6337	6341

Donor age (years)	22	22	20	71.2	39	22	20.6	26
Donor sex (M/F)	Male	Female	Female	Male	Male	Male	Female	Male
Donor BMI (kg/m ²)	23.6	24.7	31.2	23.2	23.98	22.6	17.9	21.8
Donor HbA _{1c} or other measure of blood glucose control	n/a	6.6	n/a	n/a	8.7	n/a	12.5	13.6
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	17.00	6.00	6.00	57.00	20.00	18.00	5.00	15.00
Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: Novolog	Yes: insulin	Yes: insulin	Yes: insulin	Yes: Novolog	Yes: insulin	Yes: insulin
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								

Additional notes								
------------------	--	--	--	--	--	--	--	--

Islet preparation	97	98	99	100	101	102	103	104
MANDATORY INFORMATION								
Unique identifier	6342	6360	6362	6367	6371	6380	6396	6399
Donor age (years)	14	4.8	24.9	24	12.5	11.6	17.1	17.42
Donor sex (M/F)	Female	Female	Male	Male	Female	Female	Female	Male
Donor BMI (kg/m ²)	24.3	26.1	28.5	25.7	16.6	14.6	22.6	32

Donor HbA _{1c} or other measure of blood glucose control	9.2	10.2	10	8.8	9.5	13.5	13.4	10.4
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	2.00	2.50	0.00	2.00	2.00	0.00	2.00	0.00
Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: Humalog and Lantus	None at home reportedly; insulin IV drip upon admission	Yes: Lantus and Novolog	Yes: Lantus and Novolog	No	Yes: Humalog and Lantus	No
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								

Additional notes								
------------------	--	--	--	--	--	--	--	--

Islet preparation	105	106	107	108	109	110		
MANDATORY INFORMATION								
Unique identifier	6405	6418	6435	6472	6473	6477		
Donor age (years)	29.1	24.86	24.75	10.25	13.21	19.87		
Donor sex (M/F)	Female	Male	Female	Female	Male	Female		
Donor BMI (kg/m ²)	42.5	26.4	26.9	16.6	17.9	25.3		

Donor HbA _{1c} or other measure of blood glucose control	7	7.5	11.6	9.7	12.8	10.9		
Origin/source of islets ^b Please see authors' note: N/A								
Islet isolation centre Please see authors' note: N/A								
Donor history of diabetes? Please select yes/no from drop down list	Yes	Yes	Yes	Yes	Yes	Yes		
If Yes, complete the next two lines if this information is available								
Diabetes duration (years)	0.60	11.00	14.75	4.00	6.00	8.00		
Glucose-lowering therapy at time of death ^c	Yes: insulin	Yes: insulin	Yes: Insulin and Tresiba	Yes: insulin	Yes: Lantus	Yes: Lantus, Humalog, Insulin aspart/ degludec		
RECOMMENDED INFORMATION								
Donor cause of death								
Warm ischaemia time (h)								
Cold ischaemia time (h)								
Estimated purity (%)								
Estimated viability (%)								
Total culture time (h) ^d								
Glucose-stimulated insulin secretion or other functional measurement ^e								
Handpicked to purity? Please select yes/no from drop down list								

Additional notes								
------------------	--	--	--	--	--	--	--	--