Electronic Supplementary Materials

Insulin production is sustained during DNA damage-mediated senescence in adult human beta cells

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Methods

Human islet and EndoC-βH5 culture and treatments. Upon receipt islets were rested in culture at 37°C and 5% CO_2 for 24 hours in RPMI-1640 media (ThermoFisher, Waltham, MA, USA) containing 10% vol./vol. fetal bovine serum, 2 mmol/l L-glutamine, 5.5 mmol/l glucose and 1X antibiotic-antimycotic. To induce DNA damage mediated senescence, islets were treated with 50 µmol/l bleomycin sulfate (Sigma-Aldrich, BP971, St. Louis, MO, USA) or 0.1% vol./vol. DMSO as vehicle for 48 h, followed by washout and culture for 4-6 days in drug-free islet media, as previously [1–3]. Female fetal-derived EndoC-βH5 cells were cultured according to the supplier's protocol (Human Cell Design, Toulouse, France) and were induced to a DNA damage respone using bleomycin treatment according to previous methods [1]. Experiments were carried out on three independent vials/batches of EndoC cells. Two days after plating, cells were treated with 35

μmol/l bleomycin or 0.07-15% vol./vol. DMSO vehicle for 48 h, followed by drug removal and culture of cells for 5 days before harvest for assays. For collection of conditioned media for SASP factor ELISA, the media was replaced on day 5 for collection on day 6.

Western blot analysis and quantification

Antibodies to all protein targets in this study were validated by the supplier using positive and negative control cell lysates (**ESM Table 2**), or western blots from peer-reviewed studies. We confirmed specificity using of PC1/3, CPE and ProSAAS antibodies using recombinant PC1/3 (Origene, TP760904, Rockville, MD, USA), recombinant CPE (Creative Biomart, CPE-7253H, Shirley, NY, USA) and recombinant ProSAAS (Novus Biologicals, NBP2-23370, Centennial, CO, USA), respectively. Two different antibodies were used interchangeably to detect proSAAS as shown in **ESM Fig. 1** and **ESM Table 2**. Several X-ray film exposures were taken to ensure signals were in the linear range for quantifications. Digitally scanned X-ray films were quantified using ImageJ (version 1.54i) and signals normalised to vinculin or beta-actin as the loading control. To probe the same membranes again, signals were stripped using Restore Plus stripping buffer (ThermoFisher) and blocked again prior to probing with different primary antibodies.

ELISA specificity

The insulin ELISA has negligible cross-reactivity (<0.5%) with proinsulin, proinsulin des 31-32, proinsulin split 32-33, but 98% cross-reactivity with the split 64-65 proinsulin form and 56% cross-reactivity with the des 64-65 proinsulin form (Mercodia, Uppsala, Sweden). The proinsulin ELISA detects all forms, including des 31-32, des 64-65, split 32-33 and split 65-66 and has negligible cross-reactivity with mature insulin (<0.03% cross reactivity, Mercodia).

ESM Table 1. Human donor islet preparations and pancreas sections used in this study.

Source	Donor ID (RRID)	Diabetes	Sex	Age (years)	BMI (kg/m^2)	Senescence validation	Experiments
ADI	R507 (RRID:SAMN37283209)	No diabetes	Female	59	19.9	p21 western blot	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig. 2 and 5**)
ADI	R509 (RRID:SAMN37435001)	No diabetes	Male	53	20.1	p21 western blot	Bleomycin induced senescence, western blot of insulin synthesis enzymes (**Fig. 1 and 2, ESM Fig. 2 and 5**)
ADI	R510 (RRID:SAMN37797113)	No diabetes	Female	53	21.3	p21 western blot	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig. 2 and 5**)
ADI	R515 (RRID:SAMN38060115)	No diabetes	Male	28	26.1	p21 western blot, p21 and Insulin flow cytometry Validation by flow cytometry [3]	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig. 2 and 5**) Bleomycin induced senescence, flow cytometry for p21 and Insulin (**Fig. 2**)
ADI	R434 (RRID:SAMN26419385)	No diabetes	Female	50	24.2	RNA-seq [1]	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig. 2 and 5**)
IIDP	HP-23278-01 (RRID:SAMN37735329)	No diabetes	Female	54	23.3	p21 western blot	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig. 2 and 5**)

ADI	R523 (RRID:SAMN38809984)	No diabetes	Male	59	23.4	p21 western blot	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig. 2 and 5**)
IIDP	HP-25078-01A (n/a)	No diabetes	Male	45	31.9	n/a	No treatment, C_{12}FDG assay and β-cells sorted for ELISA of insulin (**Fig. 2**)
ADI	R563 (RRID:SAMN45037497)	No diabetes	Male	59	26.6	C_{12}FDG assay	Bleomycin treatment and C_{12}FDG assay image cytometry (**ESM Fig. 4**)
ADI	R564 (RRID:SAMN45114368)	No diabetes	Male	37	28.7	C_{12}FDG assay	Bleomycin treatment and C_{12}FDG assay β-cell flow cytometry (**ESM Fig. 4**)
ADI	R566 (RRID:SAMN46230837)	No diabetes	Male	21	23.7	n/a	No treatment, C_{12}FDG assay image cytometry (**ESM Fig. 4**)
IIDP	HP-25021-01 (RRID:SAMN46428262	No diabetes	Female	54	23.0	GDF15 ELISA	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin, proinsulin and GDF15 (**Fig. 1 and 2, ESM Fig. 2 and 5**)
IIDP	HP-25073-01 (RRID:SAMN47416578)	No diabetes	Male	56	29.3	p21 western blot & GDF15 ELISA	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin, proinsulin and GDF15 (**Fig. 1 and 2, ESM Fig. 2 and 5**)
IIDP	UWHI357R (RRID:SAMN46859874)	No diabetes	Male	57	28.1	p21 western blot	Bleomycin induced senescence, western blot of insulin synthesis enzymes, ELISA of insulin and proinsulin (**Fig. 1 and 2, ESM Fig 2 and 5**)
IIDP	HP-25007-01	No diabetes	Male	57	30.1	n/a	No treatment, C_{12}FDG assay image cytometry, C_{12}FDG assay

	(RRID:SAMN46223636)						and β-cells sorted for ELISA of insulin (**Fig. 2, ESM Fig. 4**)
IIDP	HP-2350 (RRID:SAMN38040976)	No diabetes	Female	20	22.4	p21 and Ins flow cytometry, Validation by flow cytometry [3]	Bleomycin-induced senescence, flow cytometry for insulin and p21 (**Fig. 2**)
IIDP	HP2331801 (RRID:SAMN38334492)	No diabetes	Male	51	24.6	p21 and Ins flow cytometry Validation by flow cytometry [3]	Bleomycin-induced senescence, flow cytometry for insulin and p21 (**Fig. 2**)
IIDP	HP-25129-01 (RRID:SAMN48430444)	No diabetes	Male	50	25.8	n/a	No treatment, C_{12}FDG assay and β-cells sorted for ELISA of insulin (**Fig. 2**)
IIDP	ICRH159 (RRID:SAMN41775468)	No diabetes	Male	19	19.9	p21 and Ins flow cytometry	Bleomycin induced senescence, flow cytometry of insulin and p21 (**ESM Fig. 3**)
ADI	R551 (RRID:SAMN43365828)	No diabetes	Female	57	20.0	p21 and Ins flow cytometry	Bleomycin induced senescence, flow cytometry of insulin and p21 (**ESM Fig. 3**)
nPOD	6229	No diabetes control	Female	31	26.9	n/a	Immunofluorescence for p21, Proinsulin and DAPI (**Fig. 3**)
nPOD	6196	Type 1 diabetes	Female	26	26.6	n/a – 15 years diabetes, 0.16 nmol/l C-peptide	Immunofluorescence for p21, Proinsulin and DAPI (**Fig. 3**)

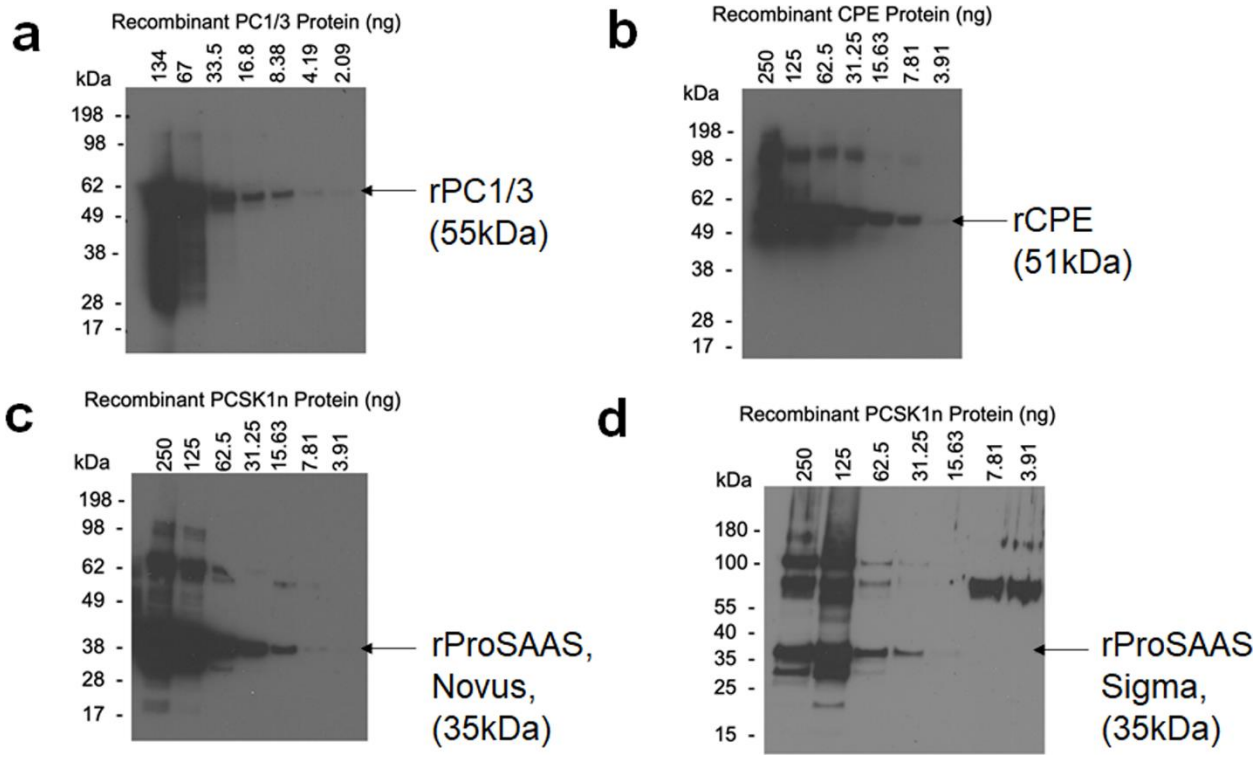
ADI – Alberta Diabetes Institute

IIDP – Integrated Islet Distribution Program

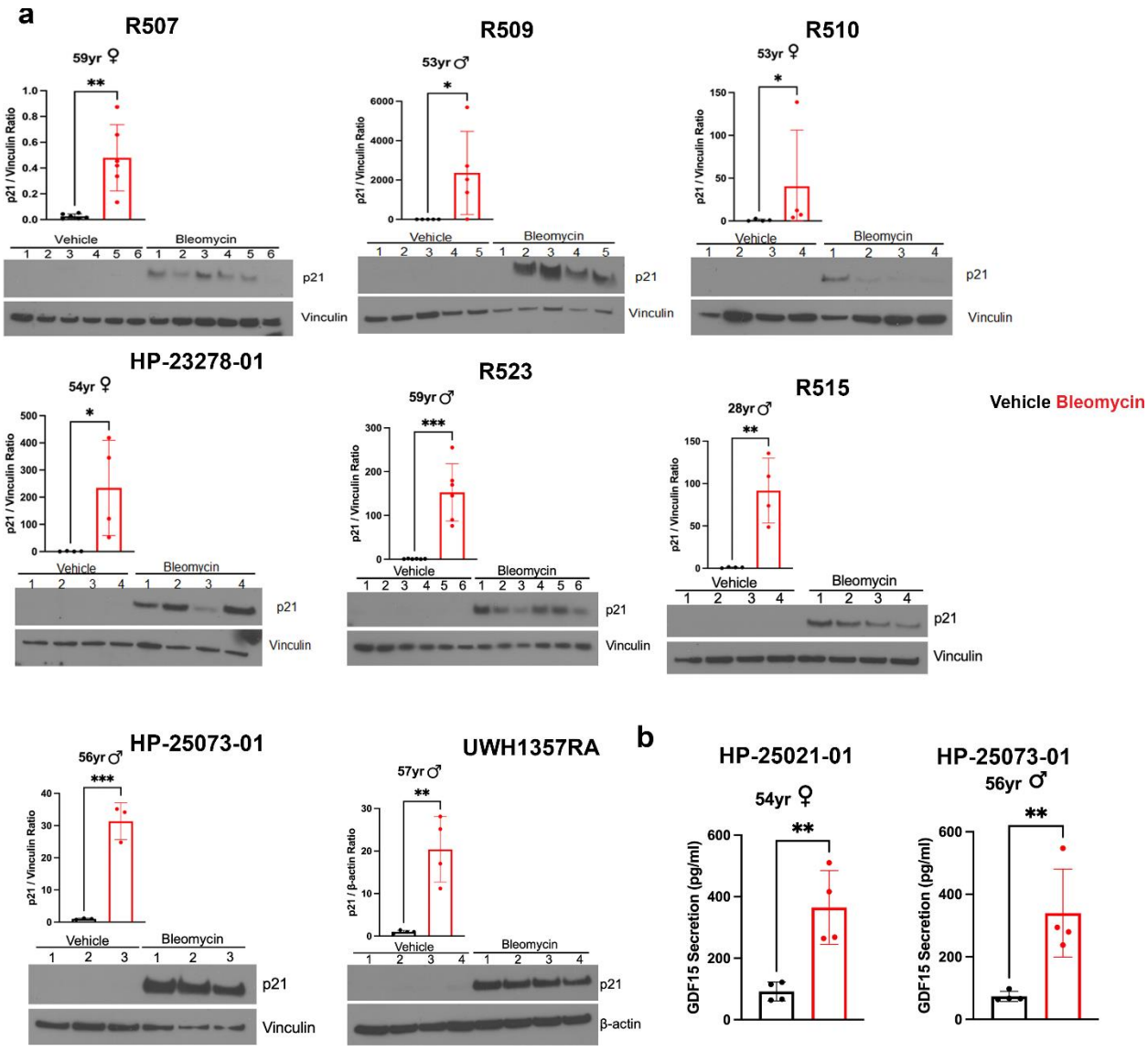
ESM Table 2. Primary antibodies used in this study.

Antibody name	Estimated band size (kDa)	Supplier	Catalogue number (RRID)	Application and Concentration used (dilution from stock)
Vinculin	124	Cell Signalling Technology	13901 (RRID:AB_2728768)	Western blot, 1:1000
PC1/3	70	Cell Signalling Technology	18030	Western blot, 1:2000
Beta-actin	45	Cell Signalling Technology	4970 (RRID:AB_2223172)	Western blot, 1:5000
PC2	65-75	Cell Signalling Technology	14013 (RRID:AB_2631285)	Western blot, 1:2000
CPE	70	R&D Systems Inc.	MAB3587 (RRID:AB_2083765)	Western blot, 1:10 000
proSAAS	19-27	EMD Millipore Corp.	ABN2268	Western blot, 1:1000
proSAAS	25	Novus Biologicals	NBP2-49423 (RRID:AB_3320347)	Western blot, 1:1000
p21	21	Cell Signalling Technology	2947 (RRID:AB_823586)	Western blot, 1:500
p21	n/a	Cell Signalling Technology	2947 (RRID:AB_823586)	Immunofluorescence, 1: 1000
Proinsulin	n/a	Developmental Studies Hybridoma Bank	GS-9A8 (RRID:AB_532383)	Immunofluorescence, 1:50

ESM Figures.

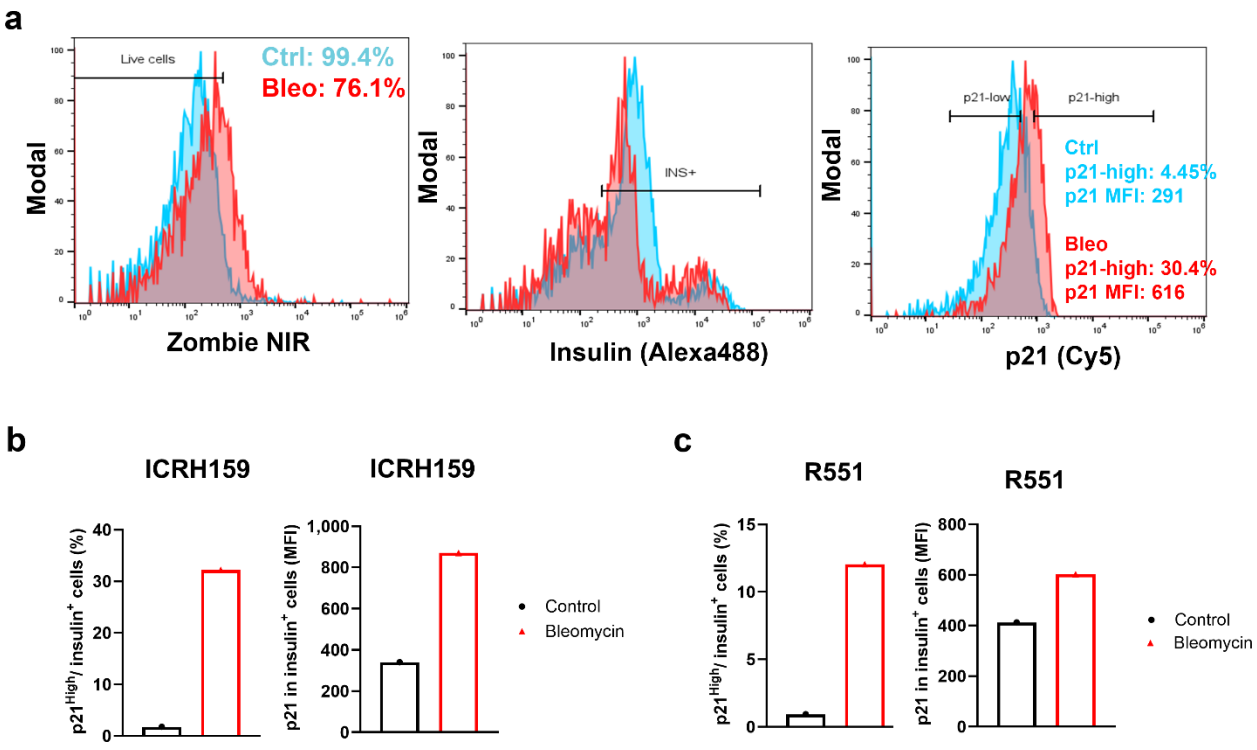


ESM Figure 1. Proinsulin processing factor antibody validations. Antibodies for PC1/3 (Origene, Cat No. TP760904) (a), CPE (Creative Biomart, Cat No. CPE-7253H) (b) and ProSAAS/PCSK1N (Novus Biologicals, Cat No. NBP2-23370) (c) and (d) were validated by western blots on purified recombinant proteins. ProSAAS was detected with two different antibodies.

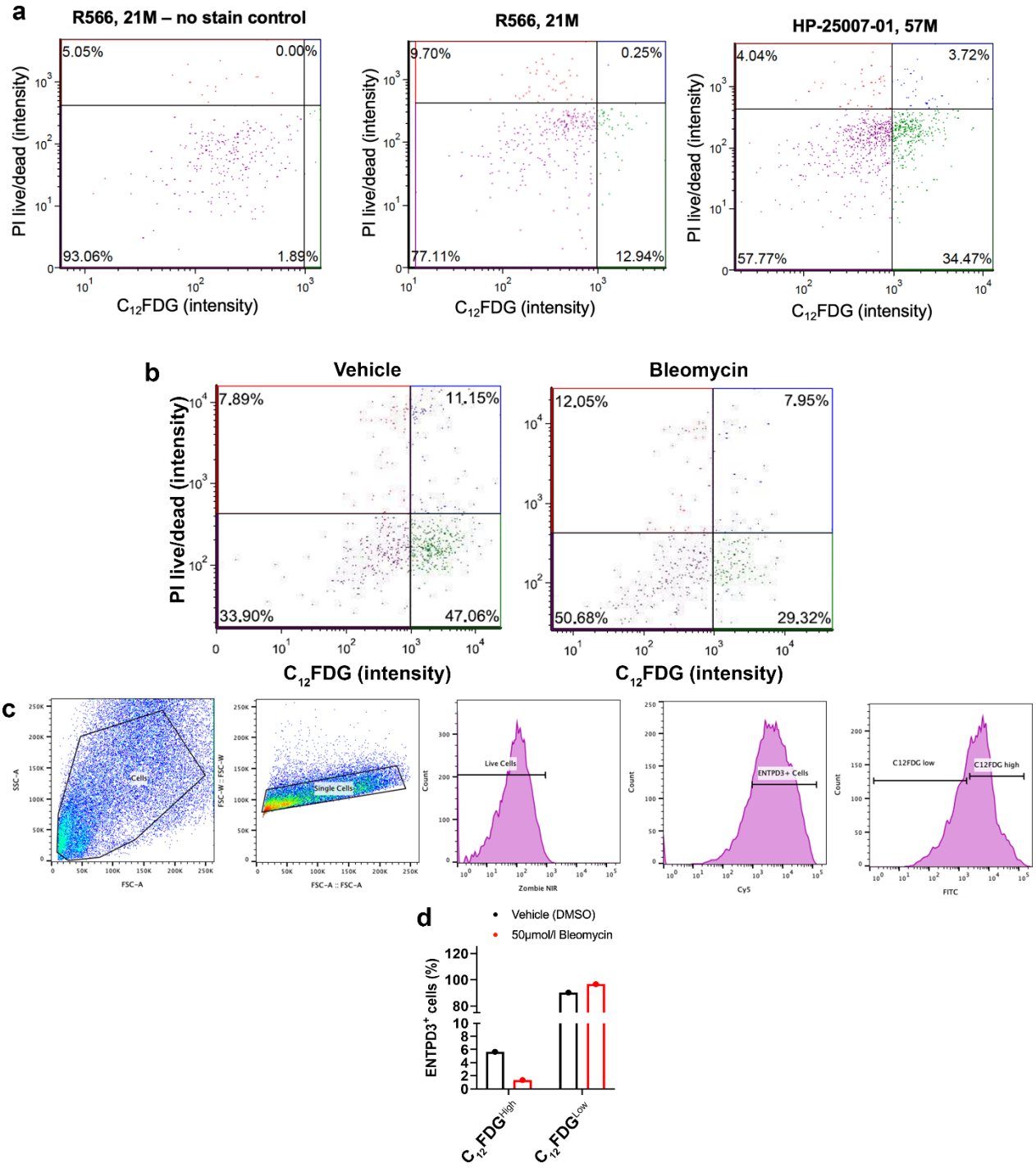


ESM Figure 2. Validation of senescence induction following bleomycin treatment in human islets. DNA damage-mediated senescence was induced in human islets with 50 μmol/l bleomycin treatment for 48 h followed by culturing islets in drug-free media for an additional 4-6 days, alongside vehicle (0.1% vol./vol. DMSO) controls. Senescence was validated in a variety of ways, such as (a) western blot analysis for p21 normalised to vinculin or β-actin as a loading control, or (b) GDF15 ELISA on the conditioned media at this timepoint. Additional detail on senescence validations across all islet preparations exposed to DNA damage and used for experiments is described for each donor in **ESM Table 1**. All data are mean ± s.d. of n=3 or 4 islet sample replicates (treated as technical replicates) per treatment group for each donor. ***p <0.001, **p<0.01, *p<0.05, two-tailed

T test. Note: loading control blots for vinculin or β-Actin for donors HP-23278-01, R515, R523, R509, R510 and UWH1357RA are the same as in ESM Fig. 5 because they were done on the same membranes after stripping and reprobing with different primary antibodies.

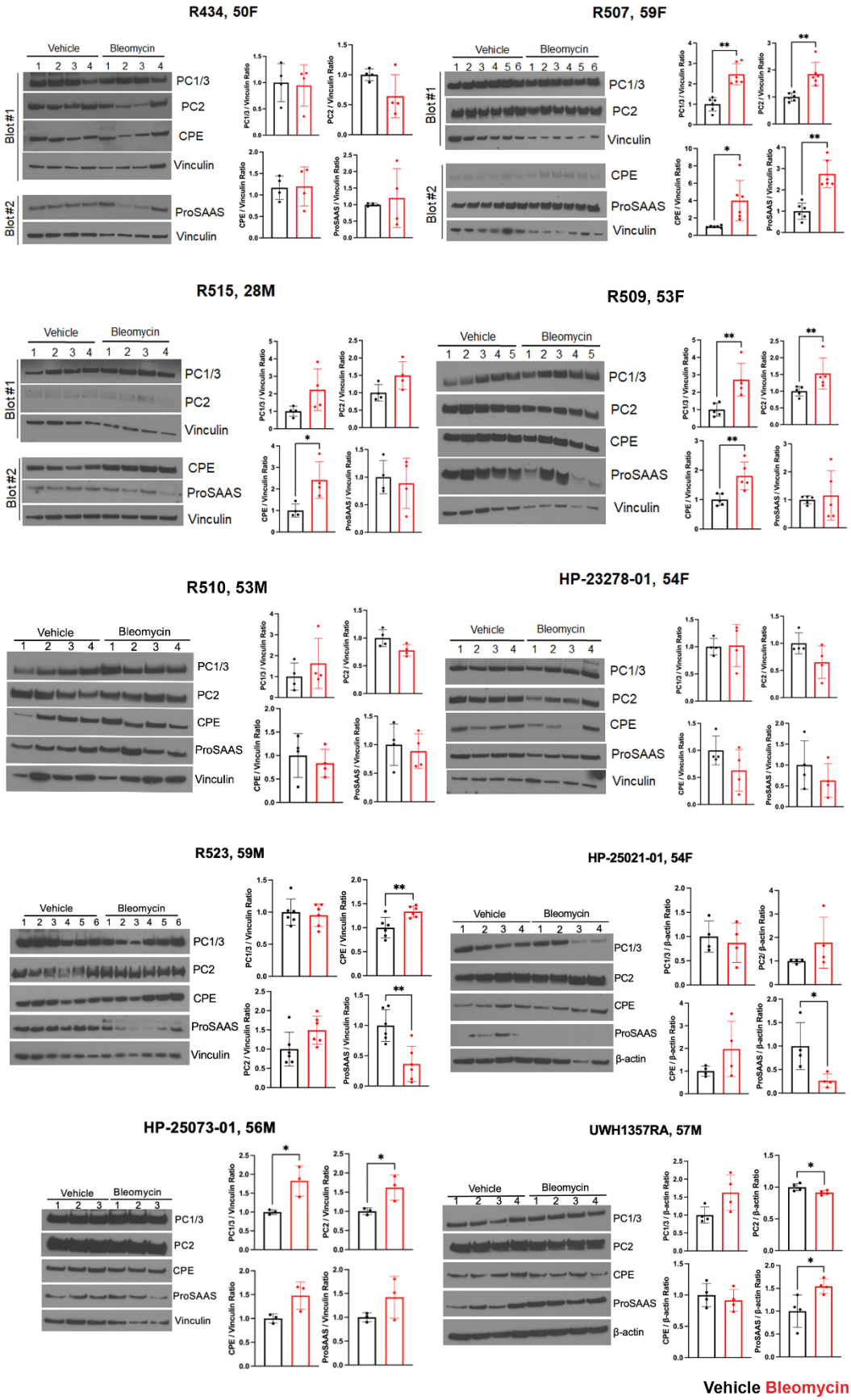


ESM Figure 3. Flow cytometry for p21 expression in beta cells following DNA damage and senescence induction with bleomycin. Senescence was induced in human islets as described in **ESM Fig. 2** and at day 5 post-drug washout islets were dissociated for flow cytometry of p21 and insulin in live islet cells. (a) Representative gating of Live cells (Zombie NIR^{-}), beta cells (insulin^{+}), and p21^{High} versus p21^{Low} in the insulin^{+} population from controls and bleomycin-treated islets (donor ICRH159). (b) and (c) Quantification plots of p21^{High}/insulin^{+} cells and p21 median fluorescence intensity (MFI) in insulin^{+} cells in control and bleomycin-induced senescent islets from two representative donors experiments: ICRH159 (male) and R551 (female). Islet donor details are found in **ESM Table 1**.

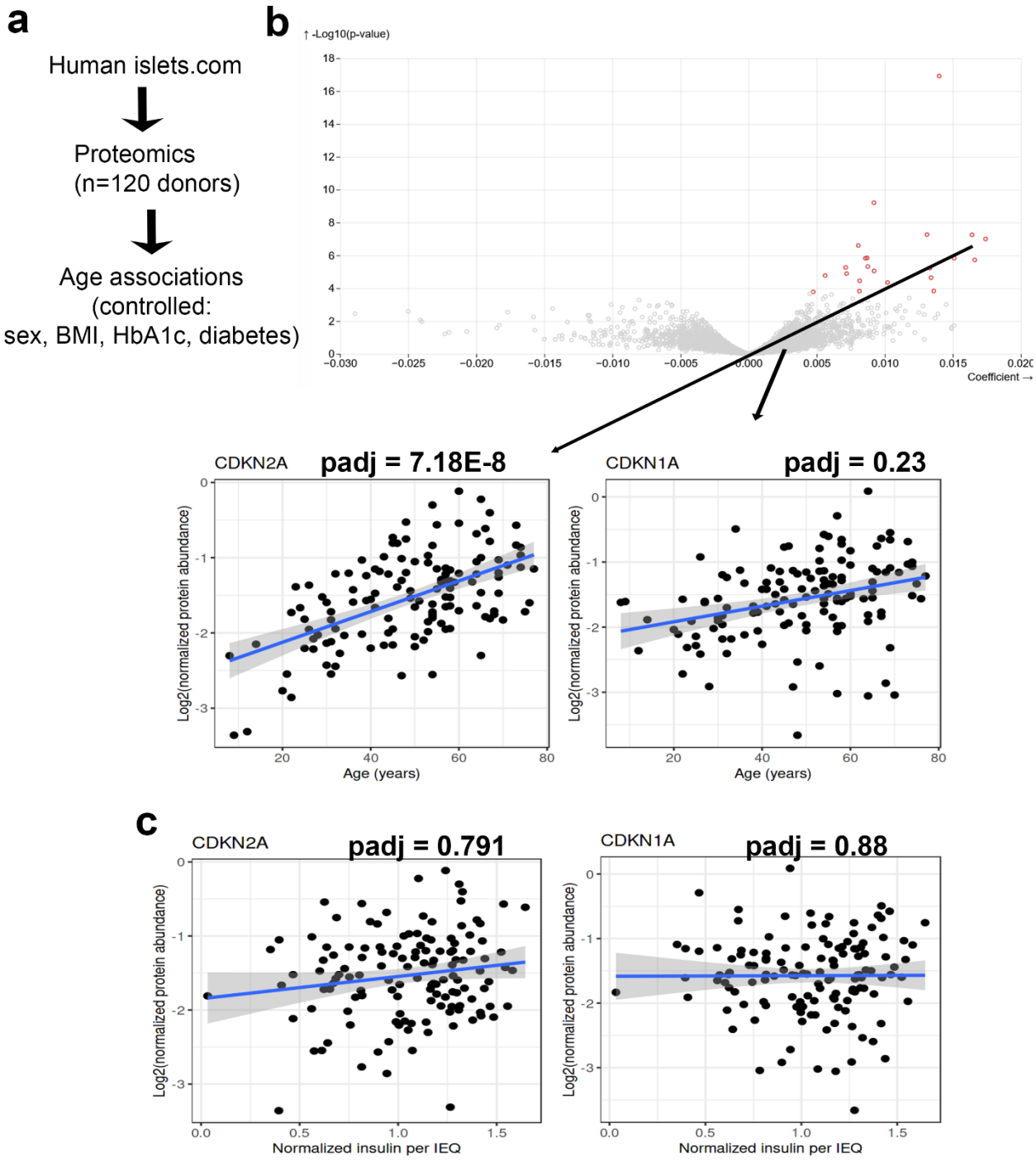


ESM Figure 4. SA-βgal activity detection with $C_{12}FDG$ in human islets. (a) Fluorogenic substrate $C_{12}FDG$ was used to assay SA-βgal activity in islet cells following co-staining with propidum iodide (PI) as live/dead marker, showing percentages of $C_{12}FDG^{+}/PI^{-}$ (bottom right), $C_{12}FDG^{-}/PI^{-}$ (bottom left), $C_{12}FDG^{+}/PI^{+}$ (top right), and $C_{12}FDG^{-}/PI^{+}$ (top left) cells in each sample by image cytometry. A no $C_{12}FDG$ control was used on donor R566 islets to confirm the assay was working. (b) Image cytometry using

the Cellometer Spectrum system to detect $C_{12}FDG^{+}/PI^{-}$ (live) islet cells from donor R563 following DNA damage and senescence induction with 50 µmol/l bleomycin and culture in drug-free media on day 4 post-drug washout. (c) Gating strategy for detecting single, Zombie Near IR^{-} (live), $ENTPD3^{+}$ (beta cells) with $C_{12}FDG^{High}$ versus $C_{12}FDG^{Low}$. (d) Senescence induction on islets with bleomycin or control vehicle treatment, as in (b) except on islets from donor R564 and using the $C_{12}FDG$ assay followed by staining with Zombie Near IR as live-dead marker and ENTPD3 antibody to mark beta cells. The percentage of live $ENTPD3^{+}$ cells were scored for $C_{12}FDG^{High}$ or $C_{12}FDG^{Low}$.

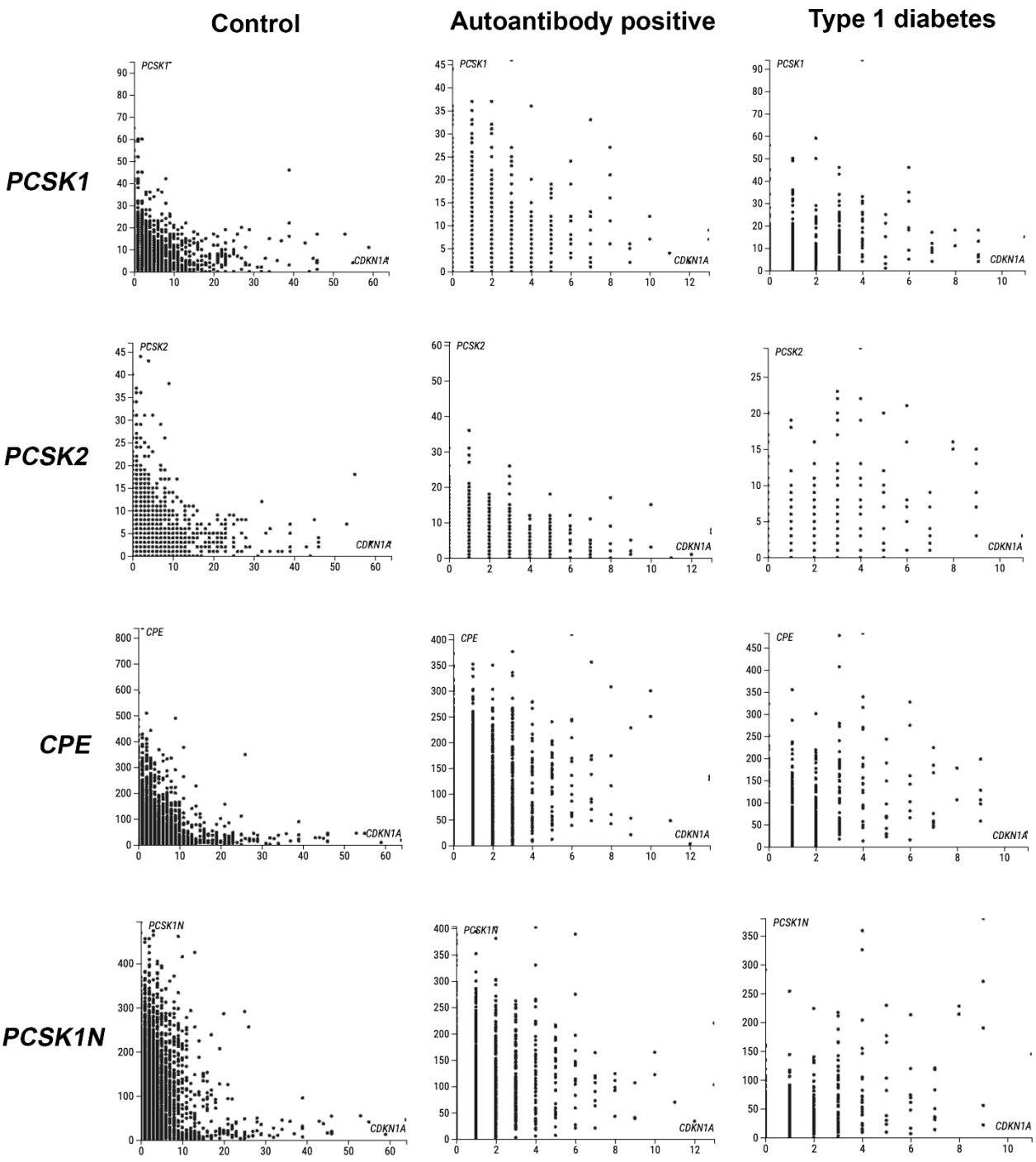

R434, 50F
R507, 59F
R515, 28M
R509, 53F
R510, 53M
HP-23278-01, 54F
R523, 59M
HP-25021-01, 54F
HP-25073-01, 56M
UWH1357RA, 57M
Vehicle
Bleomycin
Blot #1
Blot #2
PC1/3
PC2
CPE
ProSAAS
Vinculin
β-actin
PC1/3 / Vinculin Ratio
PC2 / Vinculin Ratio
CPE / Vinculin Ratio
ProSAAS / Vinculin Ratio
PC1/3 / β-actin Ratio
PC2/ β-actin Ratio
CPE / β-actin Ratio
ProSAAS / β-actin Ratio
Vehicle Bleomycin

ESM Figure 5. Proinsulin processing factor western blots for each donor islet preparation following DNA damage and senescence induction with bleomycin. Senescence was induced with 50 μmol/l bleomycin treatment for 48 h followed by drug washout and extended culture in drug-free media for 4 or 5 days. Islets were then harvested for western blot analysis of PC1/3, PC2, CPE and ProSAAS, with vinculin or β-actin detected as a loading control. Data are mean ± s.d. of n=3 or 4 islet sample replicates (treated as technical replicates) per donor experiment. $^{**}p < 0.01$, $^{*}p < 0.05$, two-tailed T test. Note: loading control blots for vinculin or β-actin for donors HP-23278-01, R515, R523, R509, R510 and UWH1357RA are the same as in ESM Fig. 2 because they were done on the same membranes after stripping and reprobing with different primary antibodies.

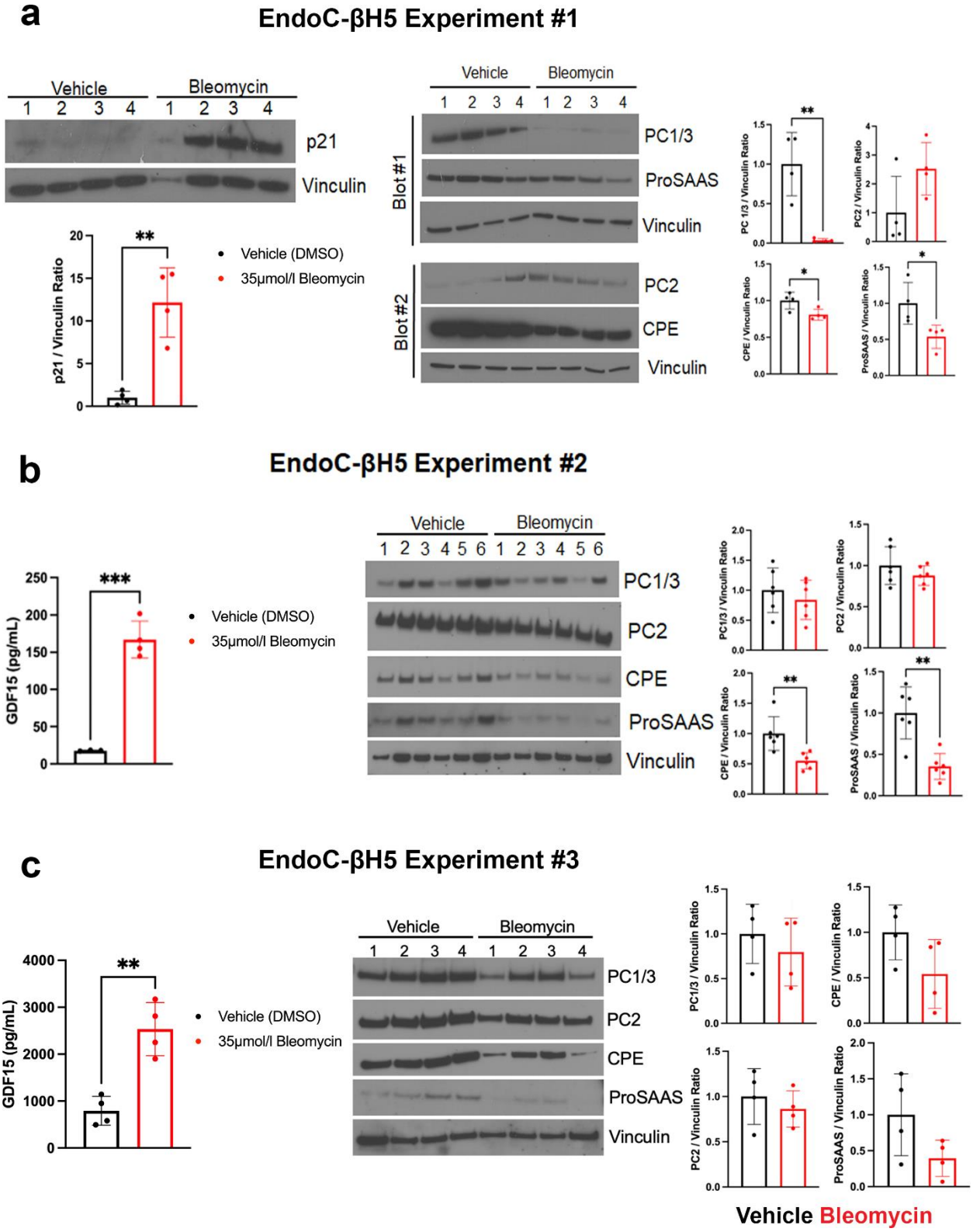


ESM Figure 6. Proteomics dataset analysis of proteins associated with aging and relationship of CDKN1A and CDKN2A to islet insulin content per IEQ. (a) Humanislets.com data portal was used to analyze donor islet proteomics datasets to identify proteins significantly associated with donor age, when controlling for sex, BMI, HbA1c and diabetes status. This analysis was run with n=120 donor islet proteomics datasets that met the criteria. (b) Volcano plot of associations with those in red showing significant positive association and those in grey showing non-significant associations.

CDKN1A (encoding p21, not significant) and CDKN2A (encoding $p16^{INK4A}$ and $p14^{ARF}$, significant positive association) are shown below with their corresponding data plots and adjusted p-values. Humanislets.com. (c) Linear regression association of CDKN2A protein and CDKN1A protein and normalized islet insulin content per islet equivalent (IEQ). Both proteins were not significantly associated with islet insulin content per IEQ.



ESM Figure 7. Single-cell RNA-seq dataset analysis of relationship between *CDKN1A* and *PCSK1*, *PCSK2*, *CPE* or *PCSK1N* in human beta cells. Human Pancreas Analysis Program (HPAP) single-cell RNA-seq datasets for beta cells in control (n=27,160 cells), autoantibody-positive (n=8,823 cells) and T1D donors (n=715 cells) were examined using bivariate plots for *CDKN1A* (x-axis) and proinsulin processing genes *PCSK1*, *PCSK2*, *CPE*, and *PCSK1N*.


a
EndoC-βH5 Experiment #1
Vehicle
Bleomycin
1 2 3 4 1 2 3 4
p21
Vinculin
p21 / Vinculin Ratio
Vehicle (DMSO)
35µmol/l Bleomycin
Blot #1
PC1/3
ProSAAS
Vinculin
Blot #2
PC2
CPE
Vinculin
PC 1/3 / Vinculin Ratio
PC2 / Vinculin Ratio
CPE / Vinculin Ratio
ProSAAS / Vinculin Ratio
b
EndoC-βH5 Experiment #2
GDF15 (pg/mL)
1 2 3 4 5 6 1 2 3 4 5 6
PC1/3
PC2
CPE
ProSAAS
Vinculin
c
EndoC-βH5 Experiment #3
GDF15 (pg/mL)
1 2 3 4 1 2 3 4
PC1/3
PC2
CPE
ProSAAS
Vinculin
Vehicle Bleomycin

ESM Figure 8. Validation of DNA damage response in EndoC-βH5 cells and proinsulin processing factor western blots per experiment. (a), (b) and (c) EndoC-βH5 human beta cells were induced to a DNA damage response with 35 μmol/l bleomycin treatment or vehicle control (0.15% vol./vol. DMSO) for 48 h followed by drug washout and culture for 5-6 days in three independent experiments on different batches of cells. Senescence was validated by western blot for p21 with vinculin as a loading control in (a) or GDF15 ELISA on the conditioned media at day 6 post-drug washout in (b) and (c). Western blot analysis for PC1/3, PC2, CPE and ProSAAS with vinculin as a loading control was performed on bleomycin-induced senescent or vehicle control-treated cells at day 5 or 6 post-drug washout. Data are mean ± s.d. of n = 3 or 4 independently treated wells of cells (replicates) per vial of cells for each experiment. ***p< 0.001, **p<0.01, *p<0.05, two-tailed T test.

Diabetologia

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

Islet preparation	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
MANDATORY INFORMATION								
Unique identifier	R507	R509	R510	R515	R434	HP23278-01	R523	HP-25078-01A
Donor age (years)	59	53	53	28	50	54	59	45
Donor sex (M/F)	F	M	F	M	F	F	M	M
Donor BMI (kg/m^2)	19.9	20.1	21.3	26.1	24.2	23.3	23.4	31.90
Donor HbA_{1c} or other measure of blood glucose control	5.30	5.80	5.90	5.30	5.70	5.60	5.50	5.60
Origin/source of islets[b]	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	IIDP	Alberta IsletCore	IIDP
Islet isolation centre	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	Prodo Labs Human Islet Isolation Center	Alberta IsletCore	Prodo Labs Human Islet Isolation Center
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)								
Glucose-lowering therapy at time of death[c]								
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	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Additional notes								

[a]If you have used more than eight islet preparations, please complete additional forms as necessary

[b]For example, IIDP, ECIT, Alberta IsletCore

[c]Please specify the therapy/therapies

[d]Time of islet culture at the isolation centre, during shipment and at the receiving laboratory

[e]Please specify the test and the results

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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

Islet preparation	9	10	11	12	13	14	15	16
MANDATORY INFORMATION								
Unique identifier	R563	R564	R566	HP-25021-01	HP-25073-01	UWH1357RA	HP-25007-01	HP-25129-01
Donor age (years)	59	37	21	54	56	57	57	50
Donor sex (M/F)	M	M	M	F	M	M	M	M
Donor BMI (kg/m^2)	26.6	28.7	23.7	23.0	29.3	28.1	30.1	25.80
Donor HbA_{1c} or other measure of blood glucose control	4.50	5.40	5.50	5.20	5.40	5.50	5.30	5.20
Origin/source of islets[b]	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	IIDP	IIDP	IIDP	IIDP	IIDP
Islet isolation centre	Alberta IsletCore	Alberta IsletCore	Alberta IsletCore	Prodo Labs Human Islet Isolation Center	Prodo Labs Human Islet Isolation Center	Prodo Labs Human Islet Isolation Center	Prodo Labs Human Islet Isolation Center	Prodo Labs Human Islet Isolation Center
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)								
Glucose-lowering therapy at time of death[c]								
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	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Additional notes								

[a]If you have used more than eight islet preparations, please complete additional forms as necessary

[b]For example, IIDP, ECIT, Alberta IsletCore

[c]Please specify the therapy/therapies

[d]Time of islet culture at the isolation centre, during shipment and at the receiving laboratory

[e]Please specify the test and the results

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Islet preparation	17	18	19	20	21	22	23	24
MANDATORY INFORMATION								
Unique identifier	ICRH159	R551	HP-2350	HP-2331801				
Donor age (years)	19	57	20	51				
Donor sex (M/F)	M	F	F	M				
Donor BMI (kg/m^2)	19.9	26.0	22.4	24.6				
Donor HbA_{1c} or other measure of blood glucose control	5.30	4.30	4.90	5.40				
Origin/source of islets[b]	IIDP	Alberta IsletCore	IIDP	IIDP				
Islet isolation centre	Prodo Labs Human Islet Isolation Center	Alberta IsletCore	University of Miami	Prodo Labs Human Islet Isolation Center				
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)								
Glucose-lowering therapy at time of death[c]								
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	Yes	Yes	Yes	Yes				
Additional notes								

[a]If you have used more than eight islet preparations, please complete additional forms as necessary

[b]For example, IIDP, ECIT, Alberta IsletCore

[c]Please specify the therapy/therapies

[d]Time of islet culture at the isolation centre, during shipment and at the receiving laboratory

[e]Please specify the test and the results

ESM References

1. Brawerman G, Pipella J, Thompson PJ (2022) DNA damage to β cells in culture recapitulates features of senescent β cells that accumulate in Type 1 Diabetes. Mol Metab 62:101524. https://doi.org/10.1016/j.molmet.2022.101524
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