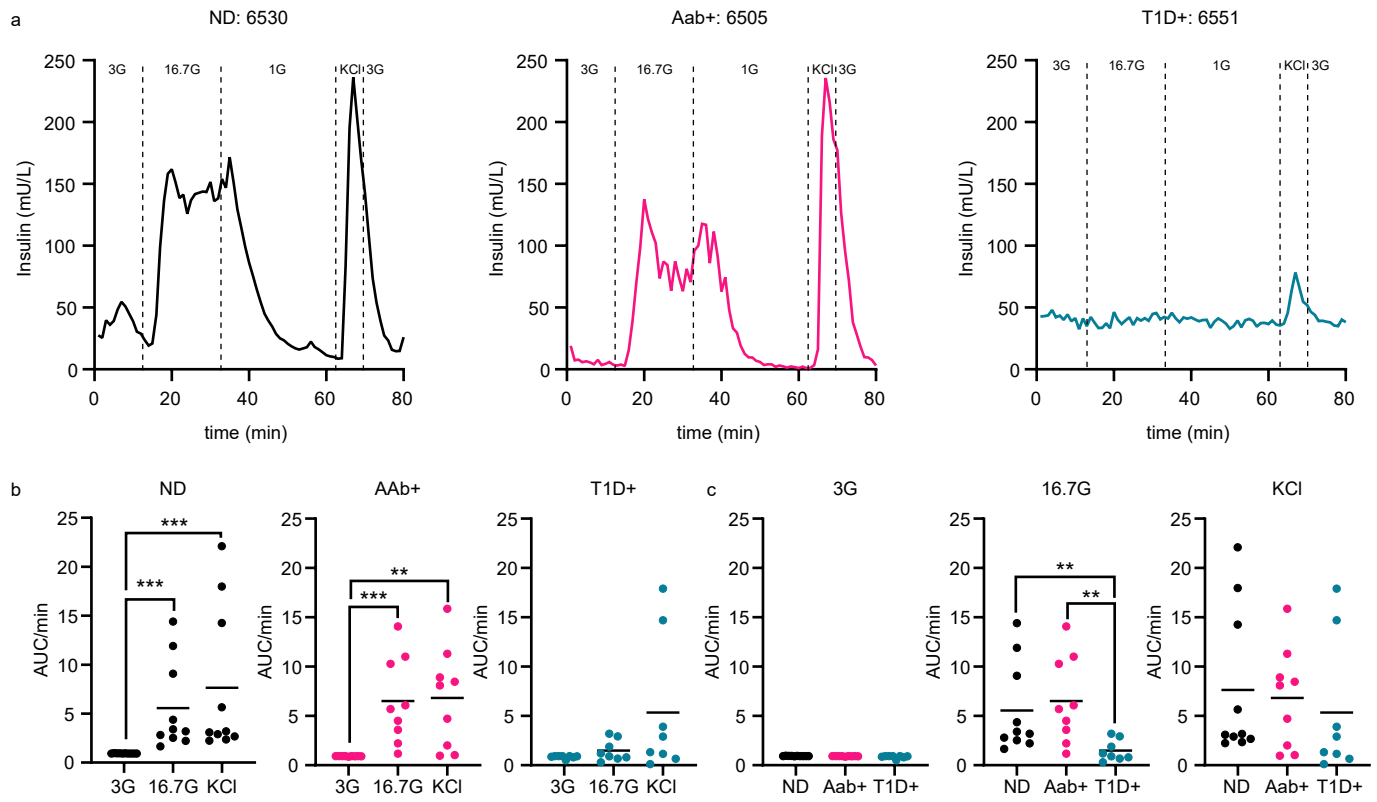
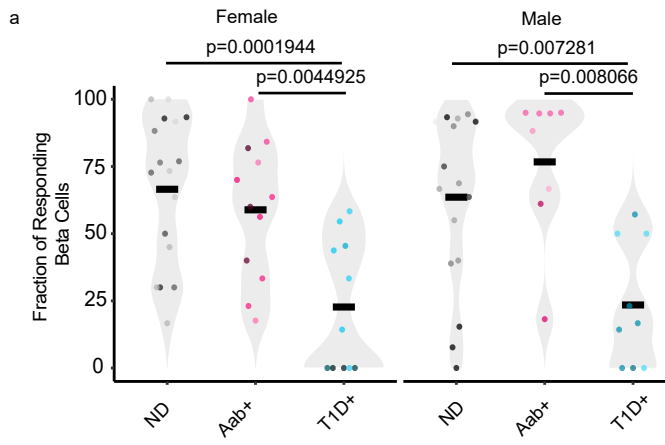


Supplementary Figure 1: UMAP of laser-capture microdissected islets. Uniform manifold approximation and projection (UMAP) plot showing clustering of 260 islets. Each dot represents an islet and each clinical phenotype is plotted with different color.

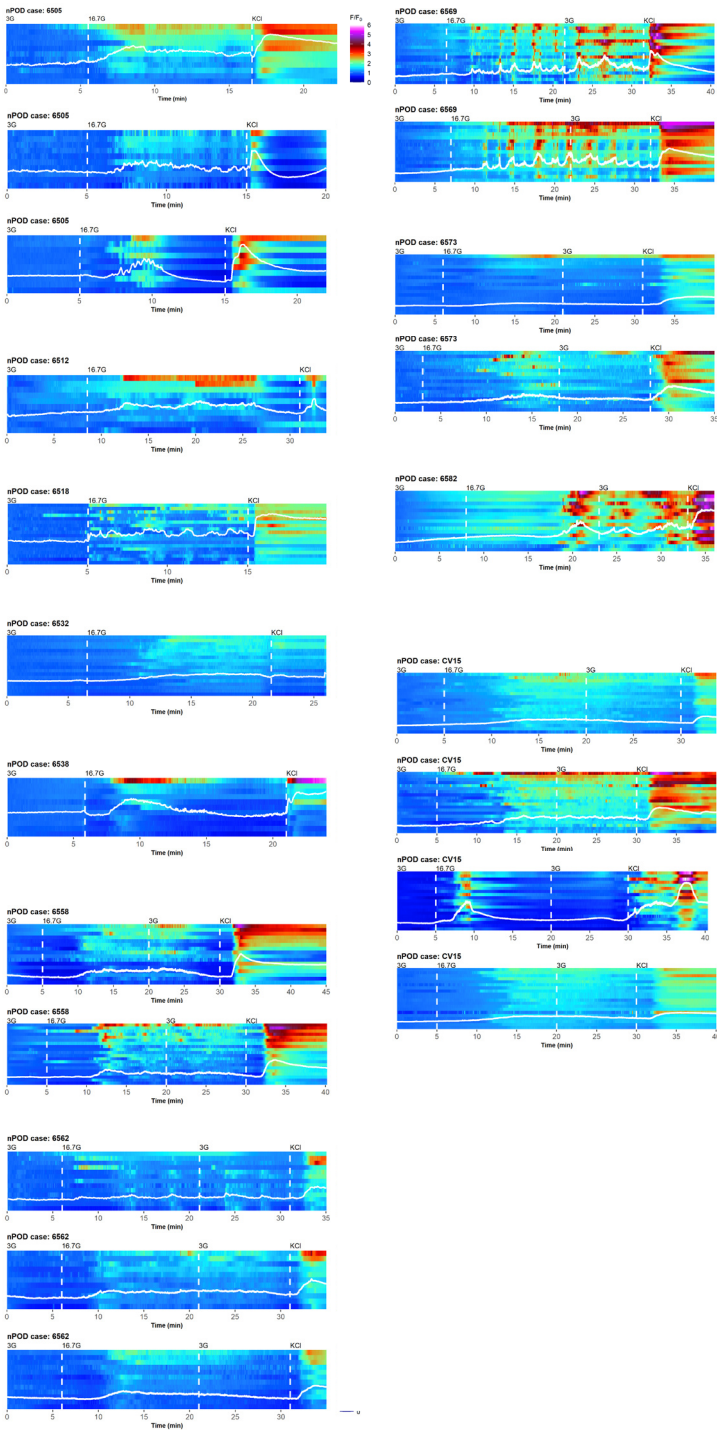


Supplementary Figure 2: Beta cell insulin secretion decreases after T1D diagnosis. a) Representative insulin secretion traces from ND, Aab+, and T1D+ donors to low glucose (3 mM), high glucose (16.7 mM) and KCl (30 mM). b) Quantification of AUC per minute of insulin secretion of live pancreas tissue slices from ND (n=10), Aab+ (n=9), and T1D+ (n=8) donors. Each dot represents one donor. c) Quantification of AUC per minute of insulin secretion of the donor groups during different glucose stimulations. One-way ANOVA with multiple comparisons run on log10 transformed data, **P<0.01, ***P<0.001.



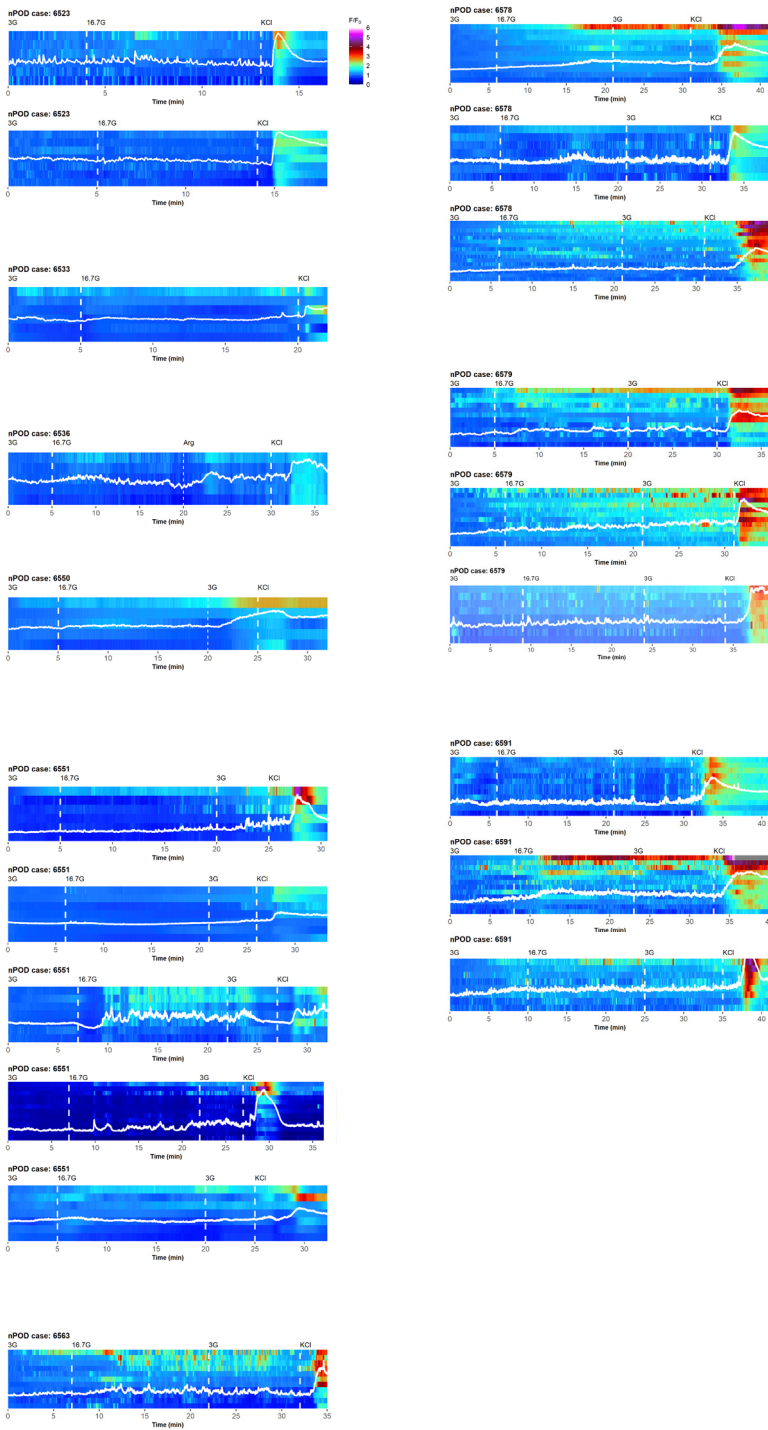
Supplementary Figure 3: Beta cell dysfunction is not driven by sex differences. The fraction of beta cells responding to high glucose within each islet in male and female donors recorded from ND, Aab+, and T1D+ cases. Each dot represents an islet recording. Center line indicates the mean. One-way ANOVA with multiple comparisons.

Aab+

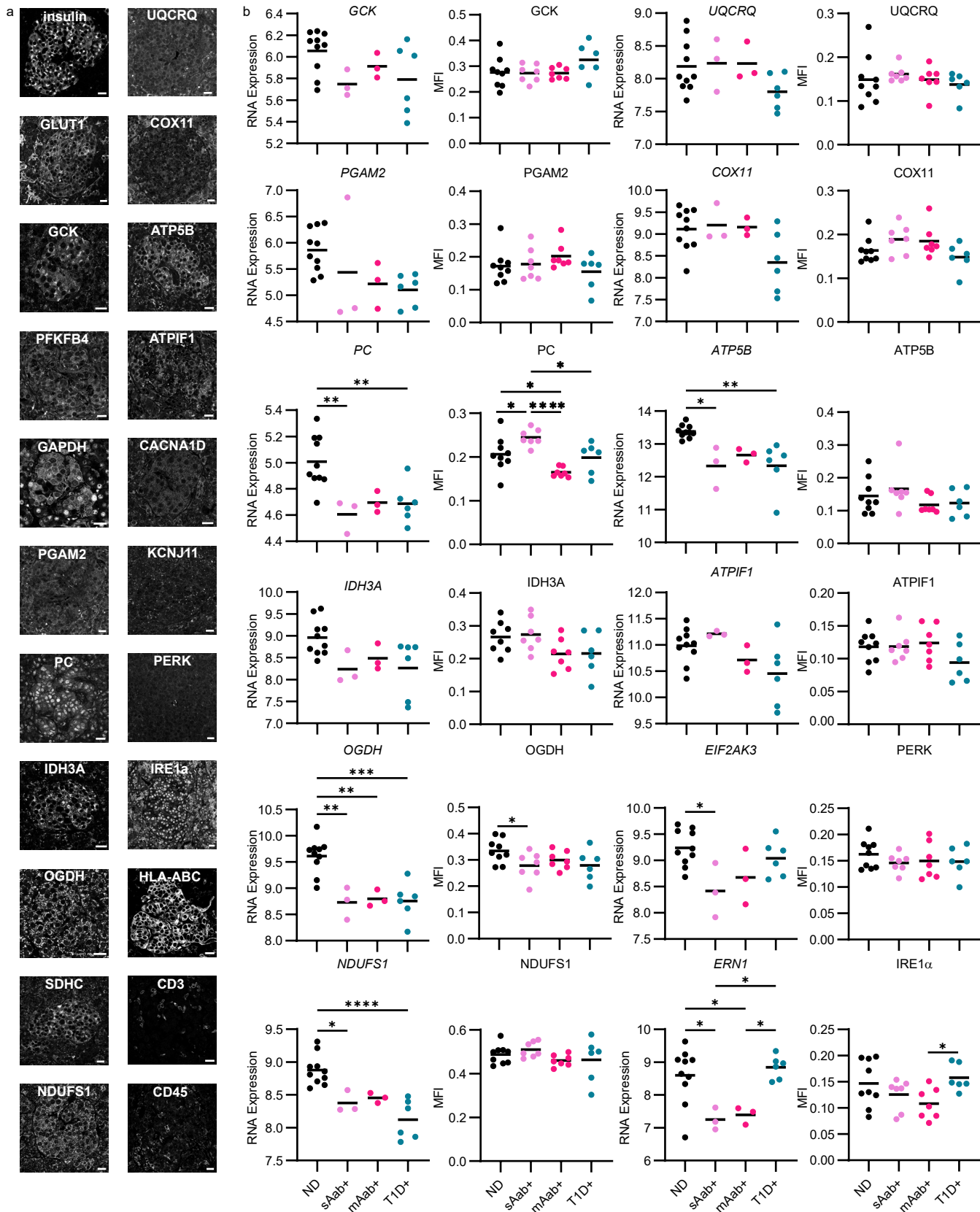


Supplementary Figure 5: Ca^{2+} responses of beta cells within Aab+ slices. Heatmaps of all Aab+ Ca^{2+} recordings showing the changes in fluorescence of the individual ROIs from Aab+ cases along with the superimposed average traces showing the glucose and KCl responses.

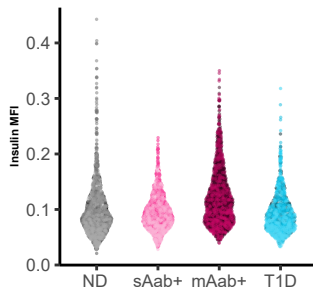
T1D+



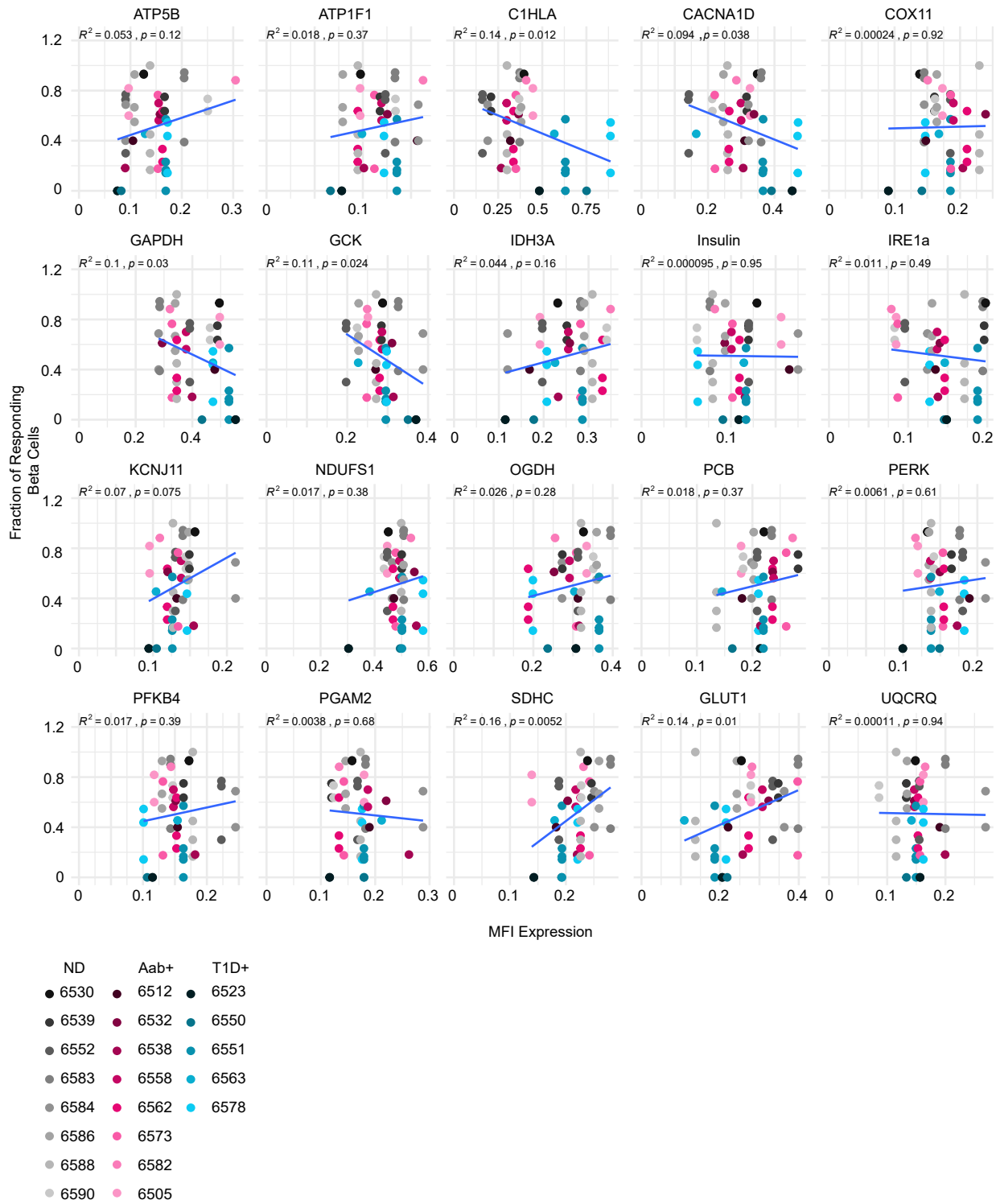
Supplementary Figure 6: Ca^{2+} responses of beta cells within T1D+ slices. Heatmaps of all T1D+ Ca^{2+} recordings showing the changes in fluorescence of the individual ROIs from T1D+ cases along with the superimposed average traces showing the lost high glucose responses and maintained KCl responses.



Supplementary Figure 7: ER stress markers and some glucose metabolism markers do not differ during T1D pathogenesis. a) Representative images of immunofluorescent staining of FFPE slides of the panel of markers used to assess immune cell infiltration and beta cell glucose metabolism in donors with ND (n=9), sAab+ donors (n=7), mAab+ donors (n=7), T1D+ donors (n=6). Scale bars, 20 μ m. b) Protein expression levels indicated by mean fluorescence intensity during the different stages of T1D development in donors with ND (n=9), sAab+ donors (n=7), mAab+ donors (n=7), and T1D+ donors (n=6) and RNA expression levels of glucose metabolism markers in laser-capture micro-dissected islets from donors at different stages of T1D development (ND, n=10; sAab+, n=3; mAab+, n=3; T1D+, n=6). MFIs: One-way ANOVA with multiple comparisons, *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001. RNA: One-way ANOVA followed by a Tukey post-hoc test, *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001.



Supplementary Figure 8: Insulin protein levels within beta cells does not change as T1D progresses. Protein expression levels of insulin within beta cells indicated by mean fluorescence intensity during the different stages of T1D development in donors with ND (n=9), sAab+ donors (n=7), mAab+ donors (n=7), and T1D+ donors (n=6). Each dot represents an islet. One-way ANOVA with multiple comparisons,



Supplementary Figure 9: Correlation of beta cell function and glucose metabolism markers. Graphs showing the relationship between the fraction of responding beta cells and protein expression of markers of glucose metabolism with the linear models indicated in blue.

Supplementary Table 1: Donor characteristics from nPOD cases. Table summarizes donor information and applied studies.

Case	RRID	Type	Duration (years)	Autoantibody	Age (years)	Sex	Ethnicity	HbA1c	C-pep (ng/mL)	HLA-DR	HLA-DQ	Data Types
CV14	SAMN38117313	No Diabetes		Negative	9.85	F	Caucasian	5.3	4.37	DR07/15	DQ02/06	Ca ²⁺ recordings, perfusion
6073	SAMN15879130	No Diabetes		Negative	19.2	M	Caucasian	0	0.69	DR13/16	DQ05/06	RNA expression
6098	SAMN15879155	No Diabetes		Negative	17.8	M	Caucasian	4.9	1.41	DR17/08	DQ02/04	RNA expression
6131	SAMN15879188	No Diabetes		Negative	24.2	M	Caucasian	0	1.01	DR17/17	DQ02/02	RNA expression
6230	SAMN15879286	No Diabetes		Negative	16	M	Caucasian	5.3	5.22	DR04/11	DQ07/08	RNA expression
6235	SAMN15879291	No Diabetes		Negative	30	M	Caucasian	0	8.1	DR04/17	DQ02/08	RNA expression
6293	SAMN15879347	No Diabetes		Negative	9	F	Caucasian	0	2.22	DR01/11	DQ05/07	RNA expression
6316	SAMN15879370	No Diabetes		Negative	6	M	Caucasian	0	4.58	DR04/13	DQ08/09	RNA expression
6336	SAMN15879390	No Diabetes		Negative	14.3	F	Caucasian	5.2	7.87	DR07/13	DQ02/06	RNA expression
6339	SAMN15879393	No Diabetes		Negative	23.3	M	Caucasian	5.3	10.56	DR03/10	DQ02/05	RNA expression
6401	SAMN15879454	No Diabetes		Negative	25.07	F	Hispanic/ Latino	5.8	12.81	DR07/13	DQ02/06	RNA expression
6516	SAMN18053200	No Diabetes		Negative	20.75	M	Caucasian	5.5	8.91	DR01/07	DQ02/05	Ca ²⁺ recordings, perfusion
6530	SAMN18053212	No Diabetes		Negative	14.52	F	African American	6	7.41	DR04/17	DQ02/08	Ca ²⁺ recordings, IF, perfusion
6535	SAMN18242779	No Diabetes		Negative	31.07	F	Caucasian		6.59	DR11/13	DQ06/07	Ca ²⁺ recordings
6539	SAMN25652250	No Diabetes		Negative	24.6	M	Hispanic	5.7	39.23	DR04/13	DQ06/08	Ca ²⁺ recordings, IF
6540	SAMN25652251	No Diabetes		Negative	6.86	F	Hispanic	5.8	2.03	DR04/11	DQ07/04	Ca ²⁺ recordings, perfusion
6552	SAMN30386842	No Diabetes		Negative	33.87	F	Caucasian	5.6	1.8	DR17/04	DQ02/08	Ca ²⁺ recordings, IF, perfusion
6559	SAMN30386848	No Diabetes		Negative	23.46	F	Asian	5.3	7.02	DR11/12	DQ07/--	IF
6583	SAMN38117303	No Diabetes		Negative	30	M	Caucasian	5	10.55	DR11/13	DQ07/06	Ca ²⁺ recordings, IF, perfusion
6584	SAMN38117304	No Diabetes		Negative	22	M	Caucasian	5.3	6.02	DR04/11	DQ07/08	Ca ²⁺ recordings, IF, perfusion
6586	SAMN38117306	No Diabetes		Negative	13	M	Caucasian	5.1	6.83	DR04/07	DQ02/08	Ca ²⁺ recordings, IF, perfusion
6588	SAMN40555580	No Diabetes		Negative	29	F	Caucasian	5.1	7.3	DR04/11	DQ07/07	Ca ²⁺ recordings, IF, perfusion
6590	SAMN38117309	No Diabetes		Negative	16	F	African American	5.3	49.65	DR08/13	DQ06/07	Ca ²⁺ recordings, IF, perfusion
6597	SAMN40555584	No Diabetes		Negative	6	F	Hispanic/Latino	5.7	5.02	DR04/04	DQB08/08	Ca ²⁺ recordings
6598	SAMN40555585	No Diabetes		Negative	17	M	Hispanic/Latino	5.4	1.36	DR04/14	DQB07/08	Ca ²⁺ recordings
CV15	SAMN40555609	Aab+		GADA+	18.93	M	Caucasian	5.2	5.03	DR07/15	DQ06/09	Ca ²⁺ recordings, perfusion
6080	SAMN15879137	Aab+		GADA+, mIAA+	69.2	F	Caucasian	0	1.84	DR01/04	DQ03/05	RNA expression

Case	RRID	Type	Duration (years)	Autoantibody	Age (years)	Sex	Ethnicity	HbA1c	C-pep (ng/mL)	HLA-DR	HLA-DQ	Data Types
6147	SAMN15879203	Aab+		GADA+	23.8	F	Caucasian	5.2	3.19	DR04/08	DQ04/07	RNA expression
6158	SAMN15879214	Aab+		GADA+, mIAA+	40.3	M	Caucasian	5.6	0.51	DR04/13	DQ06/07	RNA expression
6167	SAMN15879223	Aab+		IA2A+, ZnT8A+	37	M	Caucasian	0	5.43	DR04/02	DQ08/06	RNA expression
6181	SAMN15879237	Aab+		GADA+	31.9	M	Caucasian	0	0.06	DR01/04	DQ08/05	RNA expression
6314	SAMN15879368	Aab+		GADA+	21	M	Caucasian	0	1.49	DR103/04	DQ03/05	RNA expression
6424	SAMN15879477	Aab+		GADA+, mIAA+	17.65	M	Caucasian	5.8	6.97	DR17/04	DQ02/08	IF
6429	SAMN15879482	Aab+		GADA+, mIAA+	22.1	M	African American	5.5	2.25	DR103/17	DQ02/05	IF
6450	SAMN15879503	Aab+		GADA+, ZnT8A+	22	F	Caucasian	5.7	5.47	DR17/--	DQ02/--	IF
6505	SAMN15879558	Aab+		GADA+, mIAA+	20.59	F	Hispanic	5.1	20.8	DR04/07	DQ02/08	Ca ²⁺ recordings, IF, perfusion,
6512	SAMN15879564	Aab+		IA2A+, mIAA+, ZnT8A+	30.59	F	Caucasian	5.2	3.2	DR04/07	DQ02/07	Ca ²⁺ recordings, IF, perfusion
6518	SAMN25652247	Aab+		GADA+	21.86	M	Caucasian	6	10.93	DR01/01:03	DQ05/05	Ca ²⁺ recordings, perfusion
6521	SAMN18053204	Aab+		GADA+, IA2A+, ZnT8A+	19.77	M	Hispanic/ Latino	5.8	7.44	DR04/17	DQ02/08	IF
6532	SAMN18053214	Aab+		GADA+	20.04	M	Hispanic	5.9	22.12	DR07/11	DQ02/07	Ca ²⁺ recordings, IF, perfusion
6538	SAMN25652249	Aab+		GADA+	19.14	M	Caucasian	5.8	11.33	DR17/08	DQ02/04	Ca ²⁺ recordings, IF, perfusion
6549	SAMN25652260	Aab+		GADA+, mIAA+	4.22	M	Caucasian	6.2	1.17	DR04/07	DQ08/09	IF
6553	SAMN30386843	Aab+		mIAA+	12.34	F	Hispanic/ Latino	8.4	4.62	DR17/04	DQ02/08	IF
6558	SAMN30386847	Aab+		GADA+	21.69	F	African American	4.4	8.03	DR17/07	DQ02/--	Ca ²⁺ recordings, IF
6562	SAMN30386850	Aab+		GADA+	29.77	F	Caucasian	5.6	13.19	DR04/15	DQ06/08	Ca ²⁺ recordings, IF
6569	SAMN38117299	Aab+		GADA+	20	F	Hispanic	6	2.44	DR04/15	DQ08/06	Ca ²⁺ recordings, perfusion
6573	SAMN33284291	Aab+		GADA+	24.48	F	Caucasian	5.1	1.85	DR01/17	DQ02/05	Ca ²⁺ recordings, IF, perfusion
6582	SAMN38117302	Aab+		GADA+	22.38	M	Caucasian	5.6	2.67	DR17/04	DQ02/08	Ca ²⁺ recordings, IF, perfusion
6268	SAMN15879322	T1D+	3	mIAA+	12	F	Caucasian	9.8	0.05	DR13/17	DQ02/06	RNA expression
6306	SAMN15879360	T1D+	5	mIAA+	19	M	Caucasian	10.1	<0.02	DR04/17	DQ02/08	RNA expression
6342	SAMN15879396	T1D+	2	IA2A+, mIAA+	14	F	Caucasian	9.2	0.26	DR01/04	DQ08/05	RNA expression
6362	SAMN15879415	T1D+	0	GADA+	24.9	M	Caucasian	10	0.38	DR103/17	DQ02/05	RNA expression
6371	SAMN15879424	T1D+	2	GADA+, IA2A+, mIAA+, ZnT8A+	12.5	F	Caucasian	9.5	0.11	DR13/17	DQ02/06	RNA expression
6396	SAMN15879449	T1D+	2	Negative	17.1	F	Caucasian	13.4	0.06	DR07/17	DQ02/null	RNA expression
6523	SAMN18053206	T1D	3	GADA+, mIAA+	12.17	F	African American	11.1	0.04	DR17/07	DQ02/02	Ca ²⁺ recordings, IF

Case	RRID	Type	Duration (years)	Autoantibody	Age (years)	Sex	Ethnicity	HbA1c	C-pep (ng/mL)	HLA-DR	HLA-DQ	Data Types
6526	SAMN18053209	T1D	1	GADA+, mIAA+	29.74	M	Hispanic/ Latino	6.6	0.07	DR04/13	DQ08/06	IF
6533	SAMN18242777	T1D	0	IA2A+, mIAA+, ZnT8A+	3.75	F	Caucasian	11.4	0.17	DR04/17	DQ02/08	Ca ²⁺ recordings, perfusion
6536	SAMN18242780	T1D	4	GADA+	20.16	F	Caucasian	12.7	0.04	DR04/17	DQ02/08	Ca ²⁺ recordings, perfusion
6550	SAMN25652261	T1D	0	GADA+, ZnT8A+	25.06	M	Caucasian	14	0.02	DR17/--	DQ02/07	Ca ²⁺ recordings, IF, perfusion
6551	SAMN25652262	T1D	0.58	GADA+, IA2A+, mIAA+, ZnT8A+	20.7	M	Caucasian	6.4	0.11	DR04/07	DQ02/07	Ca ²⁺ recordings, IF, perfusion
6563	SAMN30386851	T1D	0	IA2A+	14.56	F	Caucasian	9.6	1.04	DR07/08	DQ02/04	Ca ²⁺ recordings, IF, perfusion
6578	SAMN33284295	T1D	0	IA2A+, ZnT8A+	11.95	F	Caucasian	13.6	0.35	DR04/11	DQ07/08	Ca ²⁺ recordings, IF, perfusion
6579	SAMN33284296	T1D	1	GADA+, mIAA+	13	F	Caucasian	15	0.31	DR17/13	DQB02/06	Ca ²⁺ recordings, perfusion
6591	SAMN38117310	T1D	0	IA2A+, ZnT8A+	3	M	Caucasian	12.8	0.03	DR04/13	DQ08/06	Ca ²⁺ recordings, perfusion

Supplementary Table 2: Ca²⁺ imaging summary. Ca²⁺ imaging characteristics and protocols for all recordings.

Case	Cell Selection	Slice	Ca ²⁺ Indicator	Protocol	Frame Rate (s)
6505	Reflectance	2	Fluo4	0-5 min LG, 5-15 min HG, 15 min-end KCl	2.873
6505	Reflectance	5	Fluo4	0-5 min LG, 5-15 min HG, 15 min-end KCl	1.99913
6505	Reflectance	6	Fluo4	0-5 min LG, 5-15 min HG, 16 min-end KCl	1.99886
6512	Reflectance	2	Fluo4	0-7 min LG, 7-22 min 30s HG, 22 min 30s -end KCl	1.99986
6516	Reflectance	1	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.31722
6516	Reflectance	4	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.31152
6516	Reflectance	6	Fluo4	0-5 min LG, 5-30 min HG, 30 min-end KCl	2.31424
6516	Reflectance	7	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.31447
6516	Reflectance	8	Fluo4	0-5 min LG, 5-40 min HG, 40 min-end KCl	2.31152
6518	Reflectance	4	Fluo4	0-5 min LG, 5-15 min HG, 15 min-end KCl	3.52091
6523	Reflectance	3	Fluo4	0-3 min LG, 3-18 min HG, 18 min-end KCl	2.72597
6523	Reflectance	4	Fluo4	0-3 min LG, 3-18 min HG, 18 min-end KCl	2.72598
6530	ENTPD3	1	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	1.99799
6530	ENTPD3	3	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	1.99883
6530	ENTPD3	4	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	1.99834
6532	ENTPD3	6	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	1.99933
6533	ENTPD3	10	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.55227
6535	ENTPD3	8	Fluo4	0-5 min LG, 5-20 min HG, 20-30 min arginine, 30 min-end KCl	2.31722
6536	ENTPD3	4	Fluo4	0-5 min LG, 5-20 min HG, 20-30 min arginine, 30 min-end KCl	2.31721
6538	ENTPD3	4	Fluo4	0-5 min 50s LG, 5 min 50s- 21 min HG, 21 min-end KCl	2.31696
6539	ENTPD3	1	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.31335
6539	ENTPD3	2	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.31407
6540	ENTPD3	3	Fluo4	0-5 min LG, 5-20 min HG, 20 min-end KCl	2.31721
6550	ENTPD3	2	Fluo4	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	2.31721
6551	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37442
6551	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37585
6551	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37442
6551	ENTPD3	5	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37728
6551	ENTPD3	6	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37585
6552	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-27 min LG, 27 min-end KCl	0.37585
6552	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37727
6552	ENTPD3	5	Calbryte520	0-5 min LG, 5-20 min HG, 20-25 min LG, 25 min-end KCl	0.37585
6558	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6558	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6562	RL	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl I	4.38736
6562	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37443
6562	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37443
6563	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
CV14	ENTPD3	6	Calbryte520	0-6 min LG, 6-21 min HG, 21-31 min LG, 31 min-end KCl	0.37585
CV14	ENTPD3	7	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727

Case	Cell Selection	Slice	Ca ²⁺ Indicator	Protocol	Frame Rate (s)
6569	ENTPD3	5	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6569	ENTPD3	6	Calbryte520	0-5 min 30s LG, 5 min 30s-20 min 30s HG, 20 min 30s-30 min 30s LG, 30 min 30s-end KCl	0.37585
CV15	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
CV15	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
CV15	ENTPD3	5	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
CV15	ENTPD3	6	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6573	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6573	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6578	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6578	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6578	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6579	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6579	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6579	ENTPD3	7	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.39293
6582	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6583	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6583	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6583	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6584	ENTPD3	7	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6584	ENTPD3	9	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6586	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37442
6586	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37728
6586	ENTPD3	3	Calbryte520	0-6 min LG, 6-21 min HG, 21-31 min LG, 31 min-end KCl	0.37728
6588	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6588	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6588	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20 min-30 min 40s LG, 30 min 40s-end KCl	0.37727
6588	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min 30s HG, 20 min 30s-30min 30s LG, 30 min 30s-end KCl	0.37727
6590	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6590	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6590	ENTPD3	5	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6591	ENTPD3	6	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6591	ENTPD3	9	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6591	ENTPD3	10	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6597	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6597	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37728
6598	ENTPD3	1	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727
6598	ENTPD3	2	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6598	ENTPD3	3	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37585
6598	ENTPD3	4	Calbryte520	0-5 min LG, 5-20 min HG, 20-30 min LG, 30 min-end KCl	0.37727

Supplementary Table 3: FFPE staining panels. Staining panels and protocols used for the immunofluorescent staining of FFPE pancreas tissue sections.

Panel	Primary Antibody	Dilution	Incubation Time	Catalog Information	Secondary Antibody	Dilution	Incubation Time	Catalog Information
1	ATPIF1	1:500	Overnight	Invitrogen MA5-31642 Lot WG3320449 Clone 1F3B8	Goat anti-Mouse IgG2b Heavy Chain Secondary Antibody [FITC]	1:200	10 minutes	Novus NB7520 Lot F15
1	ATP5B	1:100	Overnight	Invitrogen A21351 Lot 2747427 Clone 3D5	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
1-10	CD3	1:50	Overnight	Dako A0452 Lot 41495387	Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 405	1:100	10 minutes	Invitrogen A31556 Lot 2465047
1-10	Insulin (AF647)	1:200	1 hour	BD Pharmingen 565689 Lot 2168160 Clone T56-706	NA	NA	NA	NA
2	KCNJ11	1:100	Overnight	Invitrogen PA5-99440 Lot XC3547445	IgG (H+L) Cross-Adsorbed Goat anti-Rabbit, Alexa Fluor™ 488	1:200	10 minutes	Invitrogen A11008 Lot 2743033
2	SDHC	1:100	Overnight	Santa Cruz sc-515102 Lot A3020 Clone C-2	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
3	PCB	1:100	Overnight	Santa Cruz 271493 Lot E1923 Clone H-2	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
3	SLC2A1	1:100	Overnight	Invitrogen MA5-31960 Lot XC3541241A Clone SA0377	IgG (H+L) Cross-Adsorbed Goat anti-Rabbit, Alexa Fluor™ 488	1:200	10 minutes	Invitrogen A11008 Lot 2743033
4	GCK	1:50	72 hours	Santa Cruz sc-17819 Lot K0821 clone G-6	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
4	CACNA1D	1:100	Overnight	Proteintech 22276-1-AP Lot 00040685	IgG (H+L) Cross-Adsorbed Goat anti-Rabbit, Alexa Fluor™ 488	1:200	10 minutes	Invitrogen A11008 Lot 2743033
5	PERK	1:100	Overnight	LS Bio C353177 Lot 229684	Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 555	1:200	10 minutes	Invitrogen A21428 Lot 2527964
5	NDUFS1	1:200	Overnight	Proteintech 12444-1-AP Lot 00075263	IgG (H+L) Cross-Adsorbed Goat anti-Rabbit, Alexa Fluor™ 488	1:200	10 minutes	Invitrogen A11008 Lot 2743033
6	COX11	1:200	Overnight	Invitrogen PA5-104519 Lot XC3547445A	IgG (H+L) Cross-Adsorbed Goat anti-Rabbit, Alexa Fluor™ 488	1:200	10 minutes	Invitrogen A11008 Lot 2743033
6	IDH3A	1:50	48 hours	Santa Cruz sc-398021 Lot B1221 Clone A-10	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
7	GAPDH	1:200	Overnight	Santa Cruz sc-47724 Clone 0411	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
7	OGDH	1:50	Overnight	Proteintech 66285-1-IG Clone 1H7A2	Goat anti-Mouse IgG2b Heavy Chain Secondary Antibody [FITC]	1:200	10 minutes	Novus NB7520 Lot F15
8	UQCQRQ	1:50	Overnight	Invitrogen PA5-106446	IgG (H+L) Cross-Adsorbed Goat anti-Rabbit, Alexa Fluor™ 488	1:200	10 minutes	Invitrogen A11008 Lot 2743033

Panel	Primary Antibody	Dilution	Incubation Time	Catalog Information	Secondary Antibody	Dilution	Incubation Time	Catalog Information
8	CD45	1:200	Overnight	Cell Signaling Technologies 13917T Clone D9M8I	Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 555	1:200	10 minutes	Invitrogen A21428 Lot 2527964
9	Pan-Class I HLA	1:200	Overnight	Abcam ab70328 Clone EMR8-5	Goat anti-Mouse IgG1 Heavy Chain Secondary Antibody [DyLight 550]	1:200	10 minutes	Novus NB7508R Lot D109323
9	PGAM2	1:50	Overnight	Invitrogen MA5-25671 Clone OT14E9	Goat anti-Mouse IgG2a Heavy Chain Secondary Antibody [FITC]	1:200	10 minutes	Novus NB7515
10	PFKB4	1:200	Overnight	Invitrogen MA5-25024 Clone OT11C8	Goat anti-Mouse IgG2a Heavy Chain Secondary Antibody [FITC]	1:200	10 minutes	Novus NB7515
10	IRE1 α	1:100	Overnight	Novus Biologicals NB100-2323	Goat Anti-Rabbit IgG H&L (Alexa Fluor® 555) preadsorbed	1:200	10 minutes	Abcam ab150086