SUPPLEMENTARY DATA

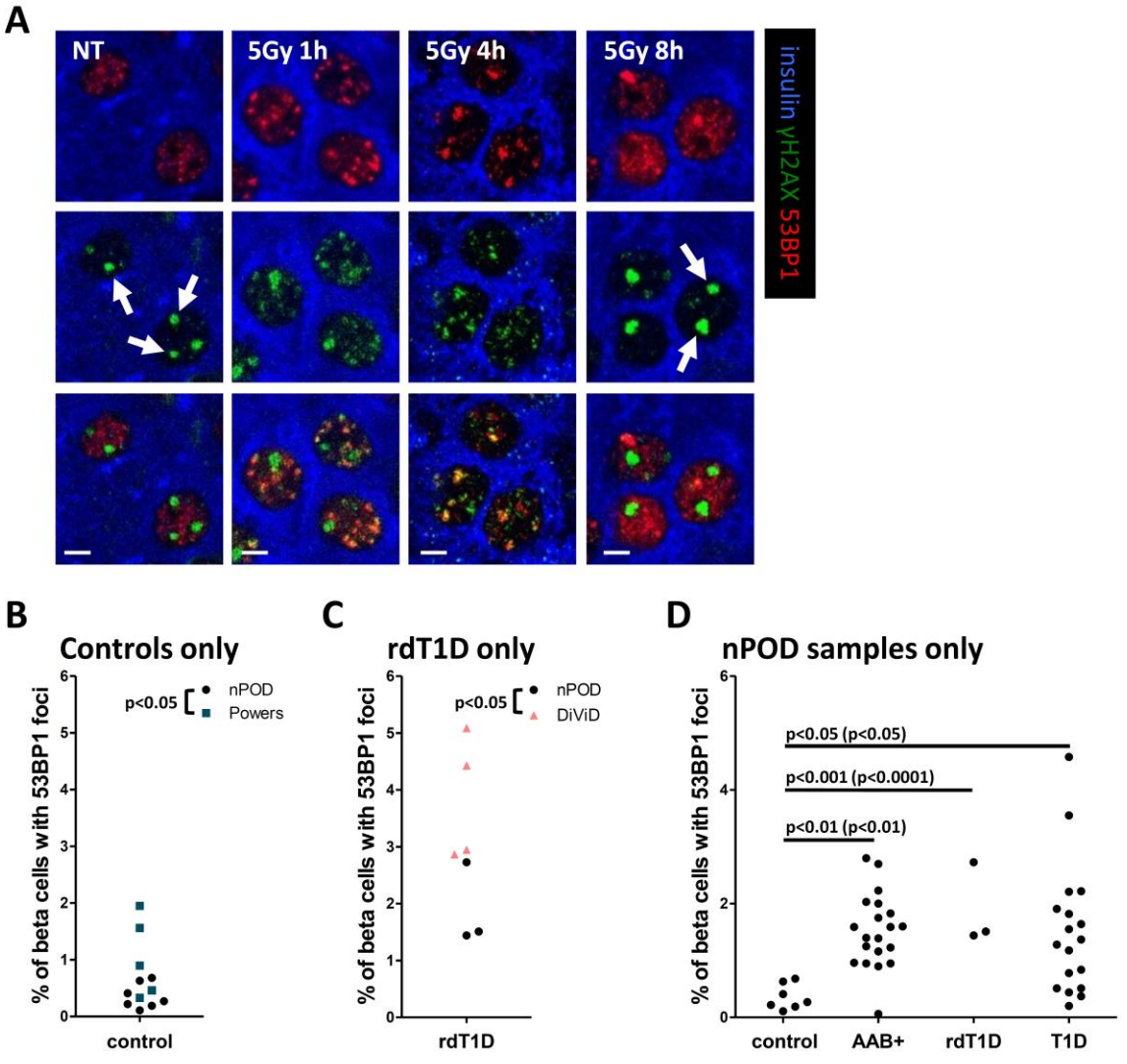
Supplementary Figure S1. DNA damage response in pancreata of recently diagnosed T1D patients.

A. The activation pattern of DDR proteins in mice following gamma irradiation. Wild type mice were subjected to 5 grey gamma irradiation and were sacrificed at different time points. Changes in markers of DDR were monitored using immunofluoresence to γH2AX and 53BP1. An atypical large focal form of γH2AX (white arrows) is found in beta cells regardless of a genotoxic condition. Note that these foci disperse at 4h past gamma irradiation and later reform.

B. The fraction of beta cells with activated 53BP1 in healthy donors originating in the nPOD repository (black dots, n=7) or at the Powers group (green squares, n=5). Each dot represents an individual case.

C. The fraction of beta cells with activated 53BP1 in recently diagnosed T1D donors originating in the nPOD repository (black dots, n=3) or at the DiViD study (pink triangles, n=4). Each dot represents an individual case.

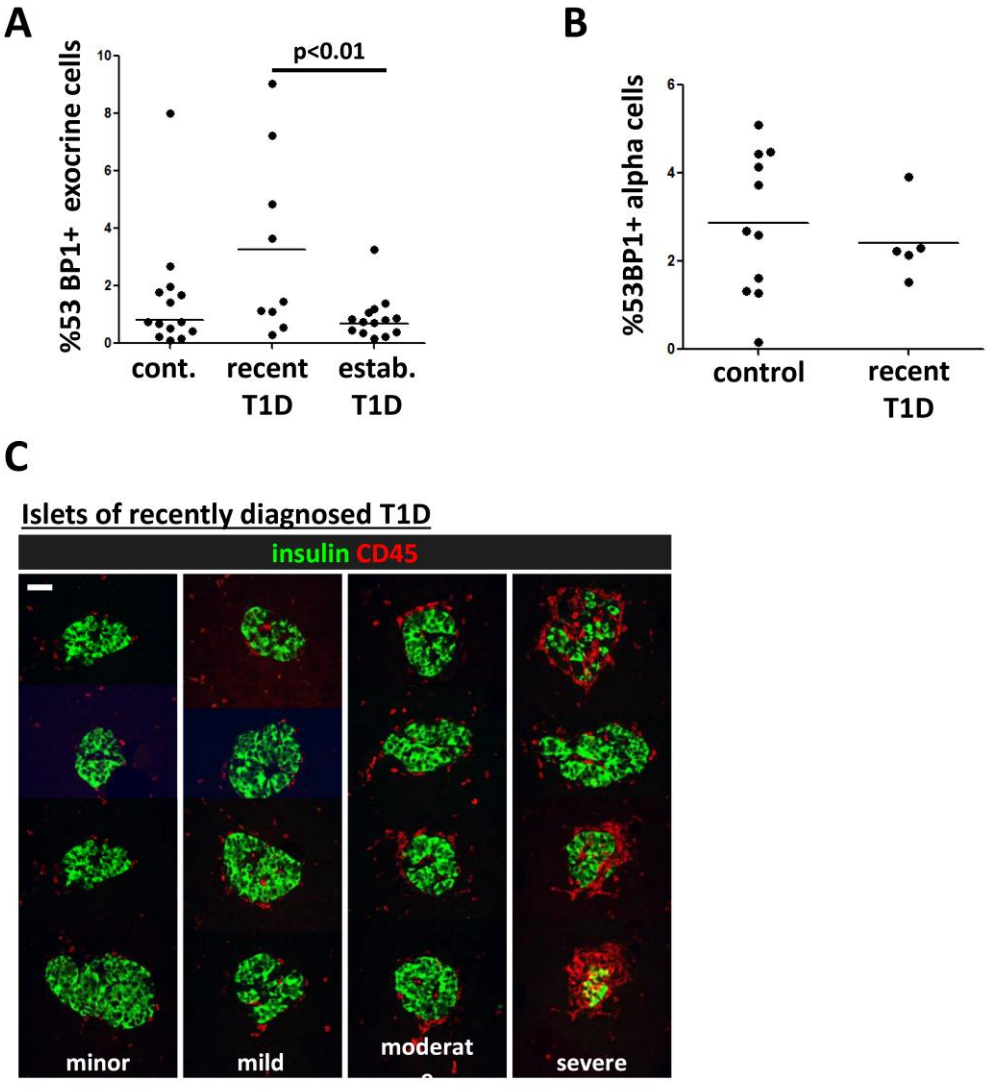
D. The fraction of beta cells with activated 53BP1 in samples originating solely from the nPOD repository. Samples groups are healthy donors (n=7), people at risk for T1D (AAB+, n=20), recently diagnosed T1D patients (n=3) and established T1D patients (n=18). Each dot represents an individual case, p-values inside brackets are from include all three tissue sources (nPOD, Powers and DiViD).



SUPPLEMENTARY DATA

Supplementary Figure S2. Classification of islets from recently diagnosed T1D patients according to the extent of inflammatory infiltrate.

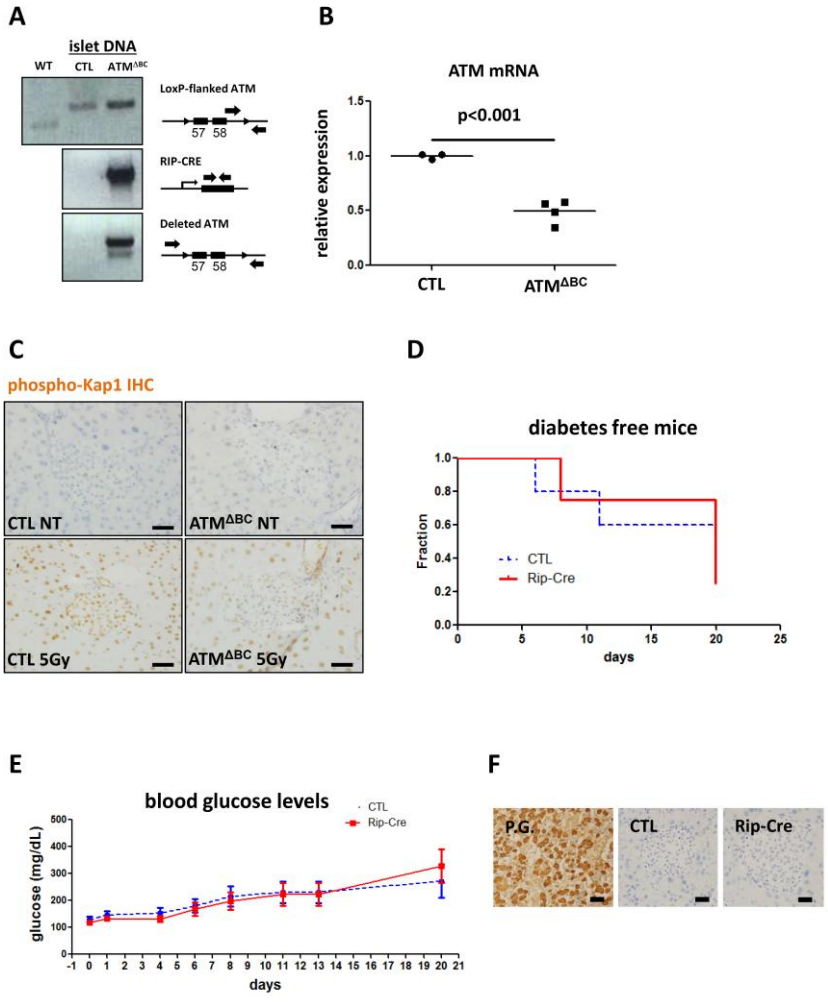
A. 53BP1 foci in cells of the exocrine pancreas. 53BP1 pattern was assessed on samples from recently diagnosed T1D patients (n=8), long standing T1D (N=12) and healthy control donors (n=13). Each dot represents an individual case.
B. Quantification of 53BP1 nuclear foci in glucagon positive cells on pancreas samples from recent T1D (n=5) and healthy control donors (n=11). Each dot represents an individual case.
C. Immunofluorescent staining for beta cells (insulin, green) and immune cells (CD45, red). The degree of infiltrate is determined by both the amount of CD45 cells surrounding the islet and their level of islet penetrance. Infiltrate definitions were: minor - up to three CD45+ cells in the islet periphery; mild – spread CD45+ cells (up to ~20) with some intra-islet infiltration; moderate - aggregated CD45+ cells (~20 cell or more) with intra-islet infiltration; severe – large aggregations of CD45+ cells with intra-islet infiltration. Scale bars, 10μm.



SUPPLEMENTARY DATA

Supplementary Figure S3. Beta cell conditional deletion of the gene for *Atm*, and lack of effect in RIP-Cre single transgenic mice.

A. ATM genomic deletion in islets of ATMf/f; insulin-Cre mice. PCR was performed of DNA from islets of wild type (WT), control (CTL, ATMf/f) and Insulin-Cre; ATMf/f (ATMΔBC) mice. A deletion product can be found only in the presence of Cre recombinase and the floxed ATM allele. Arrow indicate the location of genotyping PCR primers for each panel. Recombination deletes exons 57+58 of ATM.
B. qPCR analysis of the Atm transcript in control (CTL) and ATMΔBC mice. RNA was isolated from whole islets.
C. Immunostaining for the phosphorylated form of the ATM substrate Kap1. Control and mutant mice were non-treated (NT) or gamma irradiated (5Gy), and sacrificed 1 hour later. Note that in the mutants, acinar cells stain positive but islet cells are negative, consistent with lack of ATM. Scale bars, 20µm.
D. Hyperglycemia-free survival curve of control (CTL, n=5) and Rip-Cre (n=4) mice subjected to MLDS.
E. Average blood glucose levels of control (CTL, n=5) and Rip-Cre (n=4) mice subjected to MLDS. Day 0 is the first day of 5 consecutive daily low dose STZ injections. Bars represent one SEM.
F. Growth hormone immunostaining of pituitary gland (PG), and the pancreas of control and RIP-Cre mice.



SUPPLEMENTARY DATA

Supplementary Table S1. donor details

CaseID	Donor Type	source
BG11201122	rdT1D	DiViD
BG1160791	rdT1D	DiViD
BG1248382	rdT1D	DiViD
BG1251891	rdT1D	DiViD
H1758	rdT1D	DiViD
BG12160361	rdT1D	DiViD
6380	rdT1D	nPOD
6362	rdT1D	nPOD
6228	rdT1D	nPOD
6027	AAB+	nPOD
6044	AAB+	nPOD
6080	AAB+	nPOD
6101	AAB+	nPOD
6154	AAB+	nPOD
6156	AAB+	nPOD
6158	AAB+	nPOD
6167	AAB+	nPOD
6170	AAB+	nPOD
6181	AAB+	nPOD
6184	AAB+	nPOD
6310	AAB+	nPOD
6023	AAB+	nPOD
503	AAB+	nPOD
6123	AAB+	nPOD
6147	AAB+	nPOD
6171	AAB+	nPOD
6197	AAB+	nPOD
6303	AAB+	nPOD
6267	AAB+	nPOD
6070	T1D	nPOD
6081	T1D	nPOD
6121	T1D	nPOD
6175	T1D	nPOD
6196	T1D	nPOD
6198	T1D	nPOD
6211	T1D	nPOD
6224	T1D	nPOD
6247	T1D	nPOD
6263	T1D	nPOD
6306	T1D	nPOD
6307	T1D	nPOD
6302	T1D	nPOD
6325	T1D	nPOD
6337	T1D	nPOD
6342	T1D	nPOD
6371	T1D	nPOD
6173	T1D	nPOD
6034	No diabetes	nPOD
6178	No diabetes	nPOD
6234	No diabetes	nPOD
6235	No diabetes	nPOD
6058	No diabetes	nPOD
6292	No diabetes	nPOD
6060	No diabetes	nPOD
AB12259	No diabetes	Powers lab
ABHB279	No diabetes	Powers lab
ACEZ011	No diabetes	Powers lab
ACEZ381	No diabetes	Powers lab
ACHM315	No diabetes	Powers lab

SUPPLEMENTARY DATA

Supplementary Table S2. qPCR primers

Gene	Species	Forward	Reverse
Hprt	mouse	GTT AAG CAG TAC AGC CCC AAA	AGG GCA TAT CCA ACA ACA AAC TT
Ppia	mouse	CGCGTCTCCTTCGAGCTGTTTG	TGTAAAGTCACCACCCTGGCACAT
Atm	mouse	ATGCAGCAGGTCTTCCAGATGT	GTTCCTGTGCACCACTCGAGAA
Il1b	mouse	ACCTTCCAGGATGAGGACATGA	CTAATGGGAACGTCACACACCA
Cxcl10	mouse	CTCATCCTGCTGGGTCTGAGTG	CCTATGGCCCTCATTCTCACTG
Ccl3	mouse	TGACAAGCTCACCCTCTGTCAC	GTAGGAGAAGCAGCAGGCAGTC
Ccl4	mouse	AGACCAGCAGTCTTTGCTCCAA	GCTGCTCAGTTCAACTCCAAGTC
Ccl5	mouse	AAGTGCTCCAATCTTGCAGTCG	ACTTCTTCTCTGGGTTGGCACA
Ccl11	mouse	GAGCTCCACAGCGCTTCTATTC	TGGTCATGATAAAGCAGCAGGA
Ptprc (CD45)	mouse	TTCAAAGAAATGGGACTGCTGA	TTTCATTCCATTGACCTTGTCC