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Supplemental information

NR5A2/LRH-1 regulates the PTGS2-PGE_2-PTGER1 pathway contributing to pancreatic islet survival and function

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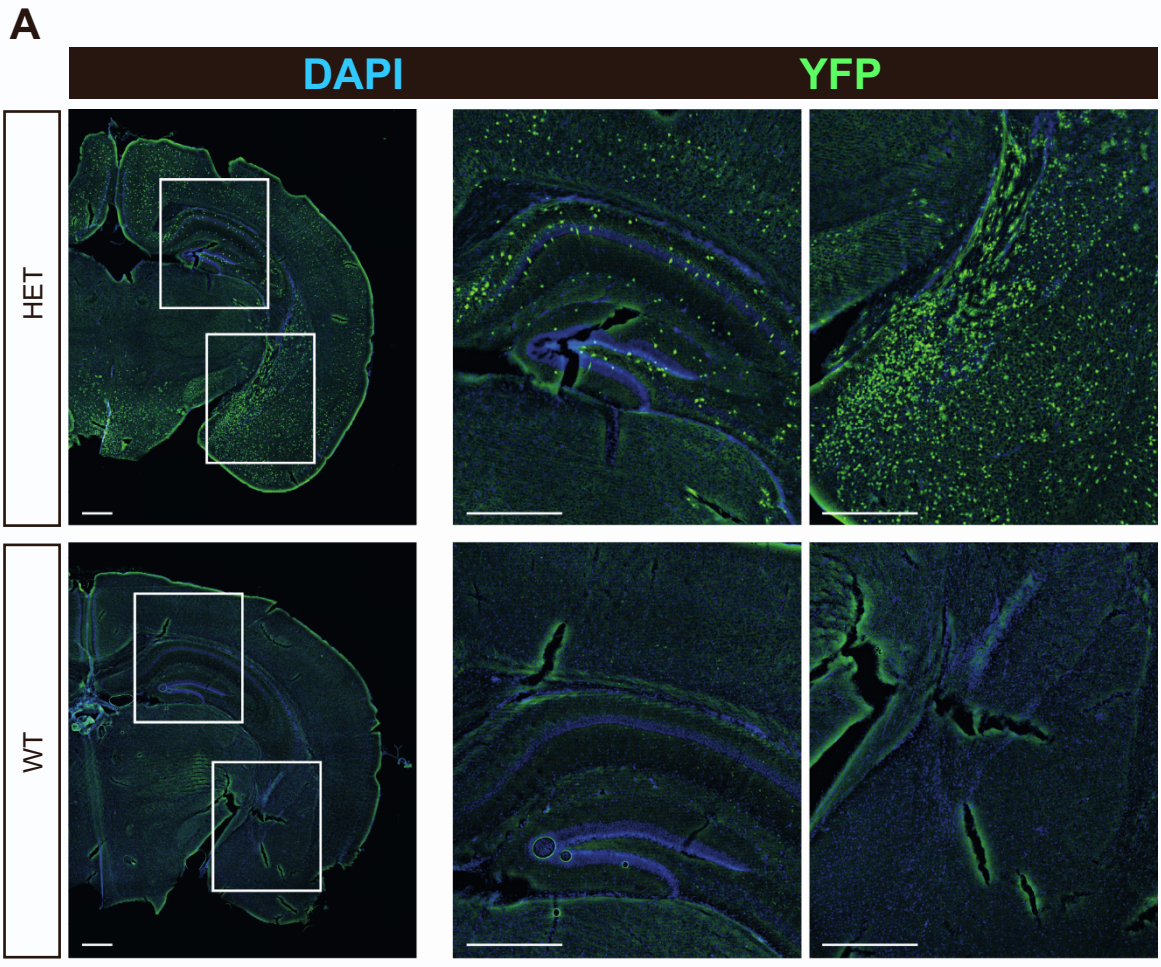
TABLE S1: List of primers used in this study (related to the RNA extraction and quantitative real-time PCR section of Star Methods).

ID	Forward primer	Reverse primer
Mouse		
Bax	CCCTGTGCACTAAAGTGCCC	CTTCTTCCAGATGGTGAGCG
Cyclophylin	ATGGCAAATGCTGGACCAA	GCCATCCAGCCATTCAGTCT
Gapdh	CACCAACTGCTTAGCCCC	TCTTCTGGGTGGCAGTGATG
Lrh1/Nr5a2	AACGATGTCCCTACTGTCG	CATGCGGTCGGCTCTTAC
Actb	GGACCAGATCCAAAAGGACA	GCTCACCCTTACCTGGAACA
Rsp9	GGAGTCACCCACGGAAGTT	CATGTTCAGCCCGTATTTGC
Ptgs2	GATGCTCTTCCGAGCTGTG	GGATTGGAACAGCAAGGATTT
Ptger1	CAGCACTGGCCCTCTTGG	ATGCCACAGCCAAGCAAAAG
Ptger2	CATCTATGGGGCCTCCTTGC	AGAGAGCTGCAGAATTGACCG
Ptger3	TGTCGGTTGAGCAATGCAAG	CAGCTGGTCACTCCACATCAG
Ptger4	CAGACTGGTCTTCACCGACC	GGAATGGTACCTCCAACCTCA
Human		
PTGS2	AGCAGGCTAATACTGATAGGAGAG	ATAGCCACTCAAGTGTTGCACAT
BAX	TCTGACGGCAACTTCAACTG	TTGAGGAGTCTCACCCAACC
ACTIN	CTGTACGCCAACACAGTGCT	GCTCAGGAGGAGCAATGATC
VAPA	TACCGAAACAAGGAAACTAATGGAA	GCCTTAAACCTTCATCTCTCAGGT



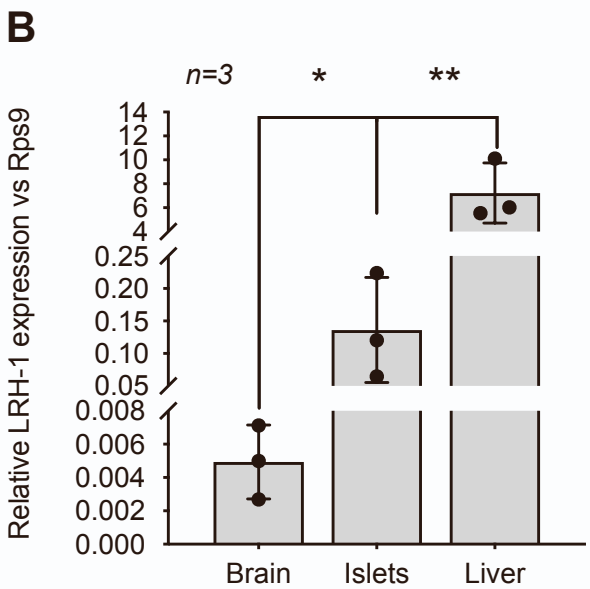


Figure S1: The RIP-Cre is expressed in the brain of IndβLRH-1 mice (related to Figure 1).
(**A**) YPF immunostaining of central nervous system sections procured from either IndβLRH-1 (HET, upper panel) or LRH-1$^{lox/lox}$::R26-stop-EYFP (WT, lower panel, green). Bar, 0.5 mm.
(**B**) LRH-1 transcript levels in brain were compared to levels in islets and liver. Relative expression levels were normalized to the housekeeping gene Rps9. *n=3*, independent samples. *p<0.05 and **p<0.001 unpaired t-test Brain versus islets and liver.

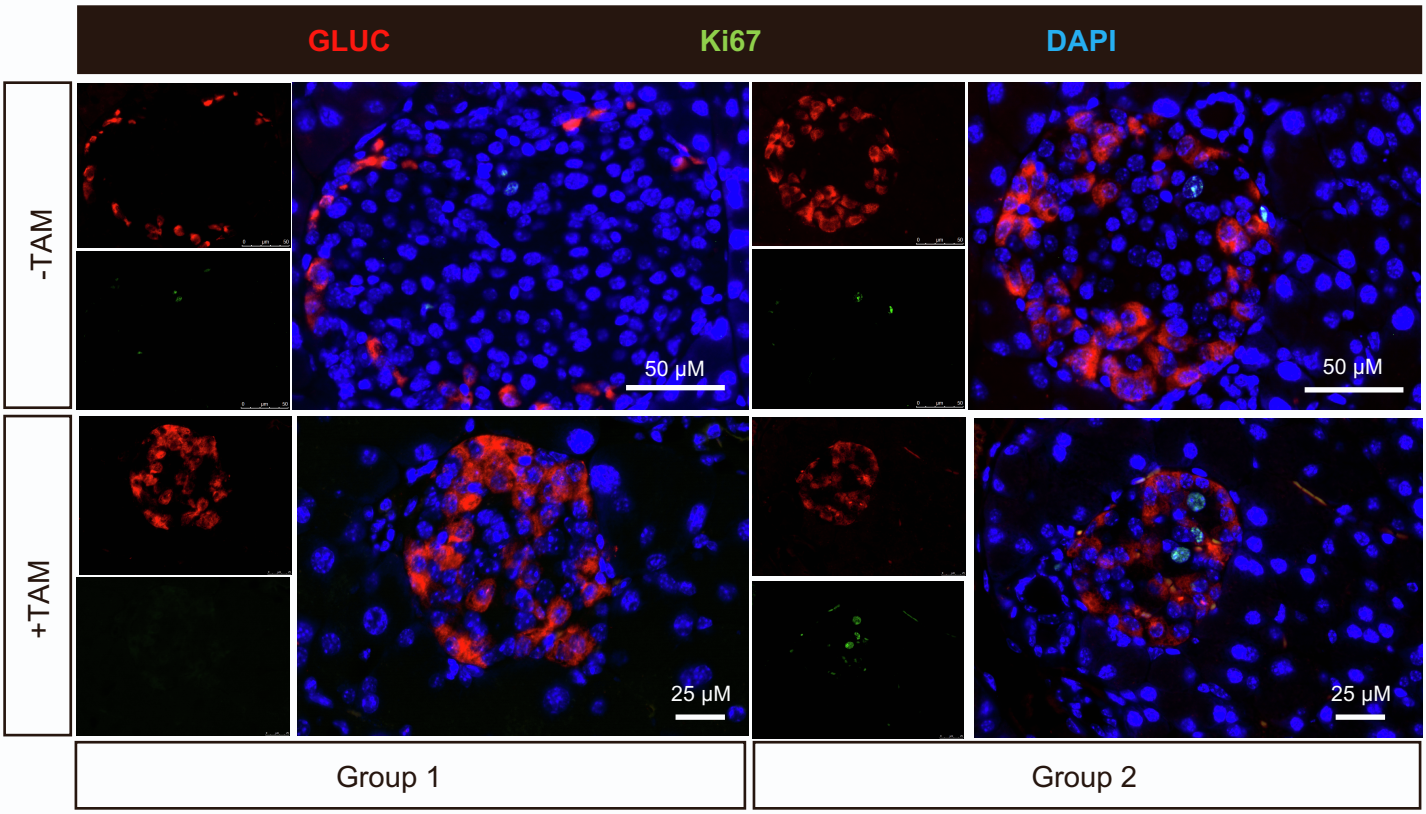


Figure S2. Islet alpha cell proliferation is not increased in TAM/STZ/BL00-treated mice (related to Figure 3). Representative immunofluorescence images (Groups 1 and 2) of glucagon (GLUC, red) and Ki67 (green) of pancreas sections from mice pre-treated or not with TAM and then exposed to STZ and BL001. Nuclei were stained with DAPI (blue).

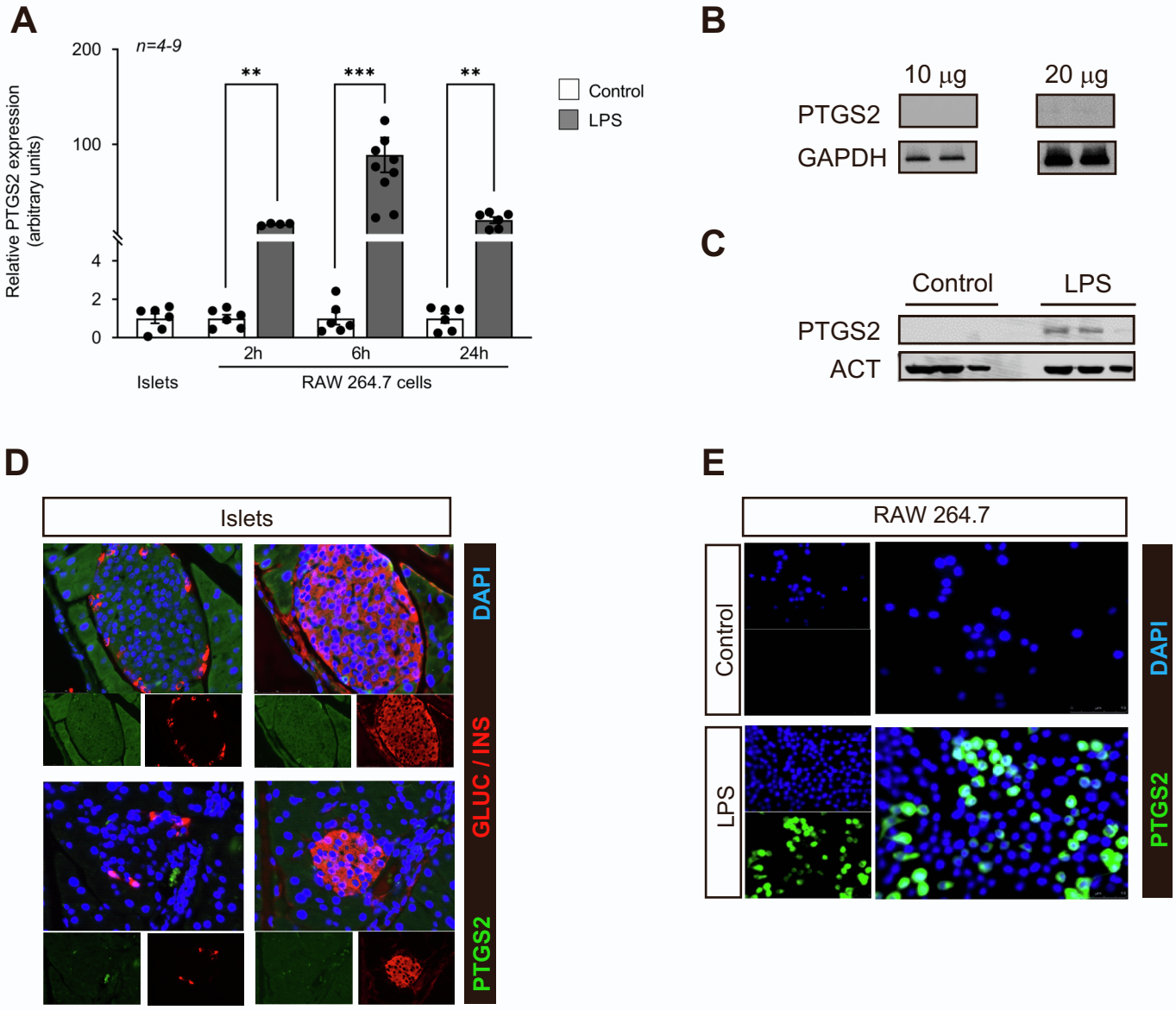


Figure S3. PTGS2 protein expression levels in islets are barely detectable (related to Figure 4).
(**A**) *Ptgs2* expression levels were assessed in mouse islets and in RAW 264.7 cells which were treated or not with LPS for different time periods. Expression levels was normalized to the housekeeping gene *Gapdh.* Results are expressed as the means + s.e.m. **p < 0.002, ***p < 0.001 Student's t test.
(**B-C**) Western blot analysis of PTGS2, Actin and GAPDH in protein extracts isolated from (**B**) islets and (**C**) RAW 264.7 cells treated or not with LPS.
(**D-E**) Representative immunofluorescence images of (**D**) islets stained for PTGS2 (green), insulin (INS, red) and glucagon (GLUC, red) and (**E**) RAW 264.7 cells (treated or not with LPS) stained for PTGS2 (green). Nuclei were stained with DAPI (blue). Magnification 40x.

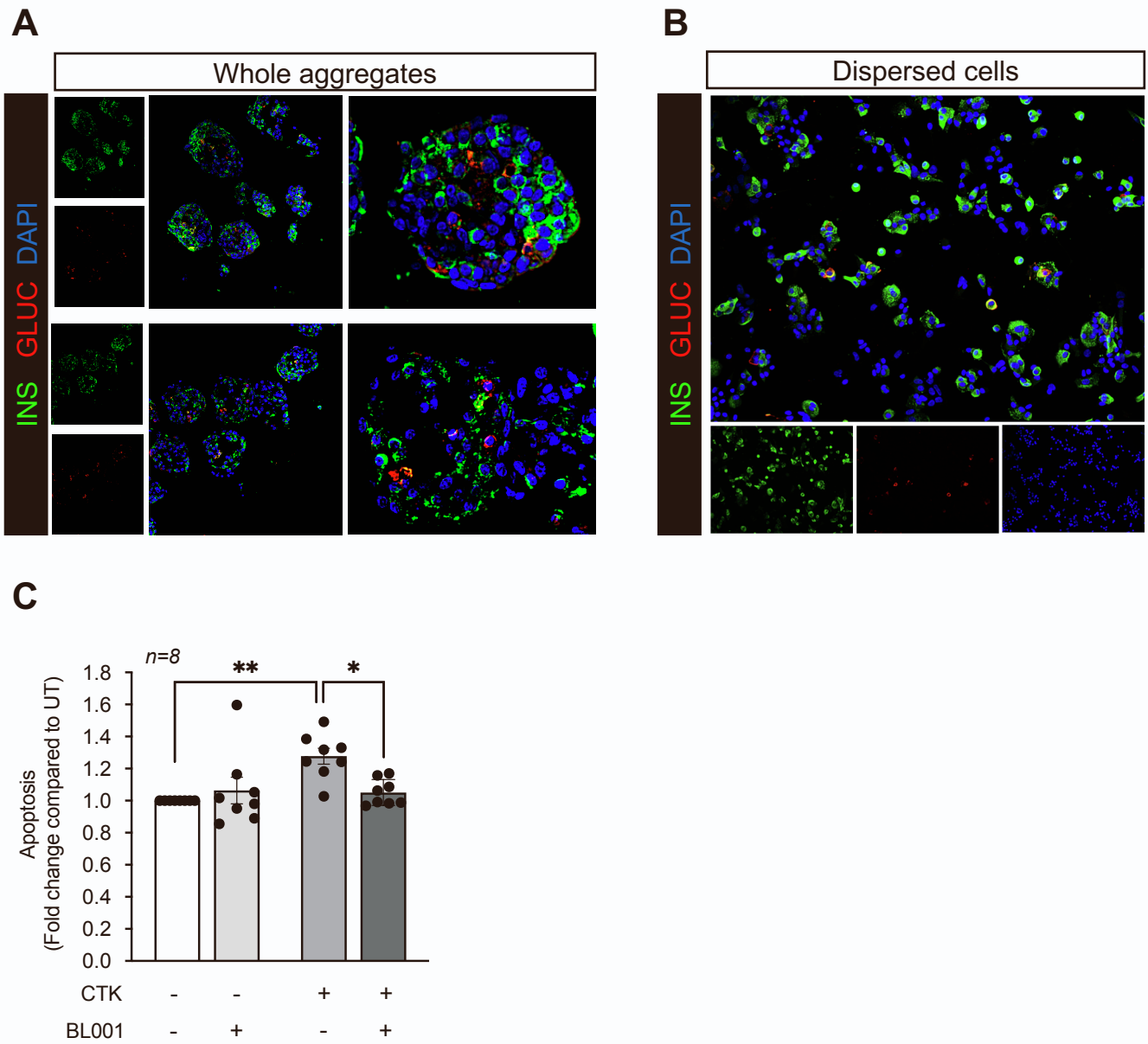


Figure S4. BL001 protects iPSC-derived pancreatic endocrine cells against cytokine-induced apoptosis (related to Figure 7). (**A-B**) Control iPSCs were differentiated into pancreatic endocrine cells using a 7-step protocol. Representative immunofluorescence images of (**A**) whole aggregates and (**B**) dispersed cells stained for insulin (INS, green) and glucagon (GLUC, red). Nuclei were stained with DAPI. 20X magnification.
(**C**) Apoptosis was assessed in iPSC-derived islet cells with a cytokine cocktail (CTK) and/or BL001 for 48 hours.