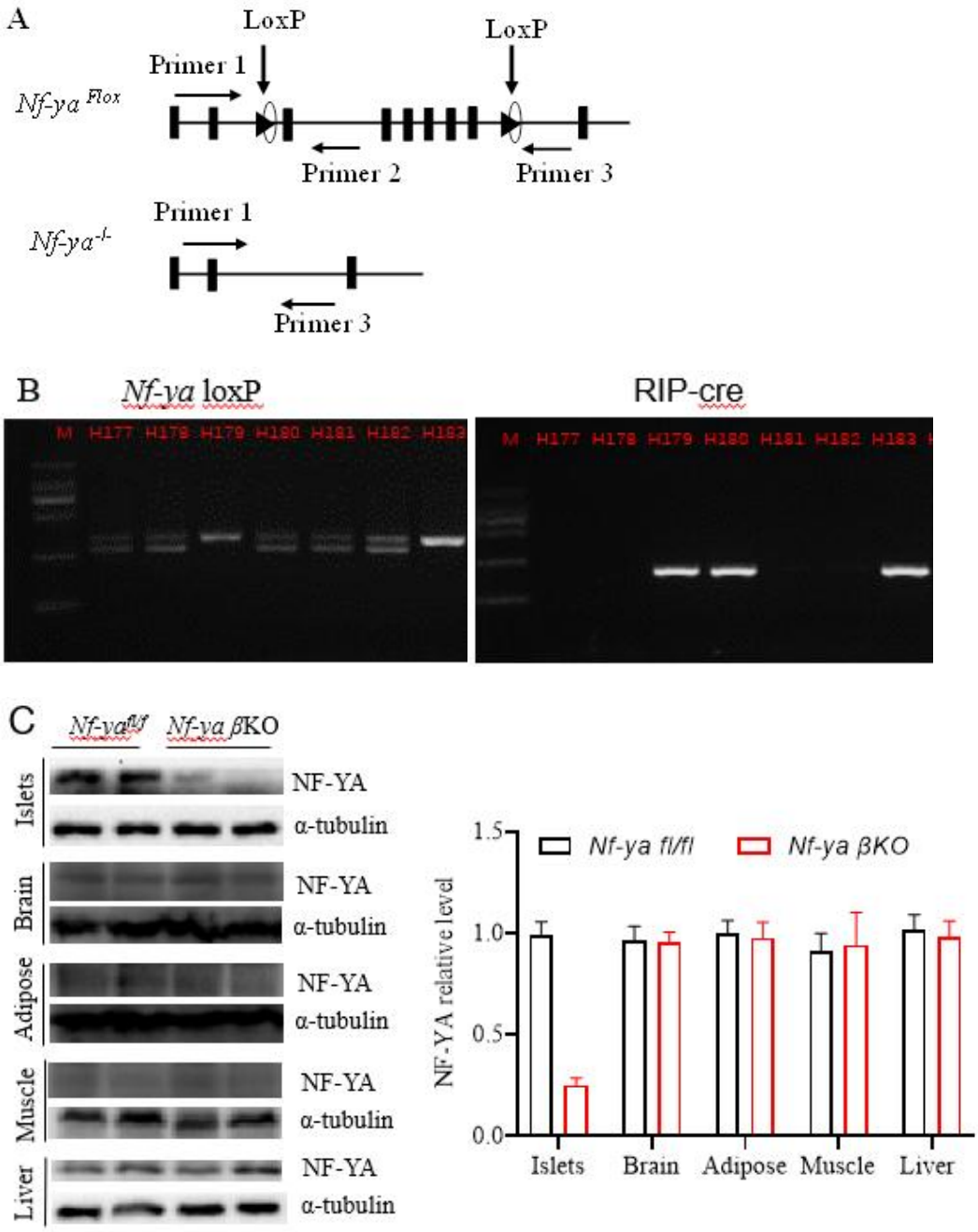

Figure S1. Generation of β cell-specific *Nf-ya* KO (*Nf-ya* βKO) mice. *Nf-ya* βKO mice were generated by crossing *Nf-ya* flox/flox mice with *RIP-Cre* transgenic mice, Cre-negative *Nf-ya* flox/flox animals were used as control. (A) Schematic diagram of the *Nf-ya* gene showing exons 3-8 flanked by two loxP sites indicated as triangles and the subsequent excision of exons 3-8 by Cre-mediated gene recombination. Vertical thick bars show relative locations of exons. (B) The genomic DNA extracted from the tails was used for PCR with primers detecting Cre, *Nf-ya* flox, *Nf-ya* WT or the deleted *Nf-ya*. (C) Western blotting analysis measured NF-YA protein levels in various tissues from *Nf-ya* βKO and *Nf-ya* $^{fl/fl}$

mice.

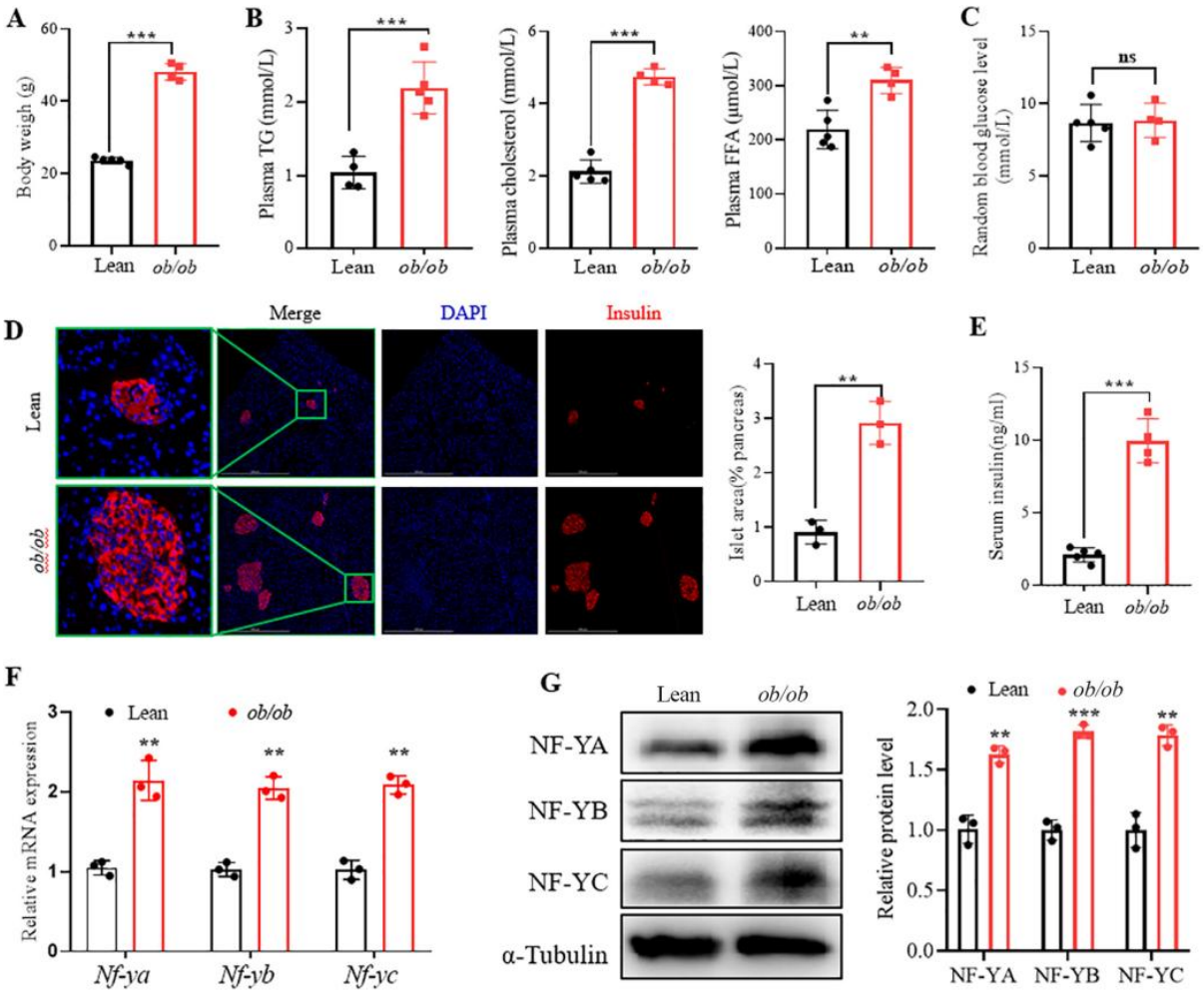

Figure S2. NF-Y expression in pancreatic islets correlates with hyperinsulinemia in obese ob/ob mice. Obese *ob/ob* and lean control mice were fed a normal chow at the age of 12 weeks. (A) body weight, (B) plasma levels of triglyceride, total cholesterol and free fatty acid (FFA), (C) random blood glucose levels, (D) immuno-fluorescent staining for insulin on pancreatic cryosections, (E) plasma insulin levels, (F-G) NF-Y (YA, YB and YC) expression at mRNA level (F) and protein level (G) in the pancreatic islets were measured. (n = 5-8 mice per group). Data are represented as means ± SD. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

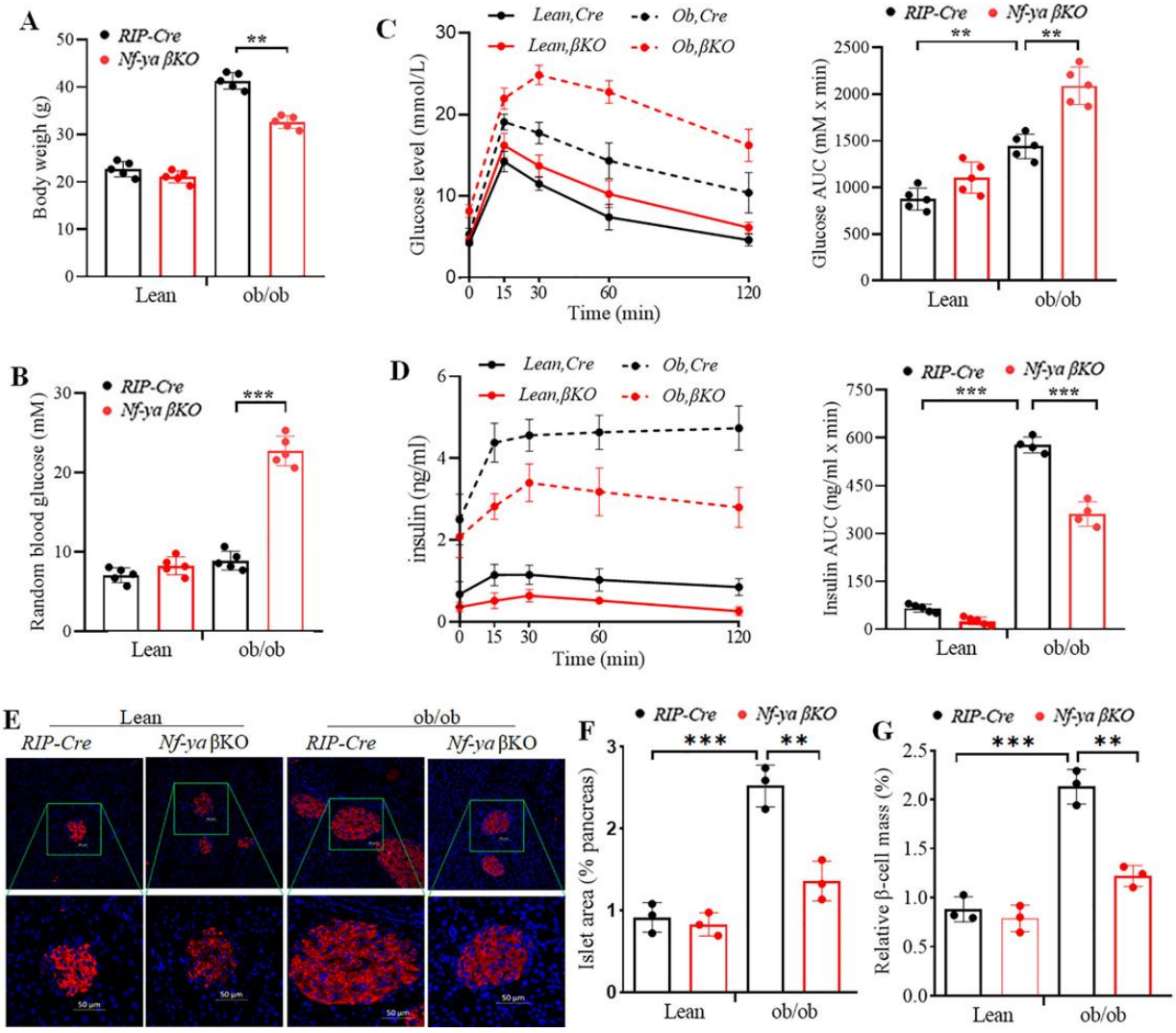

Figure S3. **NF-YA specifically deleted in pancreatic β-cells in female obese ob/ob mice leads to diabetes due to failure of β-cell compensation.** (A) body weight and (B) random blood glucose levels were examined in 12-week-old female mice (n = 5-7 for each group). (C-D) Blood glucose levels and area under the curve (AUC) for glucose (C), and plasma insulin levels and AUC for insulin (D) during intraperitoneal GTT in mice given glucose after 12 h fasting (2 g/kg body weight) (n = 5-7 for each group). (E) Example of immunofluorescent staining for insulin on pancreatic cryosections from 12-week-old female mice with the indicated genotypes. (F) Quantitative assessment of the proportion of insulin-positive area/islet area in mice pancreatic islets. A total of 20-30 islets were analyzed for each group (n = 5 mice/group). (G) β-cell mass was determined as described in the Methods. *$P < 0.05$, **$P < 0.01$, *** $P < 0.001$.

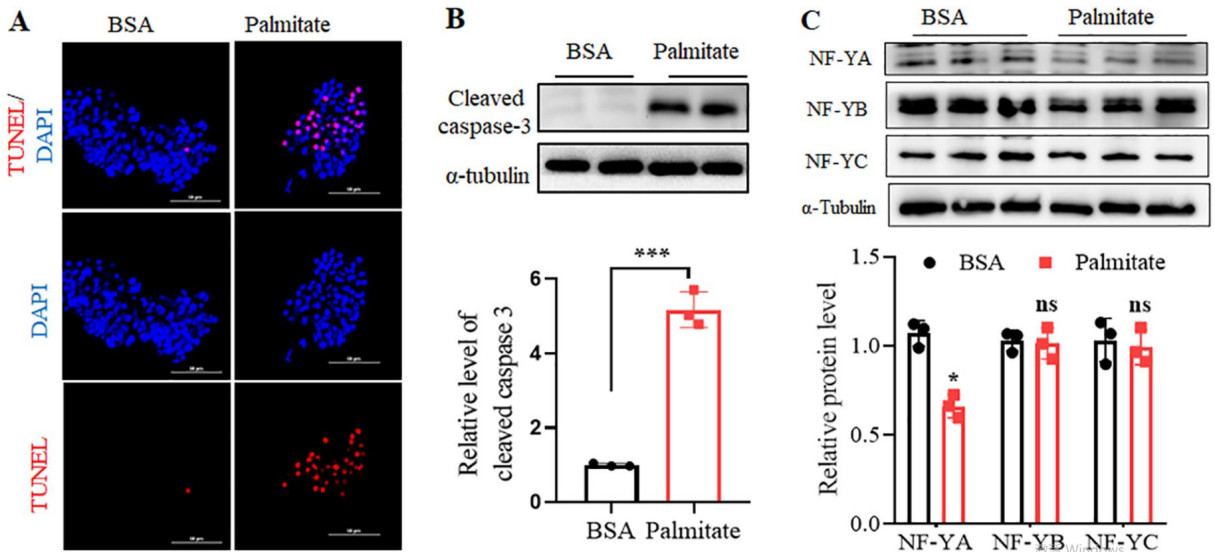

Figure S4. **Palmitate exposure decreases NF-YA expression in mouse islets and leads to apoptosis.** Mouse islets from 12-week-old C57BL/6J mice were treated with 1% BSA (BSA) or 0.2 mM palmitate complexed to 1% BSA for 24 h. (A) Representative images of immunofluorescence staining of TUNEL (red) and DAPI (blue). (B-C) Western blot (upper) and quantitative analysis (lower) of cleaved caspase 3 (B) and NF-Y (YA, YB and YC) (C) in the isolated islets (n = 4-5 mice per group). Data are presented as mean ± SD. **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

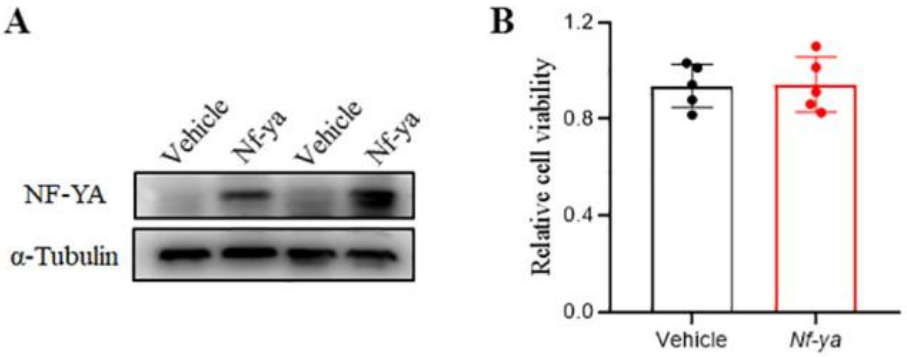

Figure S5. **Effect of *Nf-ya* overexpression on INS1-cell viability.** *Nf-ya* overexpression plasmid or control empty vector (vehicle) was transfected into INS1 cells. Stable overexpression cell line was screened by 10 μg/μl puromycin for 2 weeks. **(A)** *Nf-ya* overexpression was confirmed by Western blotting analysis. (B) Cell viability was assessed by a Cell Counting Kit-8 (CCK-8) assay.

Table S1. Primers for mice genotyping

Gene	Forward (5' to 3')	Reverse (5' to 3')
Cre	ATTTGCCTGCATTACCGGTC	ATCAACGTTTTCTTTTCGG
Nf-ya	GTAAGTCAGGCTCCAGGG	GGGTTGTCAGGATGTTCGCAG
		AGGCAAGGCAGATTTAGGAAGGTC
Leptin	GCAGTCGGTATCCGCCAAGCAG	GTGGTCTACAGGAGGGAGAGAAATG
	TAGCCAATGACCTGGAGAATCAC	CCAGCAGATGGAGGAGGTCACG

Table S2. Primers for amplifying *Nf-y* cDNAs

Gene	Forward (5' to 3')	Reverse (5' to 3')
Nf-ya	GAATTCGAGCAGTATACGACAAAC	TCTAGATTAGGAAACTCGGATGATC
Nf-yb	GAATTCGACAATGGACGGCGACAG	GGATCCTCATGAAAACTGAATTTGC
Nf-yc	GAATTCGTCCACAGAAGGAGGGTTT	TCTAGATCAGTCTCCAGTCACCTGGG

Table S3. Primers used for real-time quantitative PCR analysis

Gene	Forward (5' to 3')	Reverse (5' to 3')
Cyclin D1	ATGGAAGGACCCTTGAGGC	CTTCACGGCTTGCTCGTTCT
Cyclin B1	AAGGTGCCTGTGTGTGAACC	GTCAGCCCCATCATCTGCG
Cyclin D2	GAGTGGGAACTGGTAGTGTTG	CGCACAGAGCGATGAAGGT
Gpx1	AGTCCACCGTGTATGCCTTCT	GAGACGCGACATTCTCAATGA
Gpx4	GCCTGGATAAGTACAGGGGTT	CATGCAGATCGACTAGCTGAG
Nf-ya	GTCCAGACCCTCCAGGTAGT	AGGCACCAACTGTATCTGCT
Gapdh	AGGTCGGTGTGAACGGATTTG	TGTAGACCATGTAGTTGAGGTCA
18s rRNA	CGCCGCTAGAGGTGCAATTC	CCAGTCGGCATCGTTTATGG