Supplemental Table 1: Taqman probes used in qRT-PCR analysis in this study (Thermofischer).

Supplemental Table 2: Primer pairs used for qRT-PCR analysis

Supplemental Figure 1: AUC glucose and peak glucose during IPGTTs in NOD and B6 mice.

Supplemental Figure 2: Comparison of ER stress and cell death markers between the two populations by qRT-PCR

Supplemental Figure 3: Heat map generated from the 457 genes that are differently expressed between the Top and Btm β cells (FDR<0.05).

Supplemental Figure 4: Transcription Profiling of the two β cell populations from MIP-GFP Tg mice by qRT-PCR.

Supplemental Figure 5: Survival of Btm β cells in NOD mice with spontaneous diabetes or diabetes precipitated by cyclophosphamide treatment

Table S1, related to “Probes, primers and quantitative realtime RT-PCR”

Taqman probes used in qRT-PCR analysis (Thermofischer)

Figure S1A	*Chop, Xbp1, Bip, Wfs1, Aft4* and *Actb*
Figure S1B	*Atg5, Atg8, Becn1, Bnip3, Gabarap3, Caspas3 and Actb*
Figure 4A and Figure S3	*Ins1, Ins2, Glut2 ,Gcg, Sst, Foxo1, Mafa, Pdx1, Nkx6-1, Chga, Neurog3* and *Actb*
Figure 5B	*PD-L1, Qa-2* and *Actb*

Table S2, related to “Probes, primers and quantitative realtime RT-PCR”

Primer pairs used for qRT-PCR analysis

IGRP-F	5'AGGACTACCGGACTTACTATGGT3'
IGRP-R	5'GACCGCTACCCAGATCATCTT3'
ZnT8-F	5'GCCACCAAGATGTACGCCTT3'
ZnT8-R	5'CTTGCTTGCTCGACCTGTT3'
Gad1-F	5'AACGTATGATACTTGGTGTGGC3'
Gad1-R	5'CCAGGCTATTGGTCCTTTGTAAG3'
IA-2-F	5'TGTTTGACCGCAGACTTTGTT3'
IA-2-R	5'GGAGCACACCTTGTAGGCG3'
SOX2-F	5'GCGGAGTGGAAACTTTTGTCC3'
SOX2-R	5'GGGAAGCGTGTACTTATCCTTCT3'
SOX9-F	5'AGTACCCGCATCTGCACAAC3'
SOX9-R	5'ACGAAGGGTCTCTTCTCGCT3'
Oct4-F	5'CGGAAGAGAAAGCGAACTAGC3'
Oct4-R	5'ATTGGCGATGTGAGTGATCTG3'
L-myc-F	5'TTCTACGACTATGACTGCGGA3'
L-myc-R	5'ACGGCACCAGCTCGAATTT3'
Nanog-F	5'CACAGTTTGCCTAGTTCTGAGG3'
Nanog-R	5'GCAAGAATAGTTCTCGGGATGAA3'
Actb-F	5'GGCTGTATTCCCCTCCATCG3'
Actb-R	5'CCAGTTGGTAACAATGCCATGT3'

Figure S1

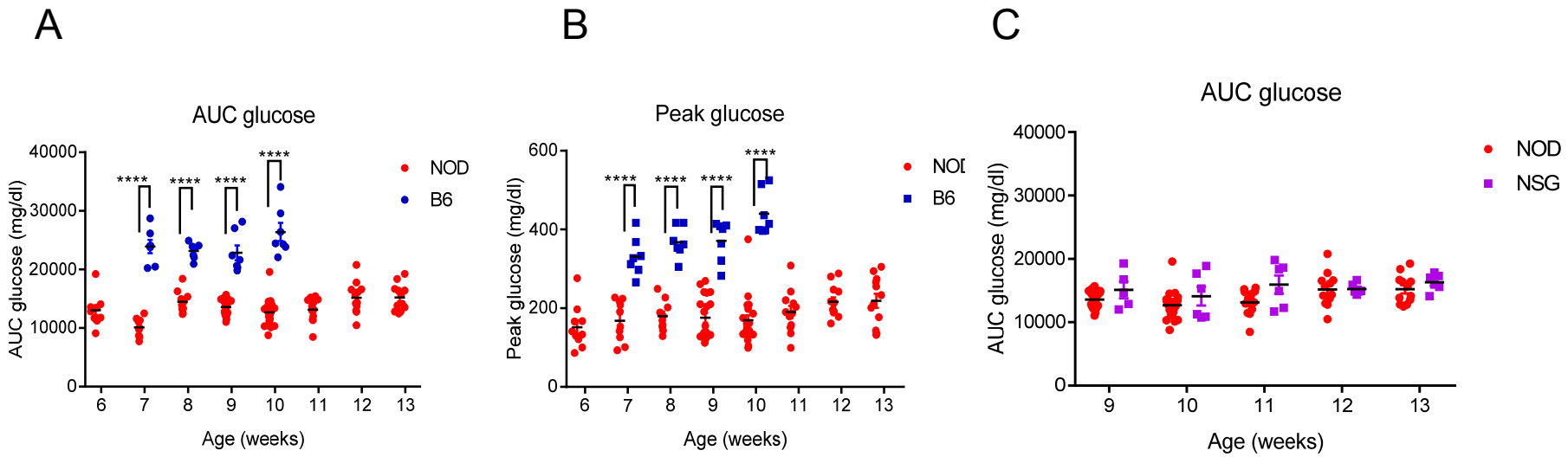

Figure S1, related to Figure 1 : AUC glucose and peak glucose during IPGTTs in NOD, B6, and NOD/scidγc-/- (NSG) mice. NOD, B6, and NSG mice of the indicated ages underwent IP glucose tolerance test. Blood glucose area under the curve (AUC) as well as peak blood glucose level were shown for each mouse. (****p<0.0001 t-tests with FDR of 5%)

Figure S2

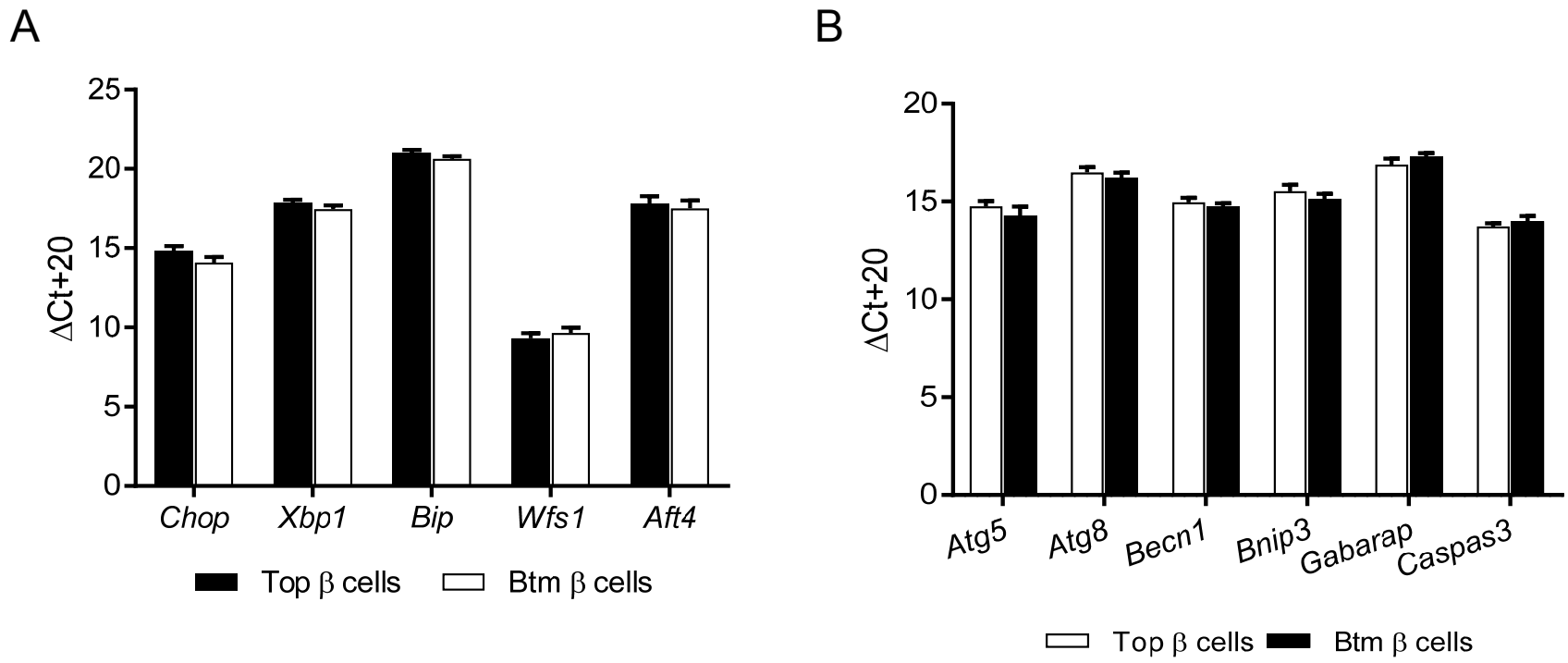

Figure S2, related to Figure 1: Comparison of ER stress and cell death markers between the two populations by qRT-PCR. Both Top and btm β cells were sorted from 8-10-wk-old NOD mice. RNA was recovered and the transcription level of (A) ER stress markers, (B) Cell Death pathways (autophagy and apoptosis) were analysed by qRT-PCR and normalised to *Actb* mRNA levels (ΔC_t=(C_t of *Actb*-C_t of *target gene)+20*). Data show the mean ± SEM of three experiments, each with 4–6 mice (Two-way ANOVA: *p*=ns).

Figure S3

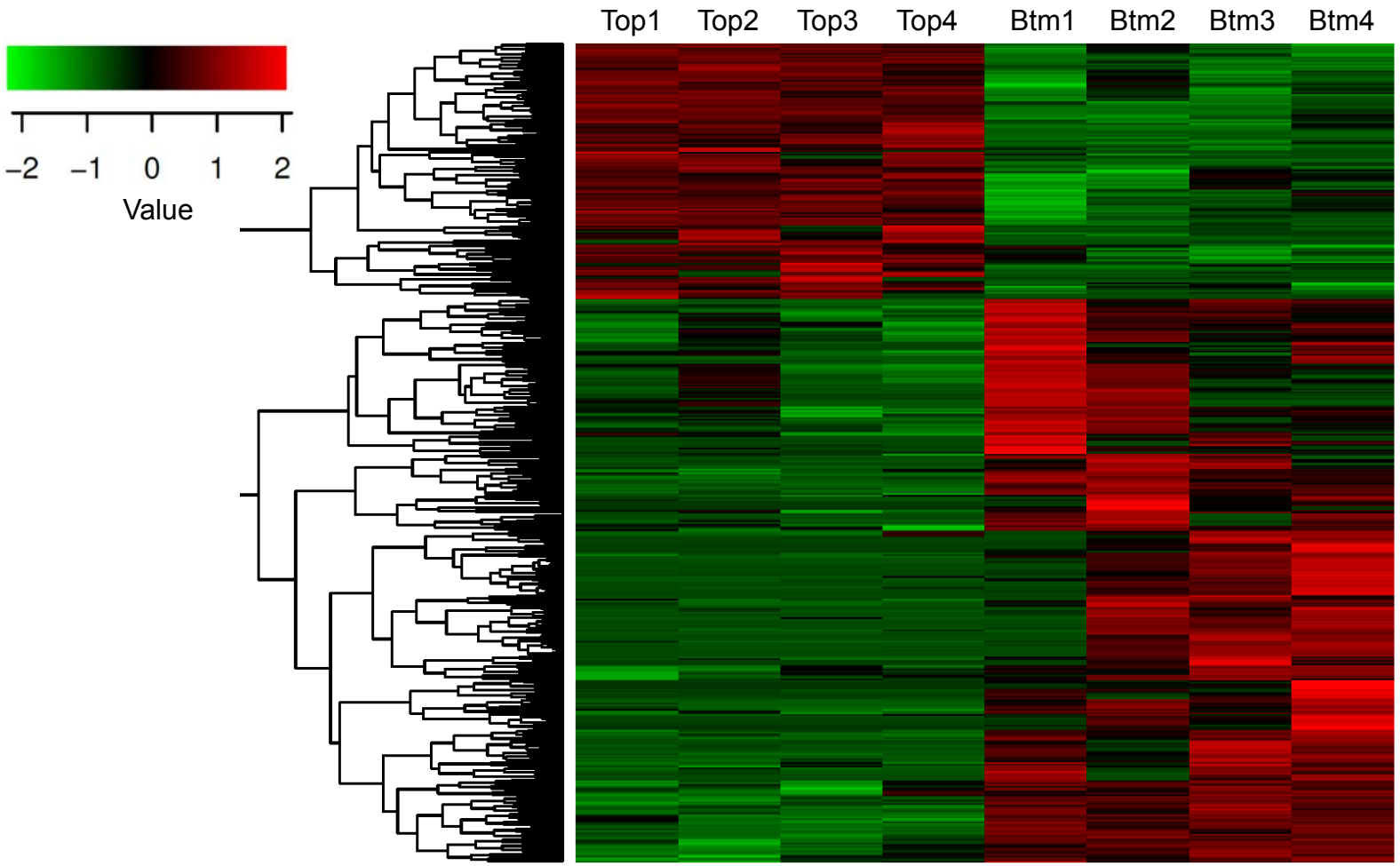

Figure S3, related to Figure 3. Heat map generated from the 457 genes that are differently expressed between the Top and Btm β cells (FDR<0.05).

Figure S4

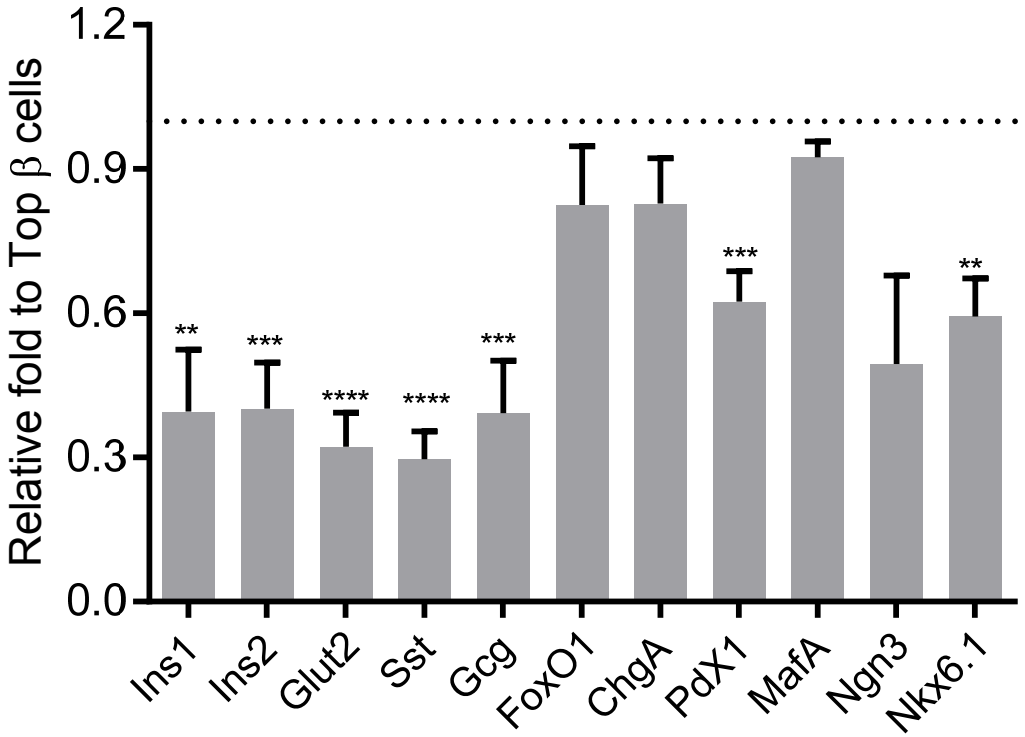

Figure S4, related to Figures 3 and 4A. Transcription Profiling of the two β cell populations from MIP-GFP Tg mice by qRT-PCR. Top and Btm GFP+ β cells were sorted from 3-5-wk-old MIP-GFP Tg mice and the transcription level of indicated β cell signatures was analysed by qRT-PCR (*Actb* was used to normalize the RNA input). The mRNA levels in Btm β cells are shown in relative to Top β cells. The dotted line shows a value of 1. Data are mean ± SEM of three experiments, each with 6 mice (one sample t-test compared to a value of 1. **p<0.01, ****p*<0.001, *****p*<0.0001).

Figure S5

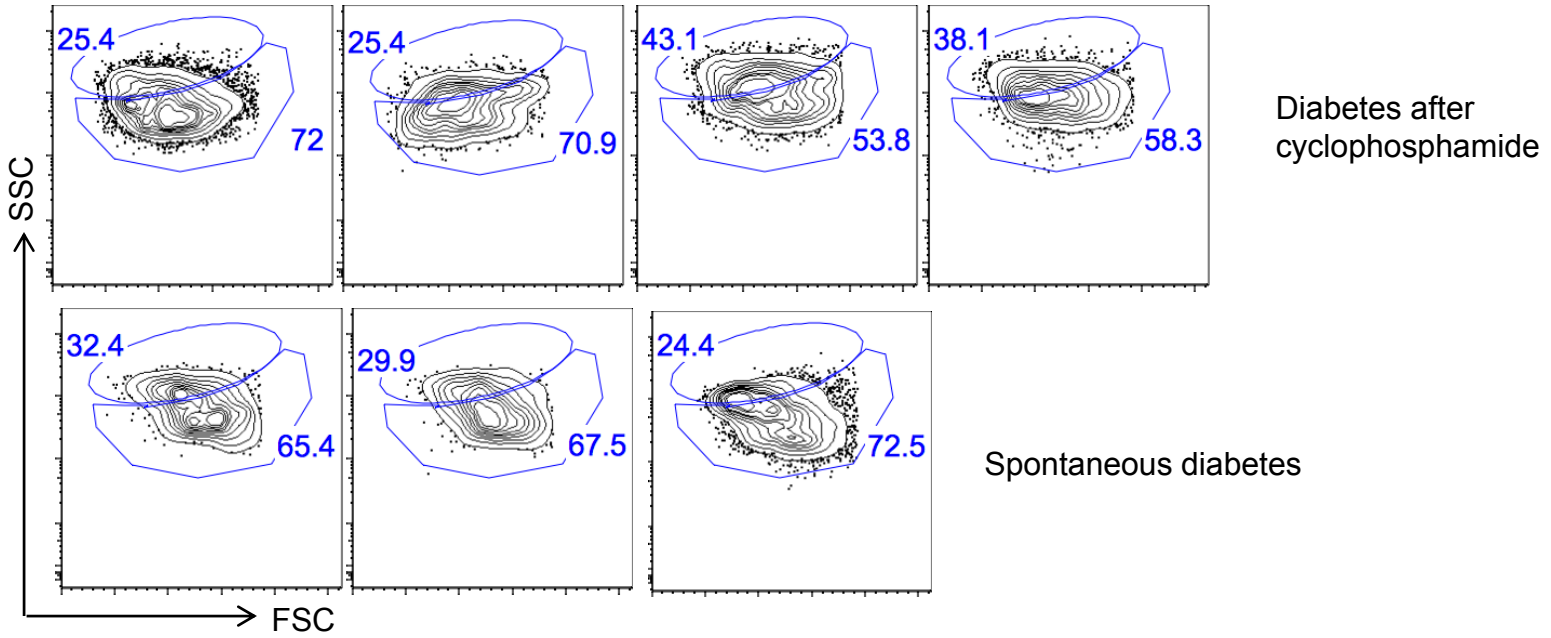

Figure S5, related to Figure 5: Survival of Btm β cells in NOD mice with spontaneous diabetes or diabetes precipitated by cyclophosphamide treatment. 9-wk-old NOD mice were given a single dose of cyclophosphamide (250 mg/kg, i.p.) to precipitate diabetes. 12 days after treatment, islets were harvested and β cell composition was analyzed by flow cytometry. β cells from NOD mice that developed diabetes after cyclophosphamide are shown (top) as well as from mice that developed diabetes at 16wks without cyclophosphamide treatment are shown. Each FACS panel shows cells from 1-2 mice.