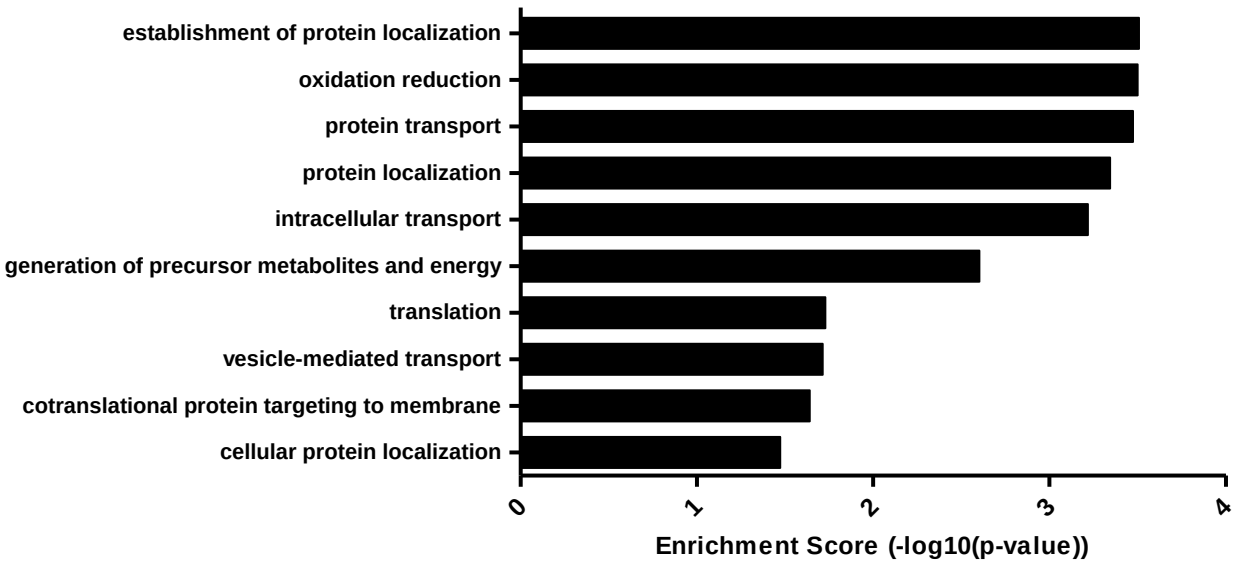
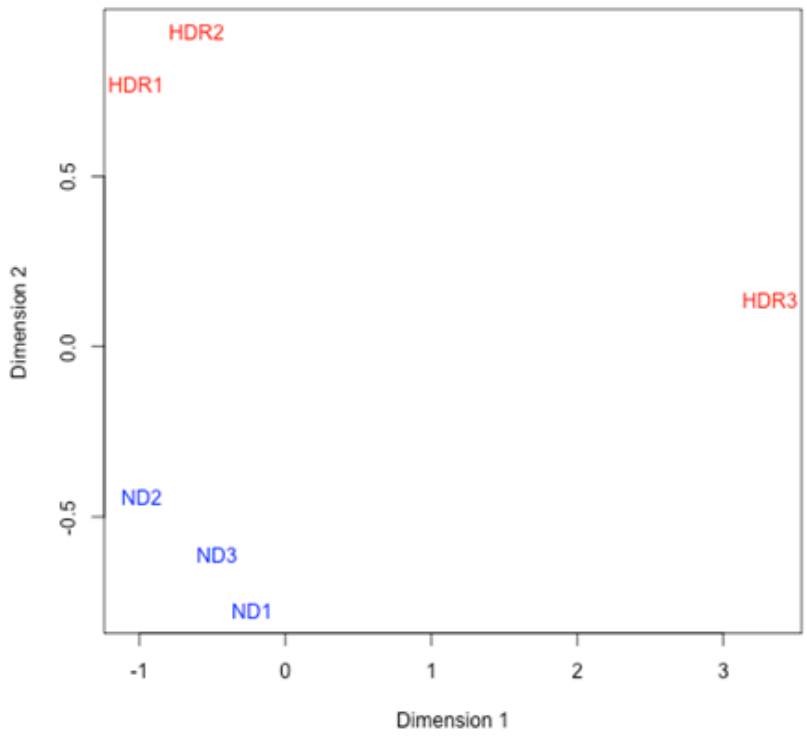
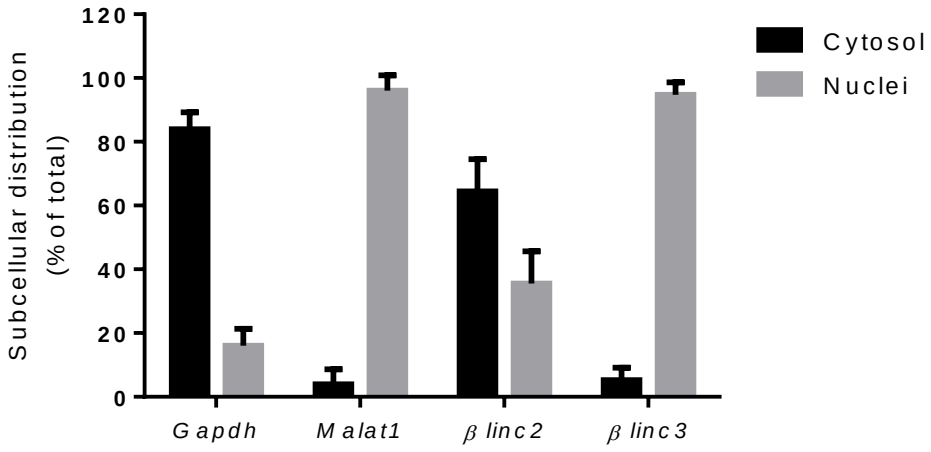


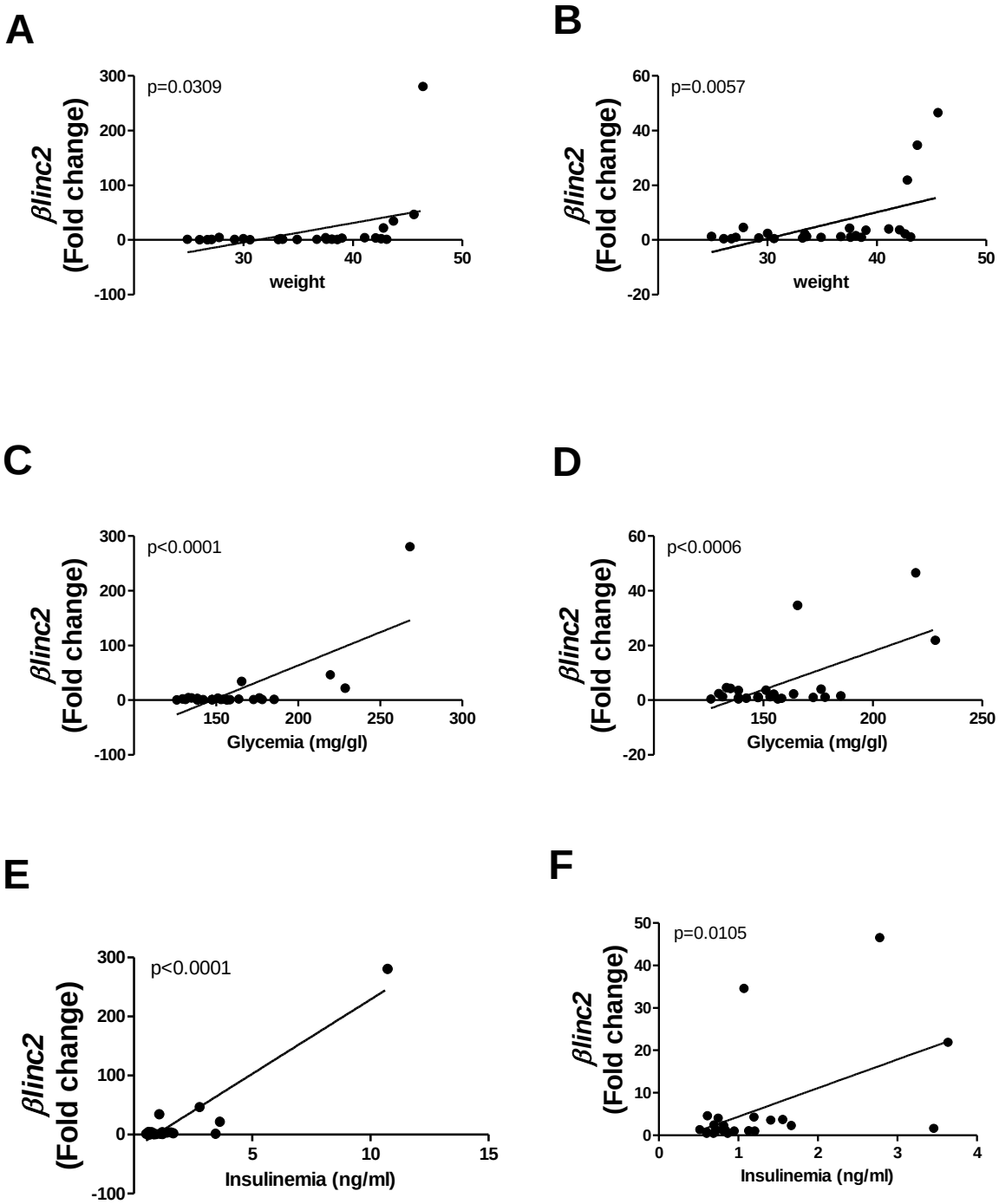
Supplemental figure 1. Gene ontology terms of differentially expressed protein coding genes. Enrichment score of biological processes terms using DAVID Functional annotation clustering tool using default parameters and databases.



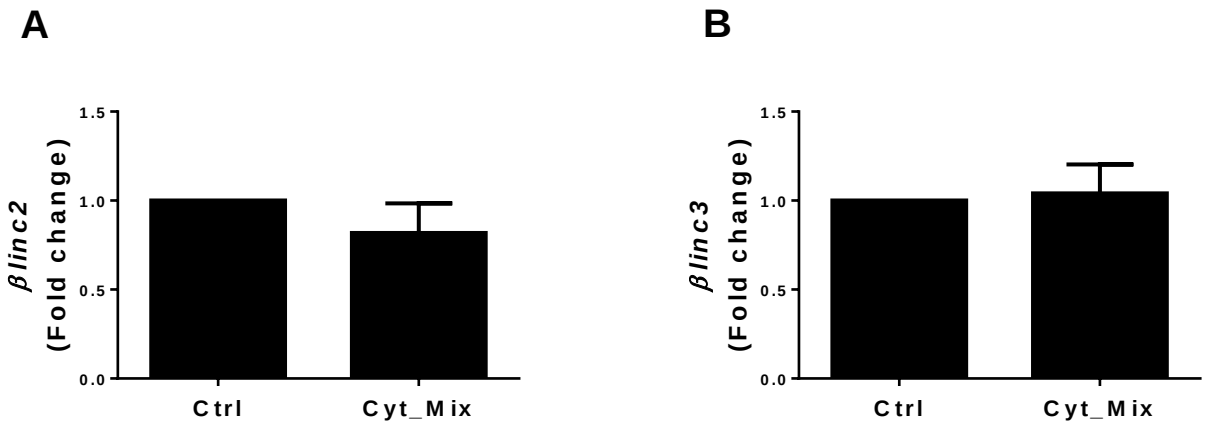
Supplemental figure 2. Multidimensional scaling plot based on the top 500 expressed genes. While ND and HDR samples display a clearly distinct pattern, HDR3 appears to display some differences compared to HDR1 and HDR2.



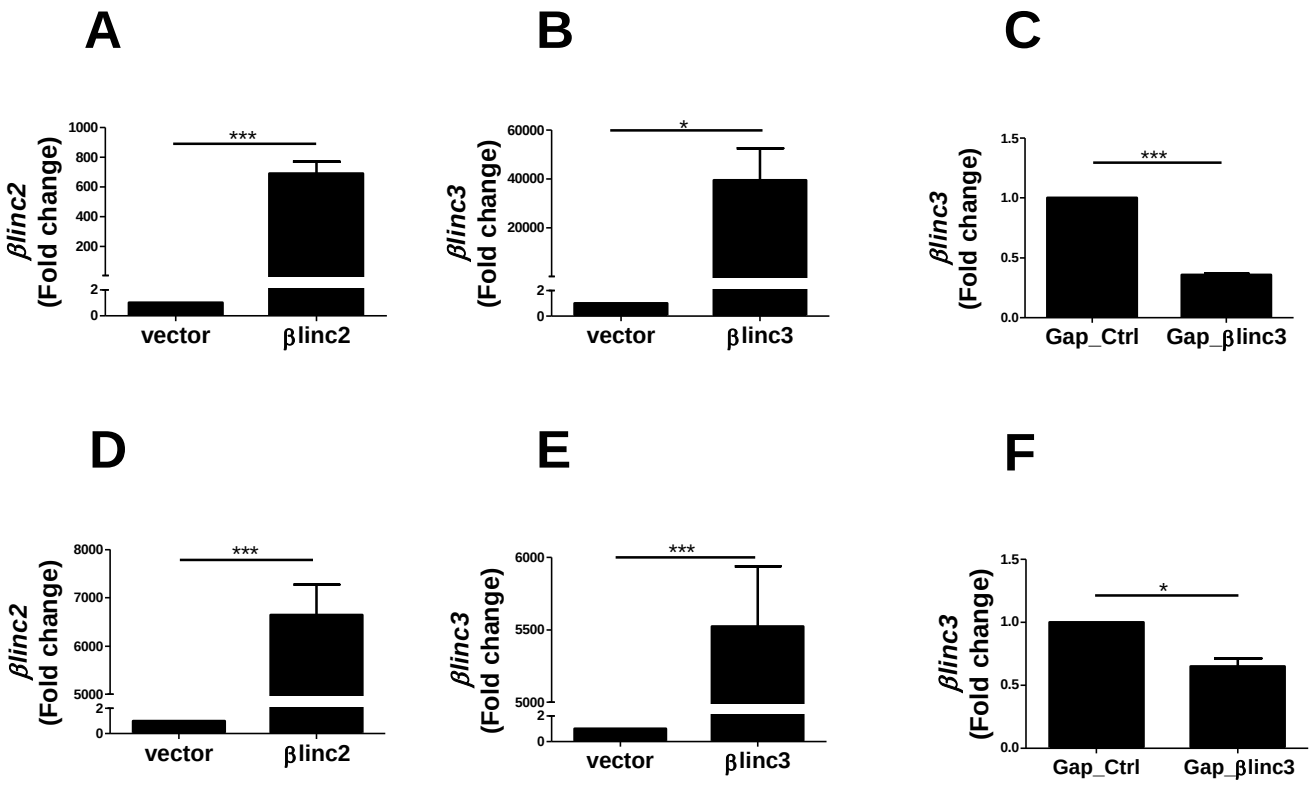
Supplemental figure 3. MIN6B1 cells were lysed and cytosolic and nucleoplasmic fractions prepared as described in the methods section. The level of *Gapdh* (cytosolic marker), *Malat1* (nuclear marker) and of the *βlinc* transcripts in each of the two compartments was assessed by qPCR. The data are the mean ± SD of 3 independent experiments.



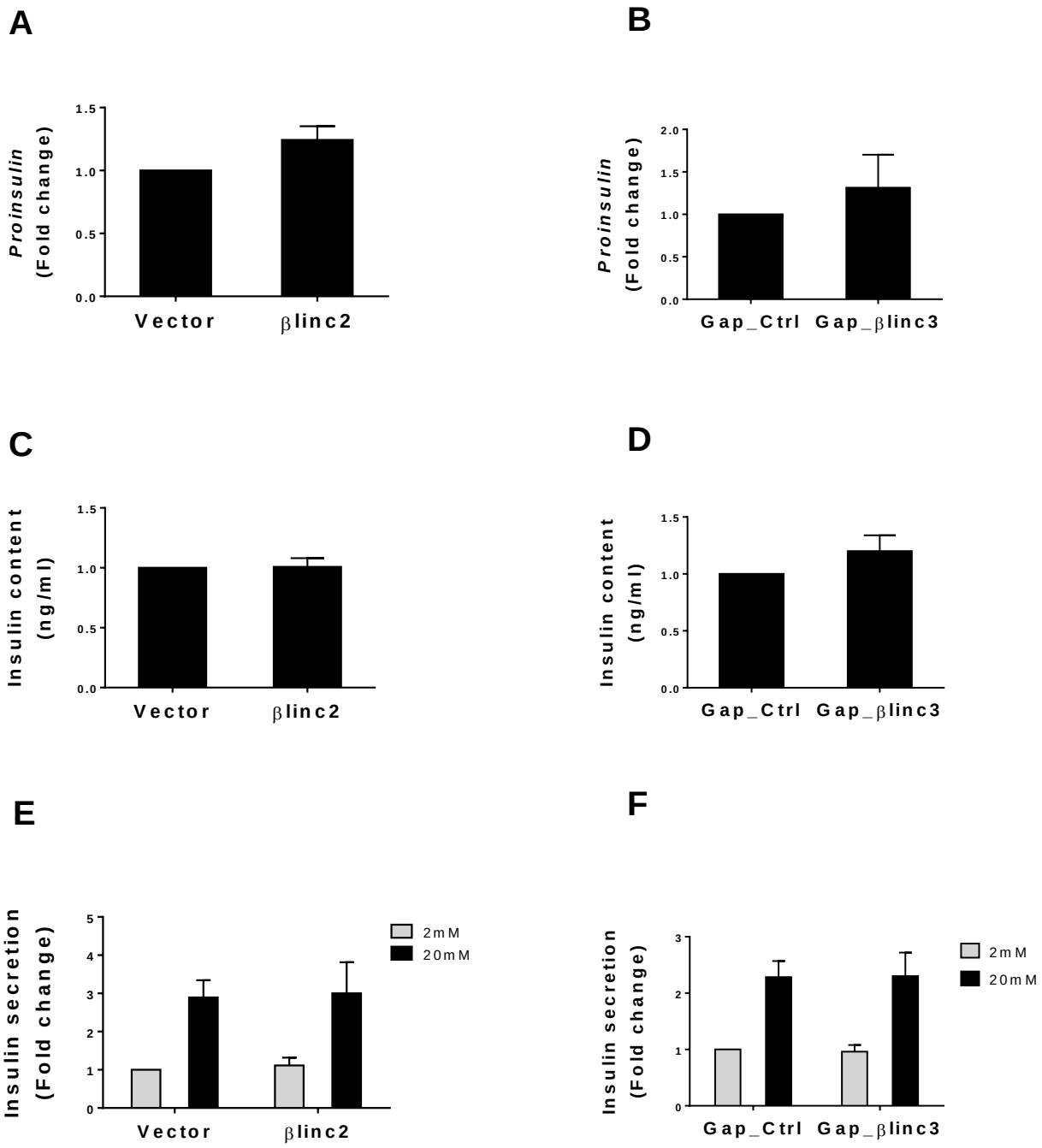
Supplemental figure 4. Correlations of the expression of *βlinc2* with body weight, insulinemia and glycaemia of C57BL/6 mice fed a normal or a high fat diet, with and without the higher expression point. Linear regression analysis of the expression of *βlinc2* versus body weight (A), glycemia (C) and Insulinemia (E). Linear regression analysis of the expression of *βlinc2* versus body weight (B), glycemia (D) and Insulinemia (F) without higher point. Body weight, Insulinemia and Glycaemia were measured at sacrifice. Fed blood glucose in HDR and ND mice was measured by a portable glucometer (Accucheck, Roche). Plasma insulin was measured by ELISA (ultrasensitive mouse insulin kit, ALPCO). The expression levels of the lncRNAs were measured by real-time PCR and normalized to Gapdh. F-test was used to determine significance at $p<0.05$.



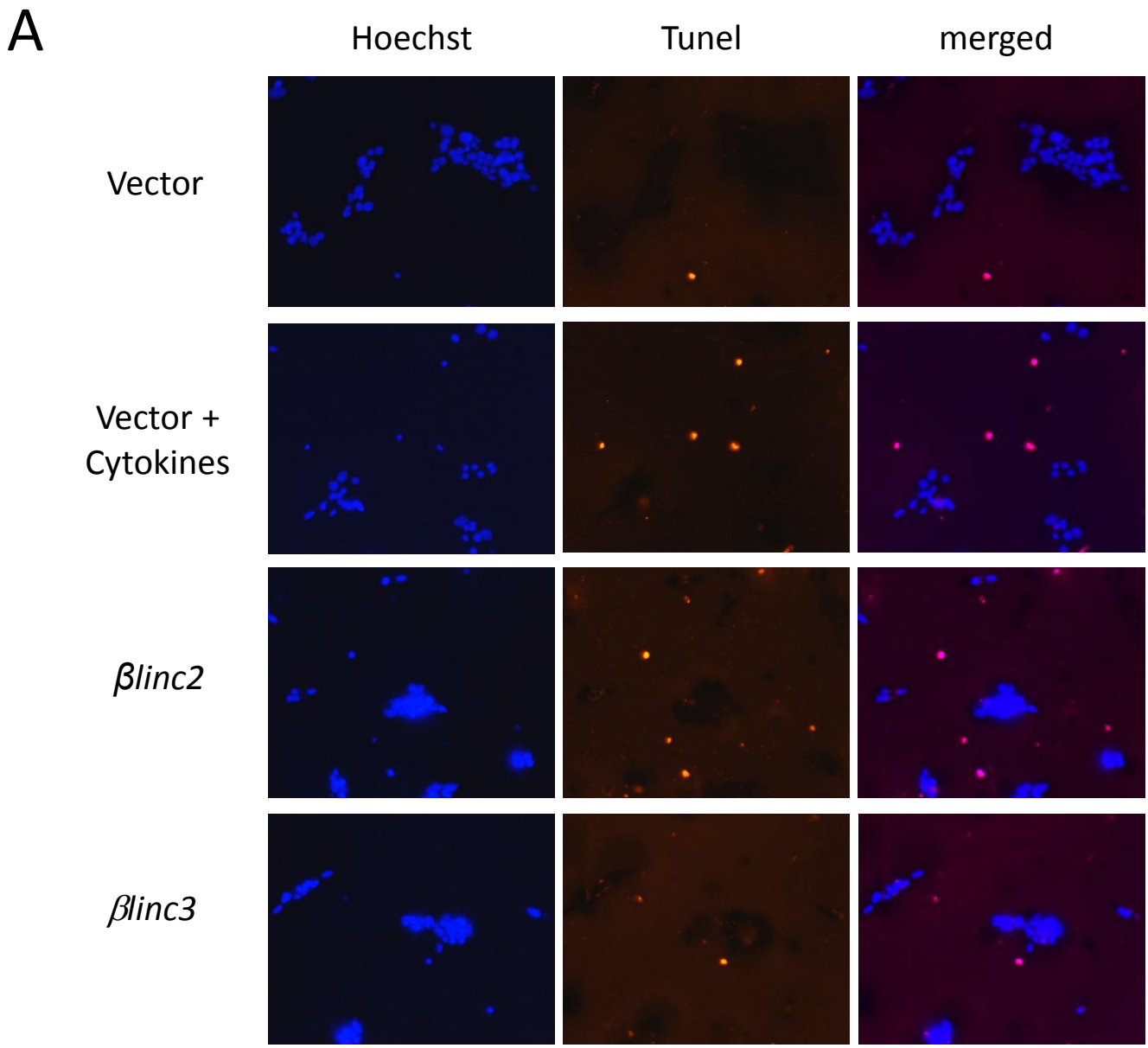
Supplemental figure 5. *βlinc2* and *βlinc3* expression is not modulated by cytokines. Dissociated islet cells were incubated in the absence (Ctrl) or presence of 0.1 ng/ml IL-1β, 10ng/ml TNF-α and 30ng/ml IFN-γ (Cyt_mix) for 24 hours. The expression levels were measured by real-time PCR and normalized to those of Gapdh. The results shown are the means ± SEM of 3 independent experiments.



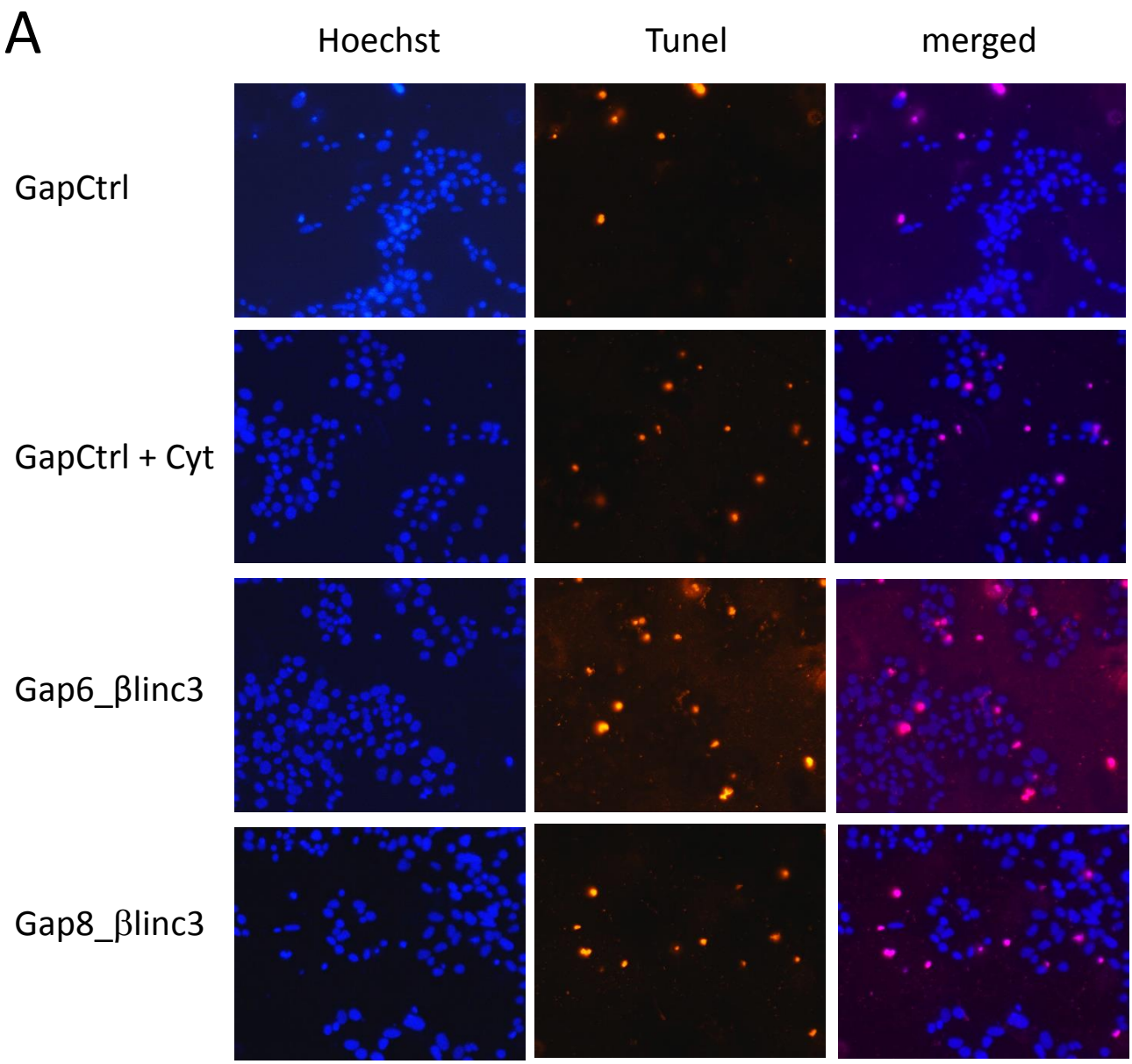
Supplemental figure 6. Confirmation of overexpression and downregulation of lncRNAs in MIN6 cells (A-B-C) and dissociated mouse islets (D-E-F). To overexpress, the cells were transfected with either the pcDNA3 plasmid (vector) or a plasmid containing the sequence to transcribe each individual lncRNA. To downregulate, the cells were transfected with either a gapmer control or a gapmer targeted against *βlinc3*. RNA isolation was performed 48h after transfection and the values normalised to the expression of *Gapdh*. The results shown are the means ± SEM of 3 independent experiments. t-test (* $p<0.5$; *** $p<0.001$).

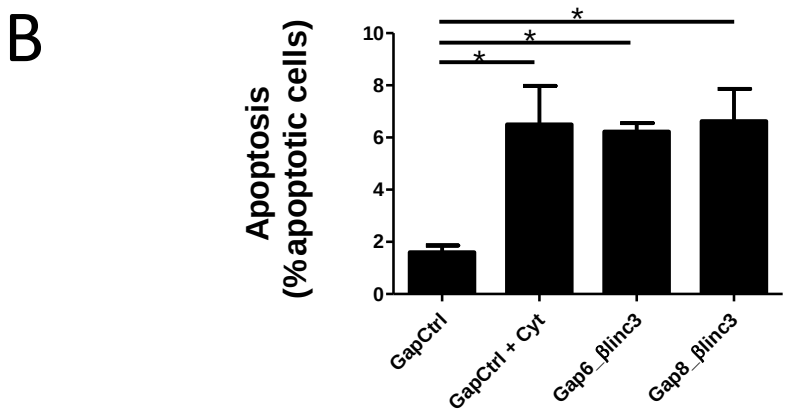


Supplemental figure 7. Overexpression and down-regulation of the two lncRNAs do not affect proinsulin mRNA, insulin content or secretion. MIN6 cells were transfected with an empty plasmid (vector) or a plasmid enabling the transcription of *βlinc2*, or a Control Gapmer (GapCtrl) and one targeted against *βlinc3* for 48 hours. RNA isolation was performed 48h after transfection and the values normalized to the expression of *Gapdh*. The cellular insulin content was measured by ELISA (C, D). Insulin secretion was also measured by ELISA after the cells were incubated with 2 or 20 mM glucose for 45min (E,F). The results represent means ± SEM of 3 different experiments. Insulin release was normalized to the amount of insulin secreted at 2mM glucose under control conditions (vector or Gap_Ctrl).



Supplemental figure 8. Overexpression of *βlinc2* but not *βlinc3* promotes apoptosis in MIN6 cells. Representative images of the TUNEL staining, after transfecting the cells for 46h with a control plasmid or a plasmid inducing the lncRNA of interest and treating or not with a mix of cytokines (A). Averages of 3 different experiments (B). Means ± SEM. ANOVA, tukey post-hoc test, *<0.05.





Supplemental figure 9. Downregulation of βlinc3 promotes apoptosis in MIN6 beta cells. Representative images of the TUNEL staining, after transfecting the cells for 46h with a control gapmer or different gapmers targeting *βlinc3* and treating one control condition with a mix of cytokines (A). Averages of 3 different experiments (B). Means ± SEM. ANOVA, tukey post-hoc test, *P<0.05.

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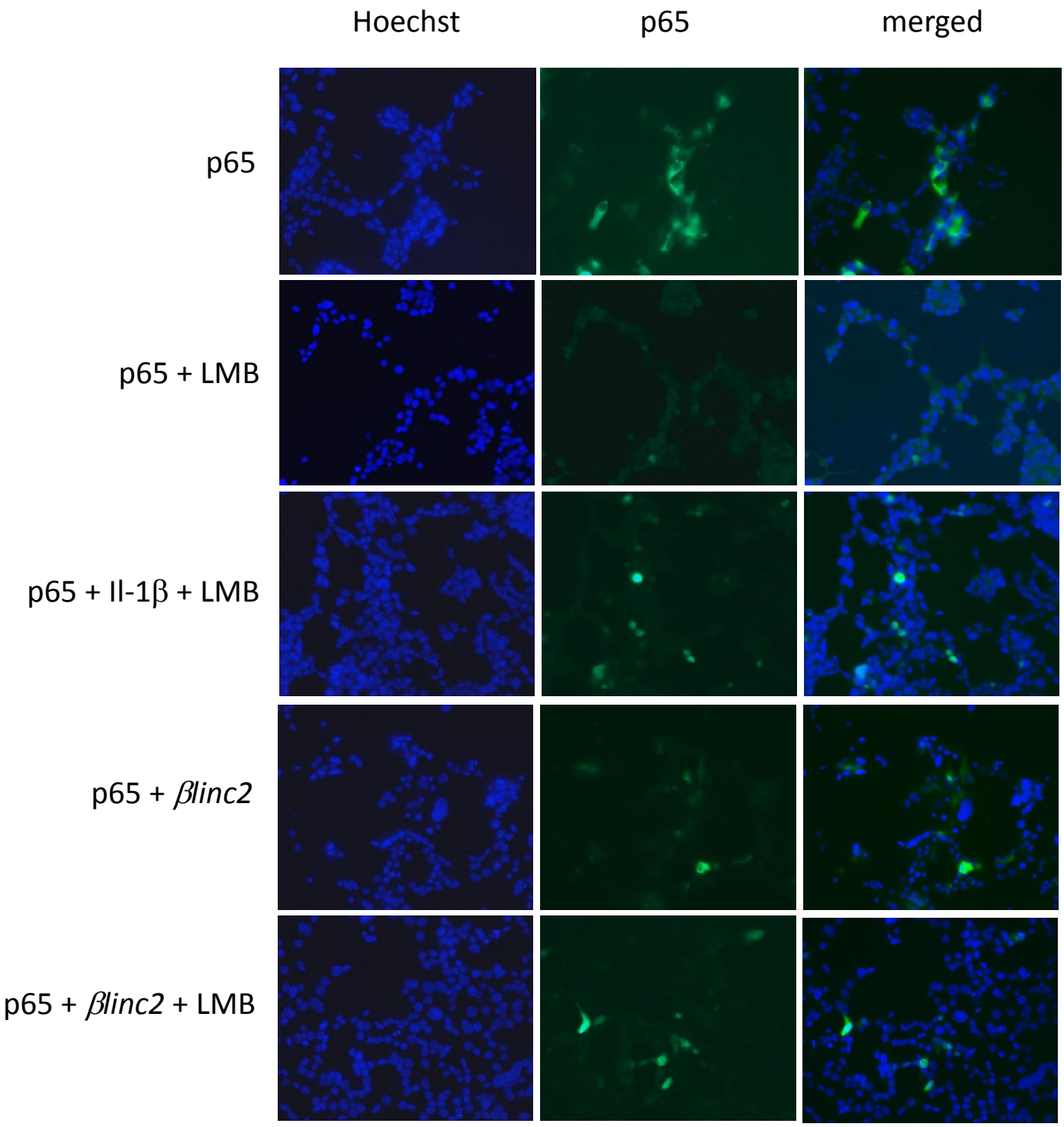
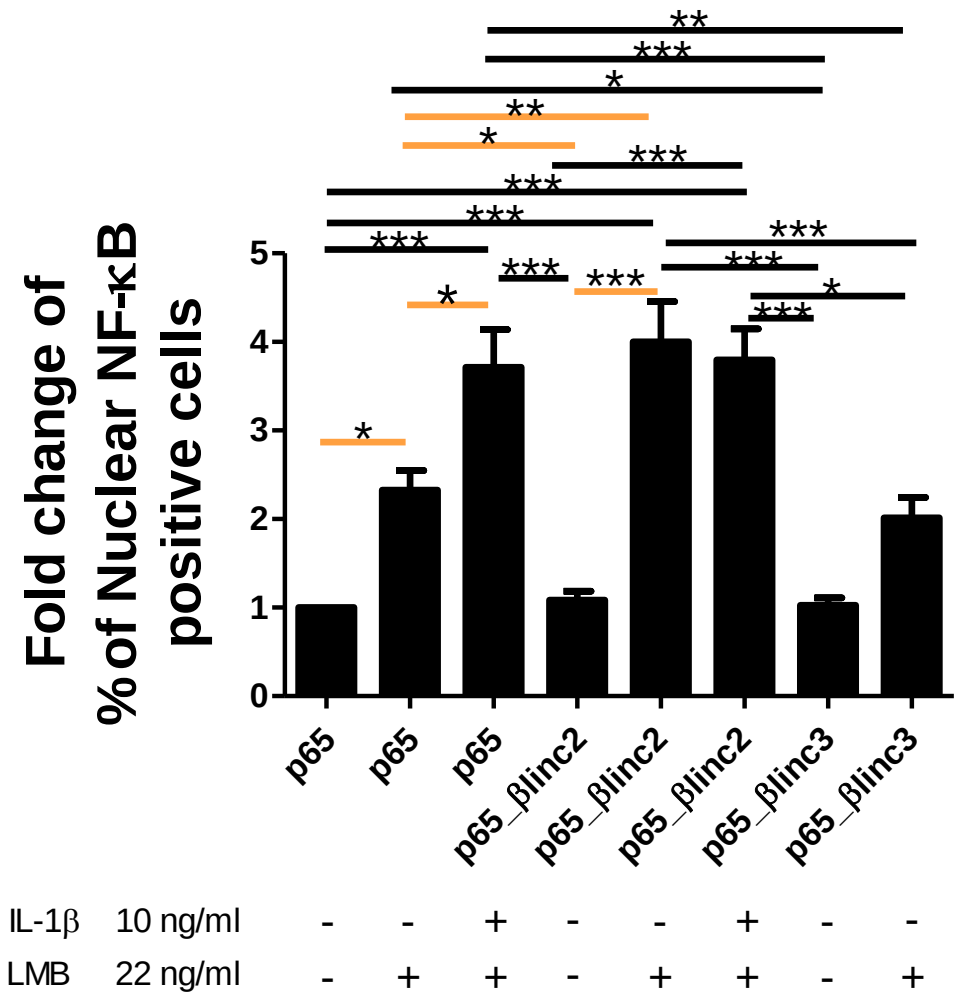
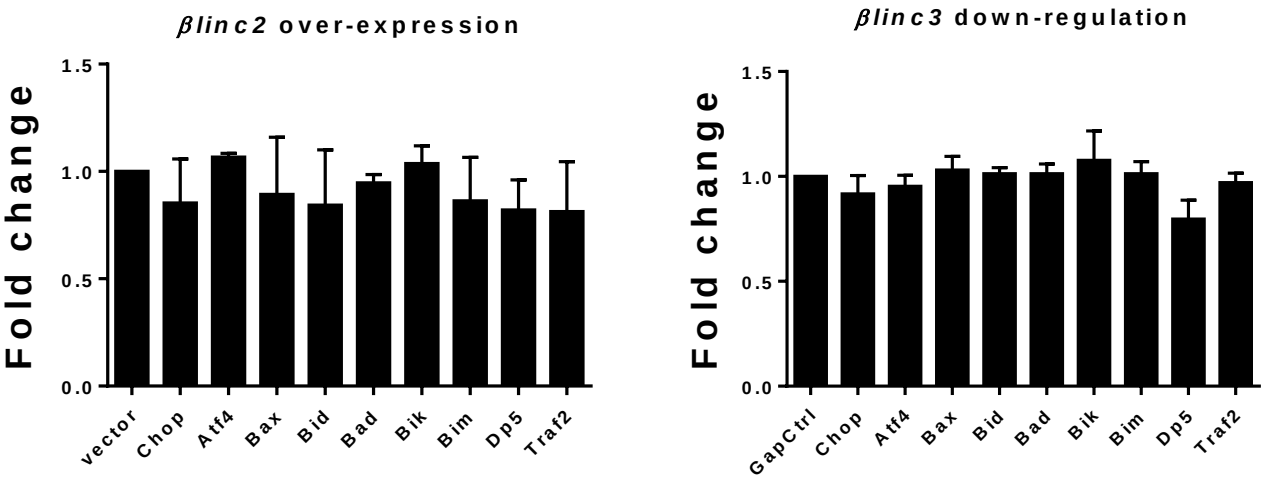


Supplemental figure 10. Representative images of the nuclear translocation of Nf-kB. MIN6B1 cells were transfected with a plasmid expressing a GFP-tagged Nf-KB subunit p65 (Rela) and/or the plasmid expressing the lncRNA of choice. 24h after the transfection, some of the cells were then treated for 3h with a high dose of IL-1β (10ng/ul) Leptomycin B (LMB) or a combination of the two. The cells were then fixed and mounted on a coverslip for microscopic examination.



Supplemental figure 11. Nuclear translocation of Nf-kB. MIN6B1 cells were transfected with a plasmid expressing a GFP-tagged Nf-KB subunit p65 (Rela) and/or the plasmid expressing the lncRNA of choice. 24h after the transfection, some of the cells (+) were treated for 3h with a high dose of IL-1β (10ng/ul), Leptomycin B (LMB) or a combination of the two. The number of cells displaying nuclear NF-kB localization were scored. Means ± SEM of 7 independent experiments. ANOVA, Tukey post-hoc test, *P<0.05, **P<0.001, ***P<0.001.



Supplemental figure 12. Effect of changes in the level of *βlinc2* and *βlinc3* on the mRNA level of genes involved in beta-cell apoptosis. Left panel: MIN6B1 cells were transfected with an empty vector or with a plasmid leading to the overexpression of *βlinc2.* Right panel: MIN6B1 cells were transfected with a control gapmer (GapCtrl) or with a Gapmer causing the down-regulation of *βlinc3.* The level of the indicated mRNAs was measured by qRT-PCR and was normalized to the respective control condition. The data are the mean ± SD of 3 independent experiments.