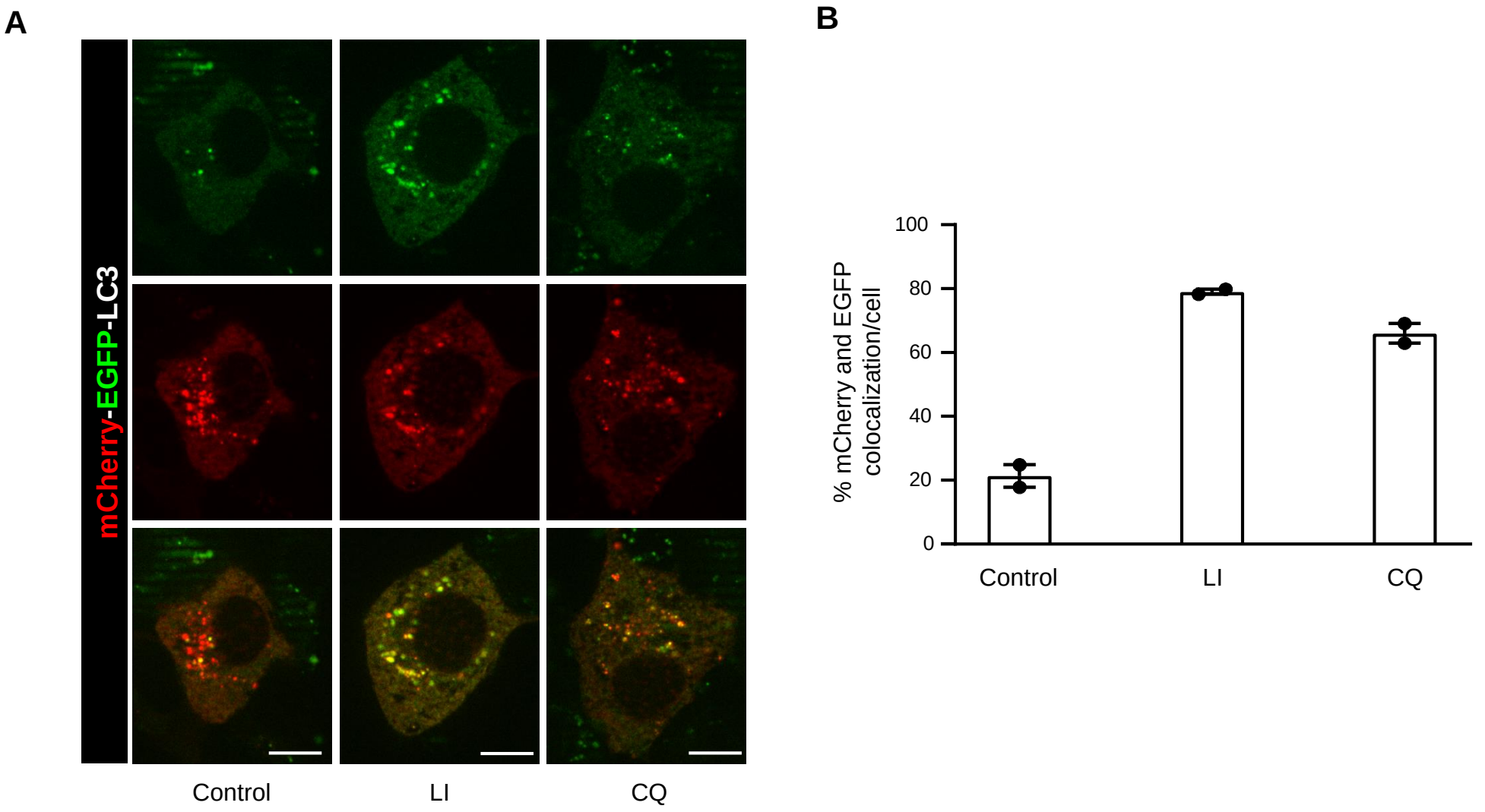
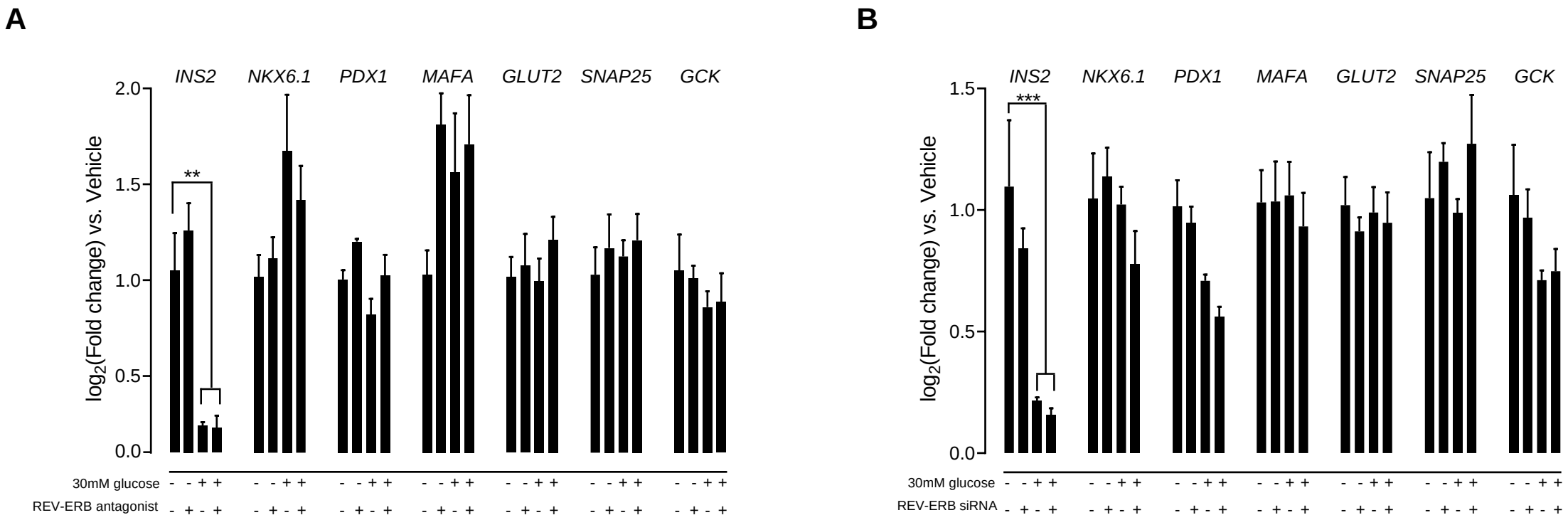


Supplemental Figure 1. Validation of mCherry-EGFP-LC3 reporter system in β-cells.
A: INS-1E cells expressing mCherry-EGFP-LC3B plasmid were either cultured in the absence or presence of lysosomal inhibitors (LI: E-64-d, 10 μg/ml and pepstatin A, 10 μg/ml, 24 h), or chloroquine (CQ: 100 μM, 2 h). **B:** Autophagic flux was assessed by quantification of mCherry and EGFP puncta colocalization using Image J software. Results are expressed as percentage of mCherry and EGFP colocalization per cell. Data are expressed as mean ± SEM of two independent experiments. Scale bar: 5 μm



<u>Supplemental Figure 2:</u> Role of REV-ERBα silencing or inhibition on β-cell function and identity gene expression under glucotoxic conditions.

A: INS-1E cells were exposed to glucotoxicity [30 mM glucose (G30) vs. control 11 mM glucose (G11)] for 48 h in the presence or absence of REV-ERB antagonist (SR8279, 10 μM). **B:** REV-ERBα was silenced in INS-1E cells by siRNA. Scramble RNA (-) was used as control. Cells were then exposed to glucotoxicity for 48 h (G30 vs. G11). For **A** and **B**, mRNA expression of key β-cell identity and functional genes is plotted and expressed as fold change relative to control expression (n=4 independent experiments per condition). Data are expressed as mean ± SEM; **P<0.01, ***P<0.001

Gene Target (Rat)	Sequence (F=forward; R=reverse)
Ins2	F-ATCCTCTGGGAGCCCCGC
	R-AGAGAGCTTCCACCAAG
Nkx6.1	F-CAGGTCAAGGTCTGGTTCCA
	TCAGTCTCCGAGTCCTGCT
Pdx1	F-GAACCGGAGGAGAATAAGAGG
	R-AGTCAAGTTGAGCATCACTGC
Mafa	F-AGGAGGTCATCCGACTGAAACA
	R-GCGTAGCCGCGGTTCTT
Glut2 (Slc2a2)	F-CGGAACCTTGGCTTTCACTGTCTT
	R-GGTGCATTGATCACACCGATGTCA
Snap25	F-GAGTCCCTGGAAAGCACC
	R-GGCATCGTTTGTTACCCT
Gck	F-AAGCCGCAGTGAGGACGTGATG
	R-AGGTGATTTCGCAGTTGGGTGTCA
Actin	F-CTCCTAGCACCATGAAGATC
	R-TCATCGTACTCCTGCTTGC

Supplemental Table 1: Gene Specific Primers