Supplementary materials and methods

Glucose-stimulated insulin secretion

The glucose-stimulated insulin secretion was performed as described by Gunawardana et al. [1] with some modifications. MIN6 cells were cultured in DMEM containing 25 mM glucose (GIBCO, 10566016, CA, USA) supplemented with 15% FBS (GIBCO, 10099141, CA, USA), 100 units/ml penicillin and 100 μg/ml streptomycin (GIBCO, 15140122, CA, USA), 55 uM β-mercaptoethanol (GIBCO, 21985023, CA, USA). Once cells reached 70% confluence, plates were rinsed once in either 5.5 mM glucose DMEM/15% FBS/55 uM β-mercaptoethanol or 25 mM glucose DMEM/15% FBS/55 uM β-mercaptoethanol and then incubated in the same medium. Metformin were added for 24 hours, and culture medium was collected and insulin level was determined by insulin ultrasensitive EIA (Alpco Diagnostics, Slemm, NH).

Supplementary Figures

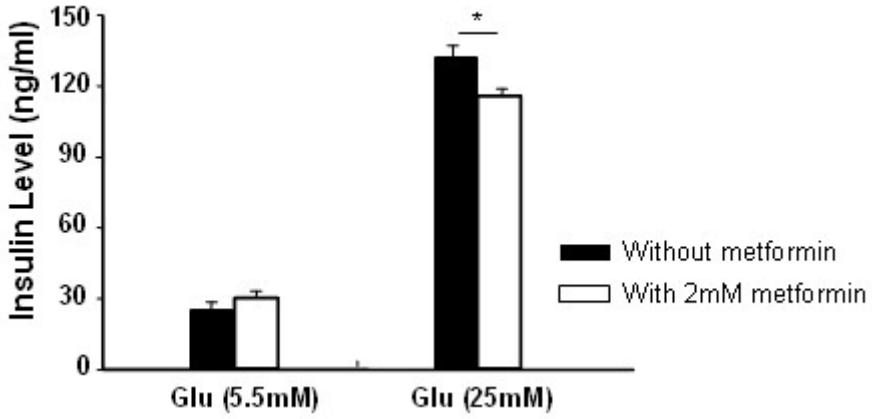

Figure S1. Metformin inhibits insulin secretion at stimulatory glucose concentration. MIN6 cells were cultured in DMEM containing 5.5mM or 25 mM glucose as indicated. 2mM Metforrmin was added and 24 hours later culture medium was collected. Insulin level was

determined by insulin ultrasensitive EIA (Alpco Diagnostics, Slemm, NH). Data are presented as means ±SEM of three separate experiments. * P<0.05.

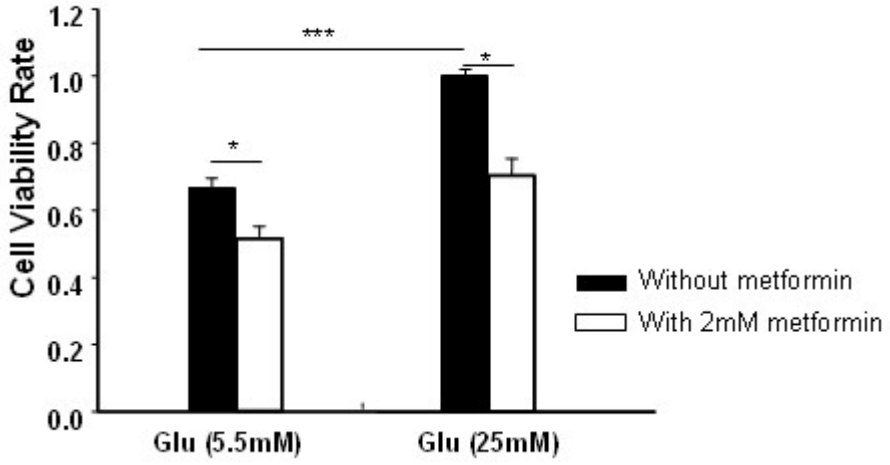

Figure S2. Glucose promotes MIN6 cell viability. MIN6 cells were cultured in DMEM containing 5.5mM or 25 mM glucose as indicated, then treated with ddH_2O as control or metformin at the indicated concentrations for 24 hours. 10 ul CCK-8 solution was added for 1 hour and cell viability rate was tested by Bio-Rad iMark™ microplate absorbance reader under 450nm wavelength. Cell viability rate= (sample OD-Blank OD)/ (Control OD-Blank OD). Data are presented as means ±SEM of three separate experiments. * P<0.05; ** P<0.01.

Reference

1. Webb, G.C., et al., *Expression profiling of pancreatic beta cells: glucose regulation of secretory and metabolic pathway genes.* Proc Natl Acad Sci U S A, 2000. **97**(11): p. 5773-8.