

Fig. S1. Quantification of RGS16 following overexpression in human islets and knockdown in mouse islets. (*A*) Isolated human islets were infected with Adv–RGS16 or Adv-GFP (n=4-7). (*B*) Isolated mouse islets were infected with Adv-shRGS16 or Adv-shCTL (n=6). mRNA levels were determined by qRT-PCR and normalized to mouse TATA-binding protein (mTbp) for mouse islets or hActin for human islets. Data are expressed as mean  $\pm$  SEM. \*\*p < 0.01; \*\*\*p < 0.001 vs. control.



Fig. S2. Effect of RGS16 overexpression on SST secretion in mouse islets. Isolated mouse islets were infected with Adv-RGS16 or Adv-GFP. SST secretion was determined in 1-h static incubations in response to 16.7 mM glucose. SST levels were normalized to the number of islets. Data are expressed as mean  $\pm$  SEM of 3 independent experiments. \*p < 0.05 vs. control.

## Overexpression



Fig. S3. Effects of RGS16 knockdown and overexpression on SSTR and Gai/o isoform expression in mouse islets. (A-C) isolated mouse islets were infected with Adv-shRGS16 or Adv-shCTL. (B-D) islets were infected with Adv-RGS16 or Adv-GFP. mRNA levels of SSTR and Gai/o were determined by qRT-PCR and normalized to mouse TATA-binding protein (mTbp). Data are expressed as mean  $\pm$  SEM of 4–6 independent experiments.



Fig. S4. Representative images of the data shown in Fig. 5B (A) and 5D (B).