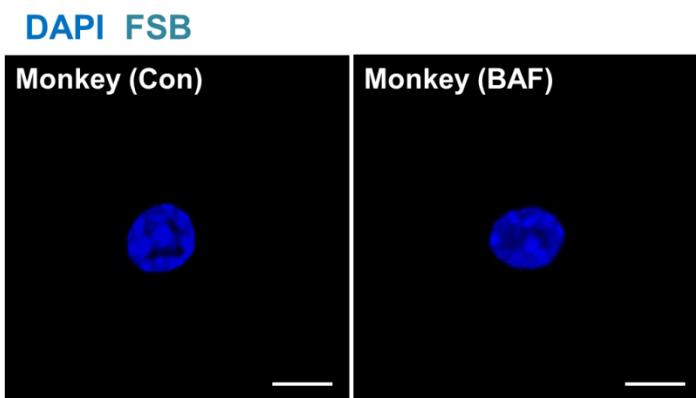
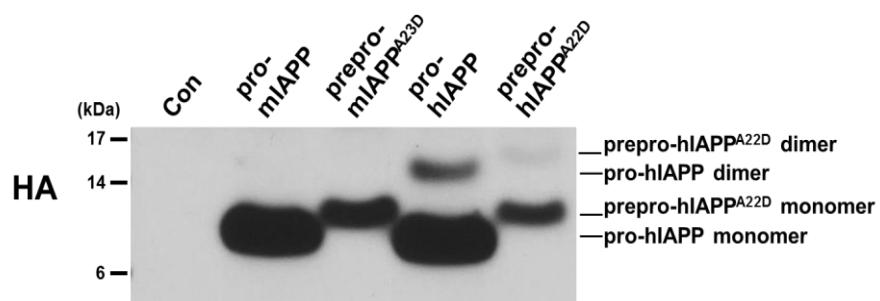


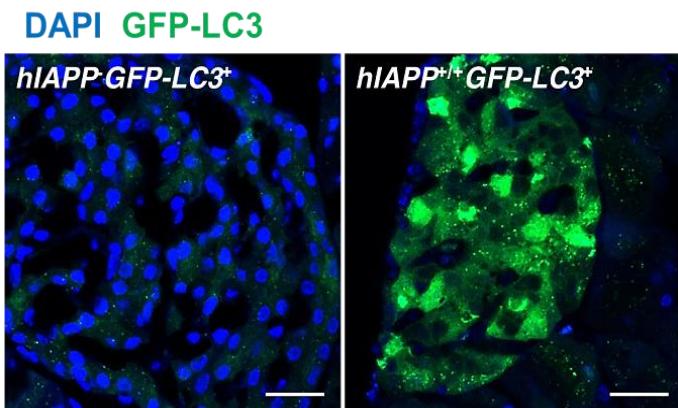
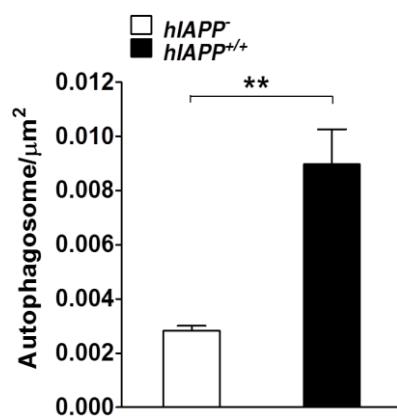
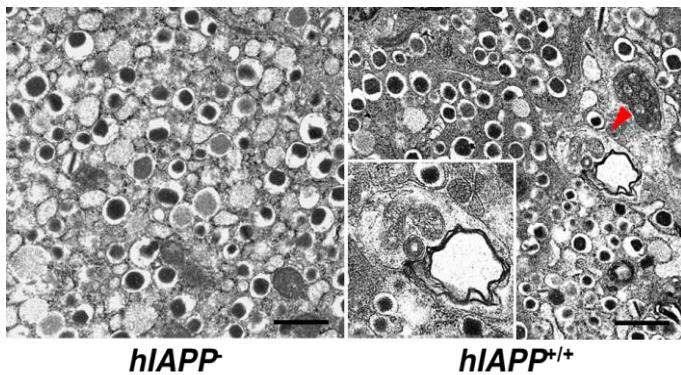
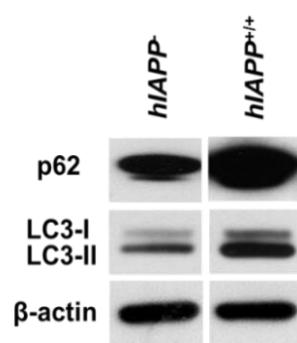
**A****Supplemental Figure 1**

No accumulation of amyloid in primary monkey islet cells in vitro. FSB staining revealed no accumulation of amyloid in the cytoplasm after incubation with 100 nM baflomycin for 24 h which induces IAPP oligomer accumulation (see Figure 4A). (scale bar, 5  $\mu$ m)

**A**

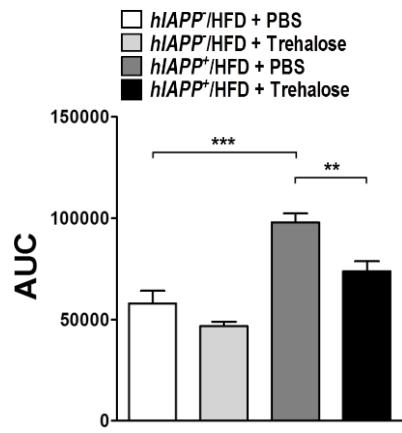
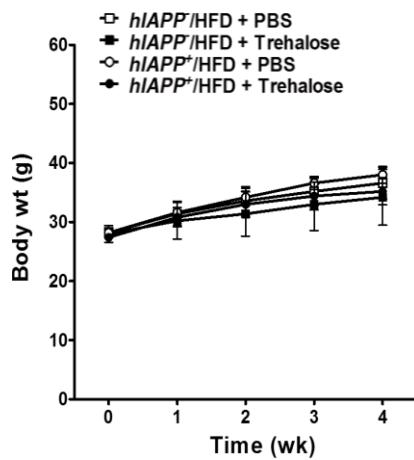
### Supplemental Figure 2

Different sizes of uncleaved prepro-hIAPP monomer and pro-hIAPP dimer. Mutation causing impaired cleavage of 'pre' sequence from prepro-hIAPP (28) was introduced by the site-directed mutagenesis of *prepro-mAPP-HA* (A23D) and *prepro-hIAPP-HA* (A22D). After transfection of INS-1 cells with the wild-type and mutant *prepro-mAPP-HA* or *prepro-hIAPP-HA*, Western blot analysis was conducted using anti-HA Ab. The size of uncleaved prepro-hIAPP monomer was apparently smaller than that of pro-hIAPP 'dimer', indicating that the 'dimer' band is not due to impaired cleavage of 'pre' sequence from prepro-hIAPP.

**A****B****C****D**

### Supplemental Figure 3

Effect of hIAPP on autophagy. (A) GFP-LC3 puncta representing autophagosomes in islets of 12-wk-old male *hIAPP<sup>+/+</sup>**GFP-LC3<sup>+</sup>* mice. (scale bar, 50  $\mu\text{m}$ ) (B) The number of autophagosomes in islets of 8 ~ 12-wk-old male *hIAPP<sup>+/+</sup>* and control mice was counted by EM as described in the Methods (n = 3 each). (C) Representative EM pictures showing a typical autophagosome in islets of *hIAPP<sup>+/+</sup>* mice. Inset is a magnified view of an autophagosome indicated by arrow head. (scale bar, 1  $\mu\text{m}$ ) (D) Western blot analysis of pancreatic islets from *hIAPP<sup>+/+</sup>* mice using anti-LC3 or -p62 Ab, indicating increased steady-state autophagy level and p62 accumulation due to autophagy blockade. The lanes were run on the same gel but were noncontiguous. (\*\*,  $P < 0.01$ )

**A****B**

### Supplemental Figure 4

Changes of AUC of IPGTT and body wt during trehalose administration. (A) AUC was calculated from data of Figure 6D (n = 5). (B) Body wt was monitored during trehalose administration to  $hAPP^+$  mice on HFD (n = 5). Food intake was also not affected by trehalose administration for 4 wk (data not shown).