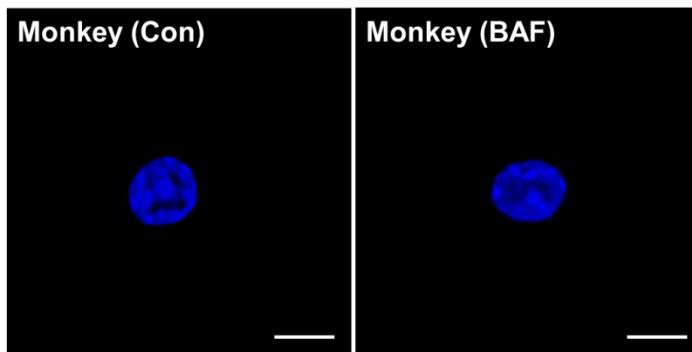


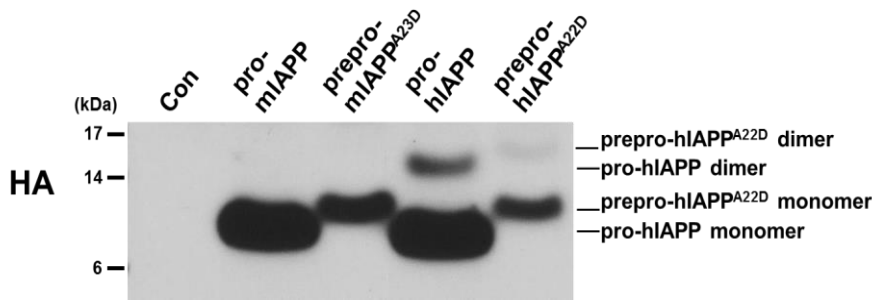
A

DAPI FSB

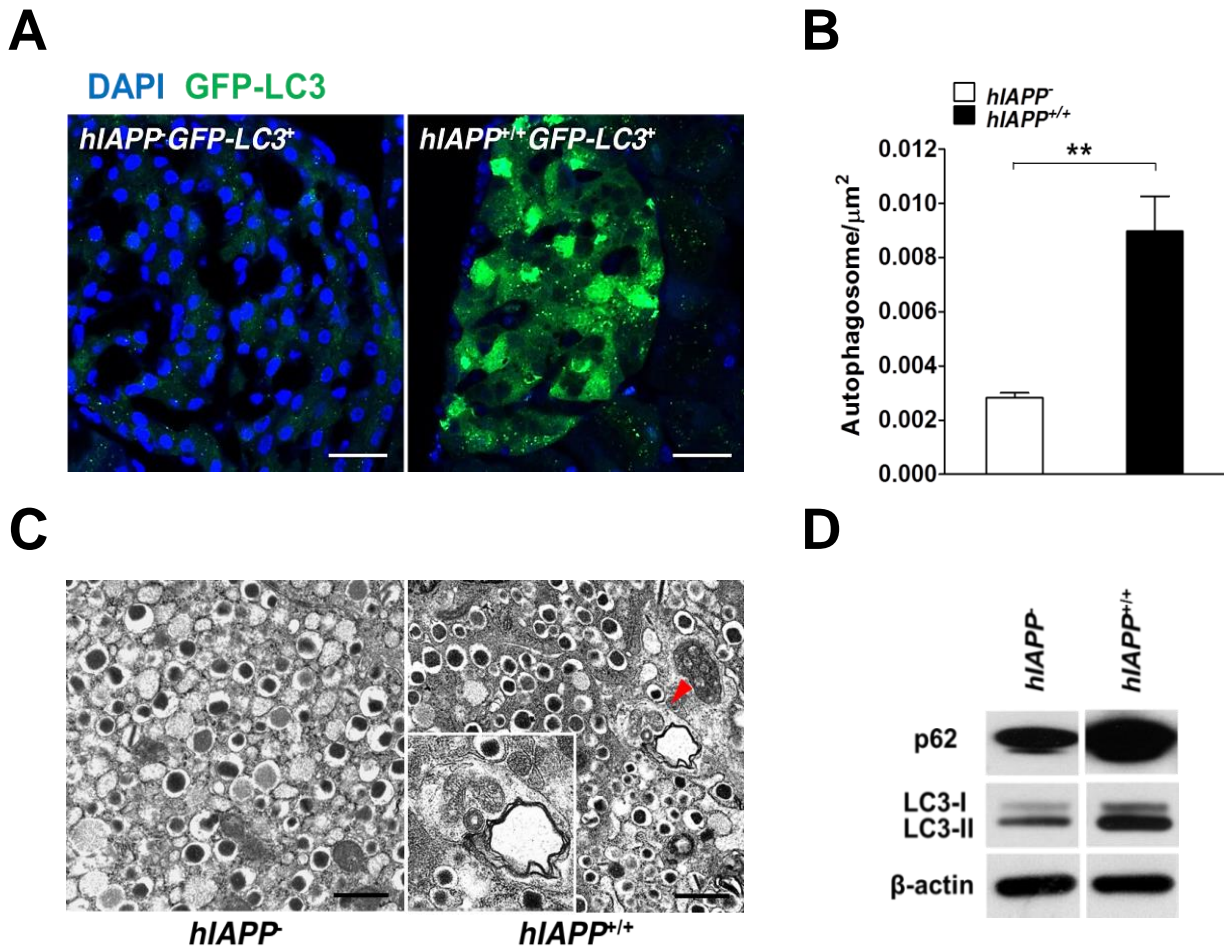


Supplemental Figure 1

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 bafilomycin for 24 h which induces IAPP oligomer accumulation (see Figure 4A). (scale bar, 5 μ m)

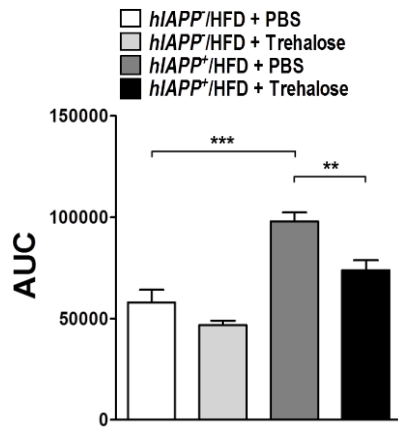
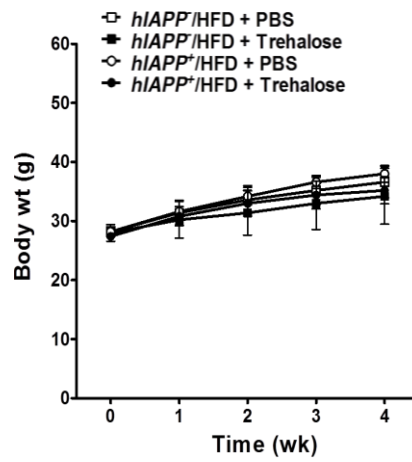
A**Supplemental Figure 2**

Different sizes of uncleaved prepro-hIAPP monomer and pro-hIAPP dimer. Mutation causing impaired cleavage of 'pre' sequence from prepro-IAPP (28) was introduced by the site-directed mutagenesis of *prepro-mIAPP-HA* (A23D) and *prepro-hIAPP-HA* (A22D). After transfection of INS-1 cells with the wild-type and mutant *prepro-mIAPP-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.



Supplemental Figure 3

Effect of *hiAPP* on autophagy. **(A)** GFP-LC3 puncta representing autophagosomes in islets of 12-wk-old male *hiAPP*^{+/+}GFP-LC3⁺ mice. (scale bar, 50 μm) **(B)** The number of autophagosomes in islets of 8 ~ 12-wk-old male *hiAPP*^{+/+} 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*^{+/+} mice. Inset is a magnified view of an autophagosome indicated by arrow head. (scale bar, 1 μm) **(D)** Western blot analysis of pancreatic islets from *hiAPP*^{+/+} 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 *hIAPP*⁺ mice on HFD ($n = 5$). Food intake was also not affected by trehalose administration for 4 wk (data not shown).