

## Description of Additional Supplementary Files

**File name:** Supplementary Movie 1

**Description:** Live-cell imaging of INS1<sup>PGCD</sup> cells endogenously expressing Phogrin-GFP (Phogrin-GFP<sup>endo</sup>, green) and CD63-DsRed (CD63-DsRed<sup>endo</sup>, red), pre-treated with Glc/Pal for 24h (shown in Supplementary Fig. 5b).

**File name:** Supplementary Movie 2

**Description:** Related to Fig. 2a: immunofluorescence of CD63 (green) and mTOR (red) in INS1 cells treated with glucolipotoxic (1% BSA, 33.3 mM Glucose and 0.4 mM Palmitate) media for 20h. Golgi-CFP was used to visualize the Golgi apparatus.

**File name:** Supplementary Movie 3

**Description:** Related to Fig. 3c, d: 3D reconstruction of the region of  $\beta$  cell with the granule-containing lysosomes (yellow), secretory granules (green) and lysosomes (red) revealed by Focused Ion Beam Scanning Electron Microscopy (FIB-SEM) of 6-week old BTBR ob/ob mice.