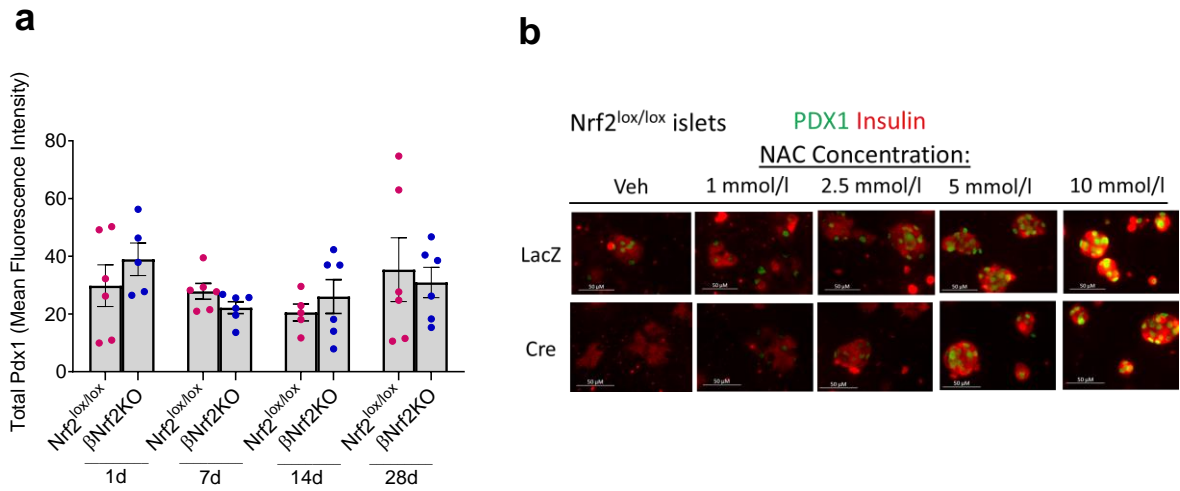
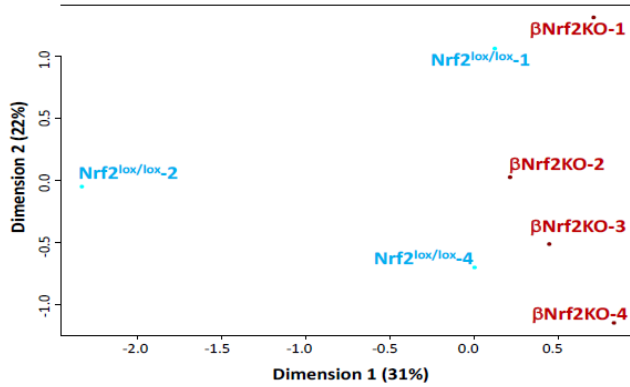
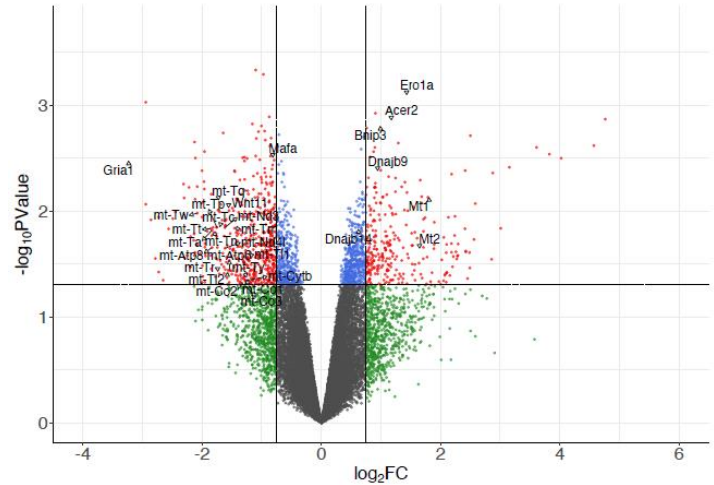
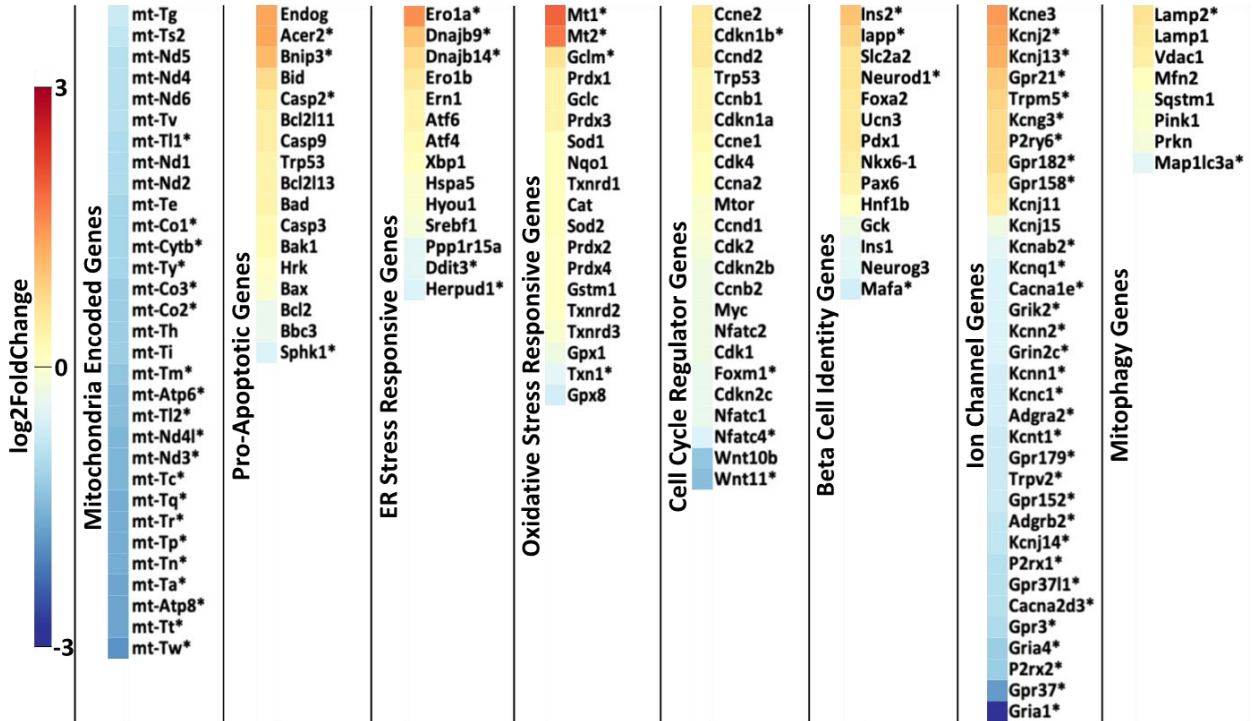


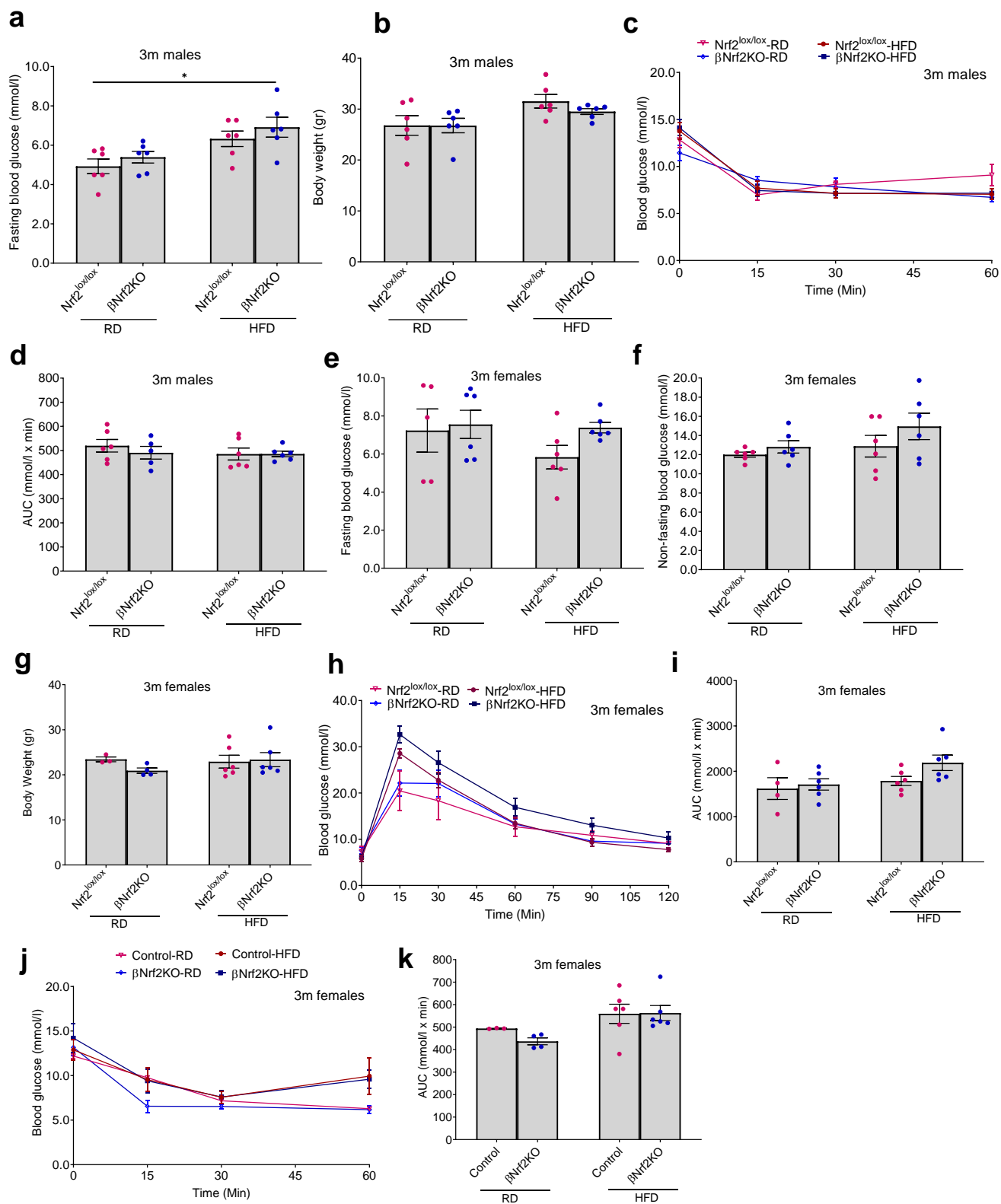
**ESM Figure 1: (a,b)** Pancreatic sections from 7-day-old male and female  $Nrf2^{lox/lox}$  control mice were immunolabeled for PCNA, NRF2 and insulin (scale bar 100  $\mu$ M). Percentage of PCNA was calculated out of NRF2-positive and insulin-positive cells. **(c,d)** Pancreatic sections from male and female 1-day-old  $Nrf2^{lox/lox}$  control mice were immunolabeled for insulin and chromogranin A (scale bar 200  $\mu$ M). b-cell area/chromogranin A area was calculated. **(e)** Pancreatic sections from 1-day-old male and female  $Nrf2^{lox/lox}$  control mice were immunolabeled for glucagon. Alpha-cell area/pancreas area was calculated. **(f)** The weight of pancreata from 7-day-old male and female  $Nrf2^{lox/lox}$  control or  $\beta Nrf2KO$  mice were recorded. (scale bar 100 or 200  $\mu$ M). Data are mean  $\pm$  SEM for n=5-9.



**ESM Figure 2:** (a) Pancreatic sections from 1,7,14 and 28-day-old male and female Nrf2<sup>lox/lox</sup> control or βNrf2KO mice were immunolabeled for PDX1 and insulin. Total PDX1 intensity was measured in insulin positive cells. (b) Nrf2<sup>lox/lox</sup> islets were dispersed, transfected with either Cre-expressing or LacZ-expressing adenovirus, followed by incubation in 20 mmol/l glucose-containing media supplemented with increasing NAC concentrations. After 72 h incubation, cells were fixed and immunolabeled with PDX1 and insulin (scale bar 50 μM). Data are mean ± SEM for n=4-8.

**a****b****c**

**ESM Figure 3: RNA-seq from islets of 7-day old b-cell-specific *Nrf2* deletion mice show differential expressed genes over *Nrf2*<sup>lox/lox</sup> control islets. (a) PCA plot shows clusters separation in gene expression profiles between  $\beta$ *Nrf2*KO and *Nrf2*<sup>lox/lox</sup> groups. (b) Volcano plot presents various differential expressed genes. (c) List of differential expressed genes. \**p* < 0.05.**



**ESM Figure 4: Glucose homeostasis in postnatal  $\beta Nrf2KO$  female and male mice fed on RD or HFD.** (a) Fasting blood glucose, (b) body weight, and (c,d) insulin tolerance test (ITT) were measured in 3-month-old male  $\beta Nrf2KO$  or  $Nrf2^{lox/lox}$  mice fed on RD or HFD for 1 month. (e) Fasting blood glucose, (f) non-fasting blood glucose, (g) body weight, (h,i) IPGTT, and (j,k) insulin tolerance test (ITT) were measured in 3-month-old female  $\beta Nrf2KO$  or  $Nrf2^{lox/lox}$  mice fed on RD or HFD for 1 month. Data are the mean  $\pm$  SEM for n=3-6. \* $p < 0.05$ .