# Supplementary Table S1. Antibodies, Source, and working dilution

Antibody	Company	Catalogue Number	Dilution
4-HNE	Abcam	Ab464545	1:100
GPX	Santa Cruz Biotechnology	sc-22145	1:200
Nrf2	Santa Cruz Biotechnology	sc-722	1:200
Galectin 3	Biolegend	125402	1:100
Glucagon	Santa Cruz Biotechnology	sc-13091	1:300
Insulin	Dako	A0564	1:500

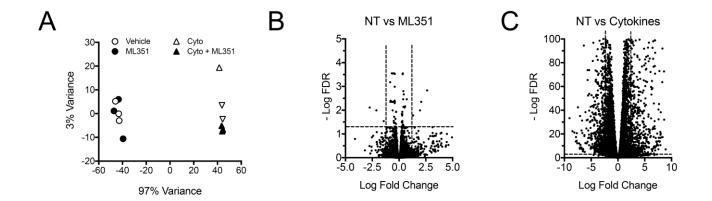
Supplementary Table S2. Docking scores of ML127 and ML351 with the human proteome forwhich comprehensive structural data are available.

Download or view data at: <a href="https://iu.app.box.com/v/SupplTableS2">https://iu.app.box.com/v/SupplTableS2</a>

Supplementary Table S3. Genes significantly altered (P<0.05, FDR<0.05) in comparison between islets treated with pro-inflammatory cytokines (PIC) and pro-inflammatory cytokines + ML353 (PIC+ML).

Download or view data at: <a href="https://iu.app.box.com/v/SupplTableS3">https://iu.app.box.com/v/SupplTableS3</a>

Supplementary Figure S1. Transcriptome analysis of mouse islets treated with cytokines and ML351. Mouse islets were treated for 24 hrs with vehicle (NT),  $10 \mu M$  of ML351 (ML351), cytokines (cyto), cytokines+ $10 \mu M$  of ML351(cyto+ML351). (A), Principal component analysis of RNA sequencing results. (B and C), Volcano plots of RNA sequencing analysis. Data are from N=3 biologic replicates.



## Supplementary Figure S2. Galectin 3 immunostaining of pancreas of CD1 and NOD mice.

Fixed pancreatic sections from CD1 and NOD mice treated with vehicle or 24 mg/kg ML351 were subjected to immunofluorescence staining. Shown are representative images (*left panel*) and galectin-3-positive cells as a percent of cellular infiltrate (*right panel*) from analysis of at least three animals pergroup. Galectin-3 (Gal-3, *magenta*), insulin (*green*), and DAPI (*blue*). Magnification x200, scale bar  $100 \ \mu m$ . \*P < 0.05 compared to NOD-MO.

