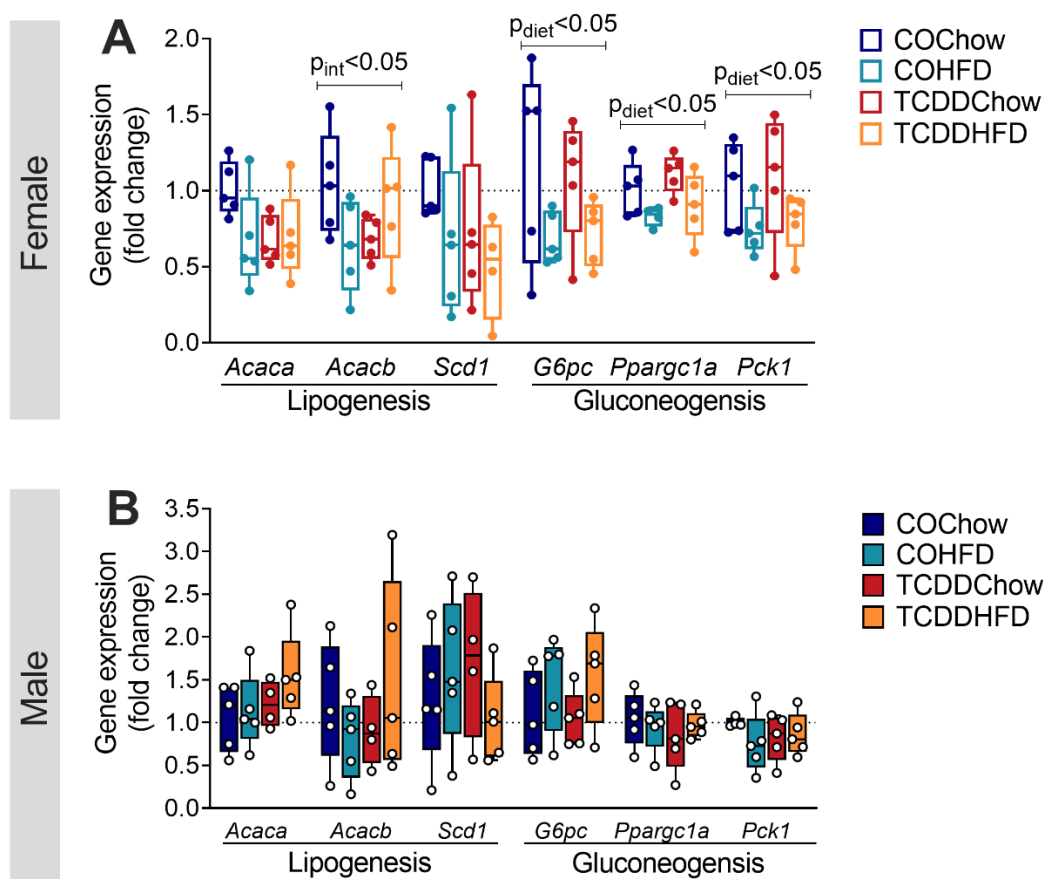
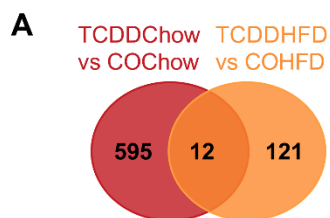


Supp. Fig. 1 TCDD exposure did not alter glucose-induced plasma insulin levels at week 4. Glucose-stimulated plasma insulin levels were assessed *in vivo* at week 4 in (A) females and (B) males (n=3-8 per group) (see Fig. 1A for study timeline). Data are presented as box and whisker plots. Individual data points on box and whisker plots represent biological replicates (different mice). The following statistical tests were used: (A-B) one-way ANOVA with Tukey's multiple comparison test at each time point.



Supp. Fig. 2 TCDD exposure did not alter hepatic expression of genes involved in insulin-dependent lipogenesis and gluconeogenesis. Liver was harvested at week 12 of the study for gene expression analysis by qPCR (see Fig. 1A for study timeline). Expression of genes involved in lipogenesis and gluconeogenesis were measured in (A) females and (B) males. All data are presented as median with min/max values in box and whisker plots. Individual data points on box and whisker plots represent biological replicates (different mice). The following statistical tests were used: (A-B) two-way ANOVA with Tukey's multiple comparison test.



B Most downregulated genes

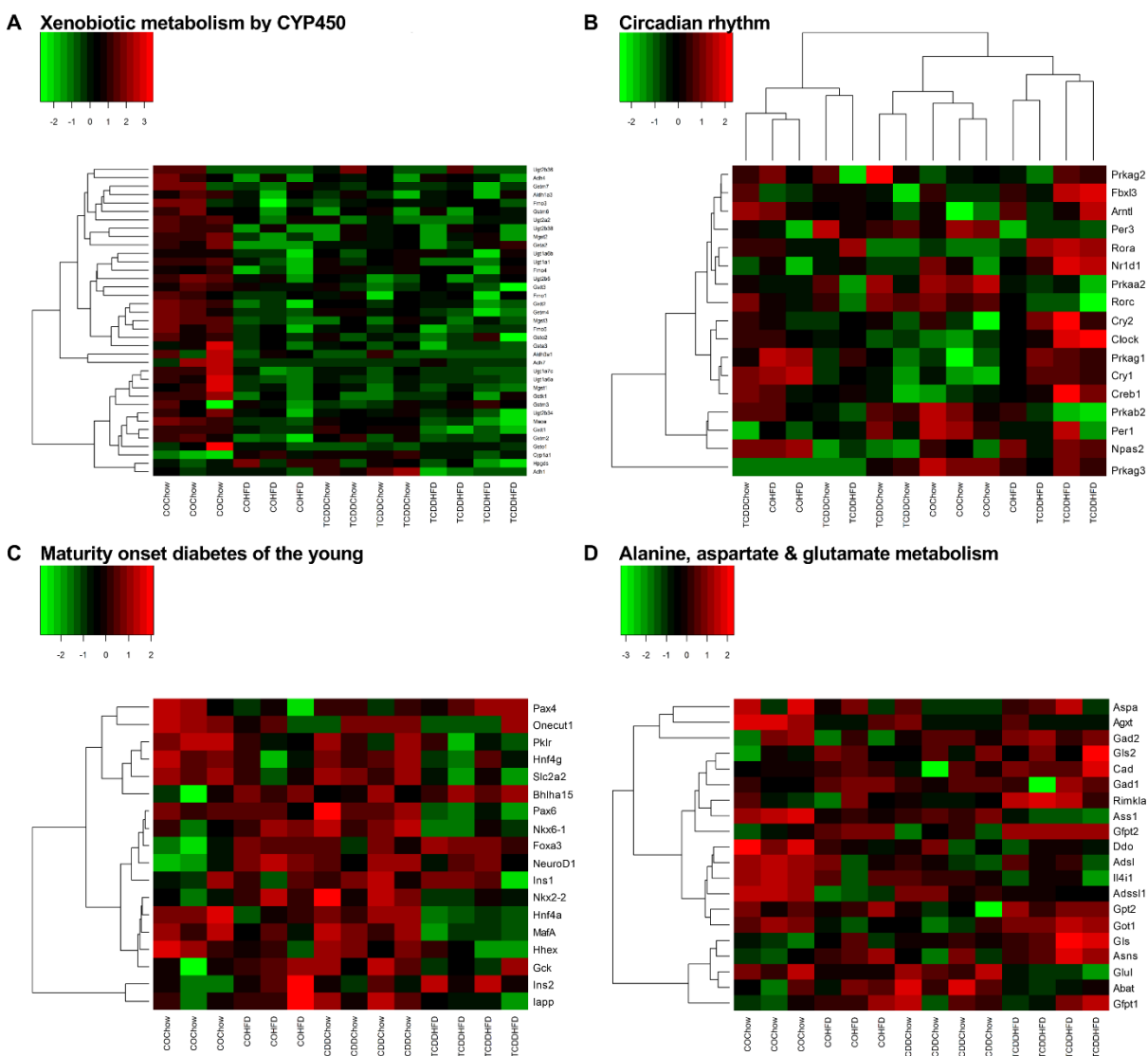
| Gene | Fold Change | p-value |
|---------------|-------------|----------|
| <i>Slc2a2</i> | -3.69 | 1.29E-09 |
| <i>G6pc2</i> | -3.20 | 6.15E-15 |
| <i>Mrln</i> | -3.11 | 8.66E-05 |
| <i>Rbm3</i> | -2.85 | 2.70E-14 |
| <i>Igfbp3</i> | -2.68 | 6.22E-12 |

Most upregulated genes

| Gene | Fold Change | p-value |
|-----------------|-------------|----------|
| <i>Akr1b3</i> | 3.91 | 3.25E-21 |
| <i>Vmn1r121</i> | 2.67 | 0.001033 |
| <i>Tfdp2</i> | 2.46 | 2.19E-05 |
| <i>Gm648</i> | 2.41 | 0.000147 |
| <i>Ephx1</i> | 2.39 | 3.26E-06 |

Supp. Fig. 3 TCDD-induced changes in gene expression relative to CO-exposed controls.

Female mice were injected with corn oil (CO) or 20 ng/kg/d TCDD 2x/week for 12 weeks, and either fed standard chow or 45% HFD (see **Fig. 1A** for study timeline). Islets were isolated at 12 weeks for TempO-Seq® analysis. **(A)** Venn diagram displaying differentially expressed genes (DEGs) (adjusted $p < 0.05$, absolute fold change ≥ 1.5) in TCDD-exposed females relative their respective CO-exposed control female. **(B)** Five most down- and up-regulated genes in TCDDHFD females when compared to COHFD females.



Supp. Fig. 4 Heatmaps displaying gene expression profiles for “Xenobiotic Metabolism by CYP450”, “Circadian Rhythm”, “Maturity Onset Diabetes of the Young”, and “Alanine, Aspartate & Glutamate Metabolism”. Female mice were injected with corn oil (CO) or 20 ng/kg/d TCDD 2x/week for 12 weeks, and either fed standard chow or 45% HFD (see Fig. 1A for study timeline). Islets were isolated at 12 weeks for TempO-Seq® analysis. Heatmaps arranged by experimental group showing expression levels of genes involved in (A) “Xenobiotic Metabolism by CYP450”, (C) “Maturity Onset Diabetes of the Young”, and (D) “Alanine, Aspartate and Glutamate metabolism”. (B) Hierarchical heatmap showing “Circadian Rhythm” gene expression profile.

Supp. Table 1: qPCR primer sequences.

| Target | Forward Primer | Reverse Primer |
|-----------------|-------------------------------|-------------------------------|
| <i>Acaca</i> | CCT GAC AAA CGA GTC TGG CT | CAT TCC ATG CAG TGG TCC CT |
| <i>Acacb</i> | TCC GTG CCT TTG TAC AGT CC | CAG GCT CCA AGT GGC GAT AA |
| <i>Cyp1a1</i> | ATC ACA GAC AGC CTC ATT GAG C | AGA TAG CAG TTG TGA CTG TGT C |
| <i>G6pc</i> | TAC TAC AGC AAC AGC TCC GTG | TCC CAA CCA CAA GAT GAC GTT |
| <i>Mafa</i> | AGT CGT GCC GCT TCA AG | CGC CAA CTT CTC GTA TTT CTC C |
| <i>Pck1</i> | TGG GAA CTC ACT ACT CGG GA | TTC TTC TTG CCT TCG GGG TT |
| <i>Ppargc1a</i> | CTT GAC TGG CGT CAT TCG G | CGC TAC ACC ACT TCA ATC CAC |
| <i>Ppia</i> | AGC TCT GAG CAC TGG AGA GA | GCC AGG ACC TGT ATG CTT TA |
| <i>Scd1</i> | CTG AAC ACC CAT CCC GAG AG | GTG GTG GTG GTC GTG TAA GA |