

# Supplemental Information

## Supplemental Methods

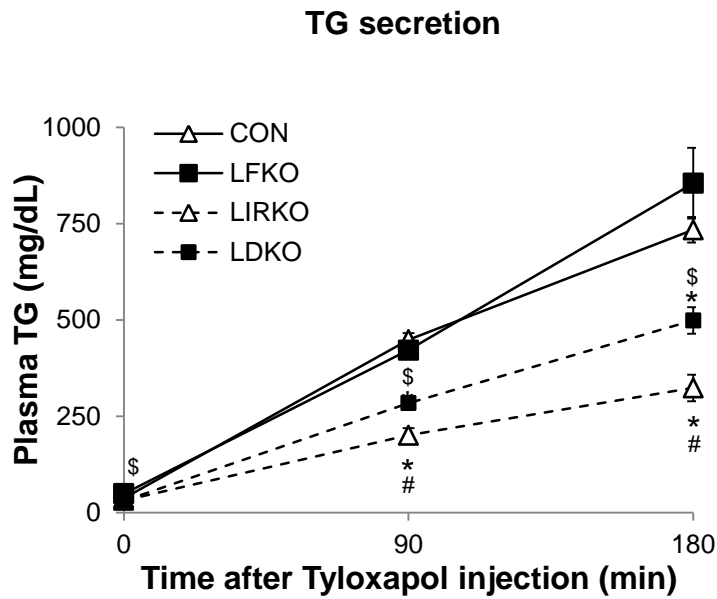
### Triglyceride secretion

Mice were fasted for 4 hours before being injected retro-orbitally with Tyloxapol (Sigma Aldrich; 0.45 mg/gr body weight). Blood was collected via retro-orbital bleeding at 0 and 90 minutes, and via cardiac puncture at 180 minutes after Tyloxapol injection. Plasma triglyceride levels were measured using a colorimetric assay (Infinity).

### Statistical analysis

Data are represented by the mean  $\pm$  SEM, unless otherwise indicated. Knockout mice were compared to their littermate Cre-negative controls as well as the pooled controls; in addition, LDKO mice were compared to LFKO and LIRKO mice. Significance was assessed by a 2-tailed Student's t-test with unequal variance. Data are pooled from two independent cohorts (triglyceride secretion) or are from a single cohort (lipidomics and gene expression in heat map).

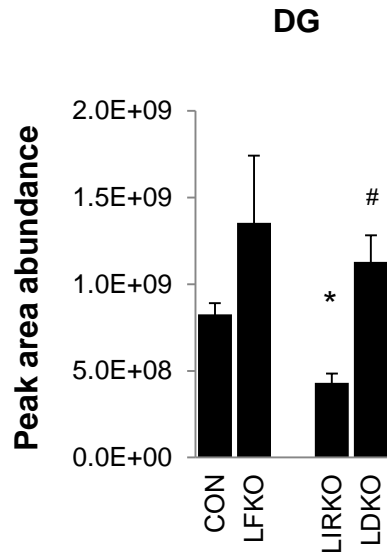
# Supplemental Figure 1



## Supplemental Figure 1: Triglyceride secretion in LFKO, LIRKO, and LDKO mice.

Plasma triglyceride (TG) levels in female control (CON), LFKO, LIRKO, and LDKO mice (8-10 weeks old) after Tyloxapol injection. Error bars represent SEM; n=9-29 mice; \*p<0.05 versus CON; #p<0.05 LIRKO vs LDKO; \$p<0.05 LFKO vs LDKO.

## Supplemental Figure 2

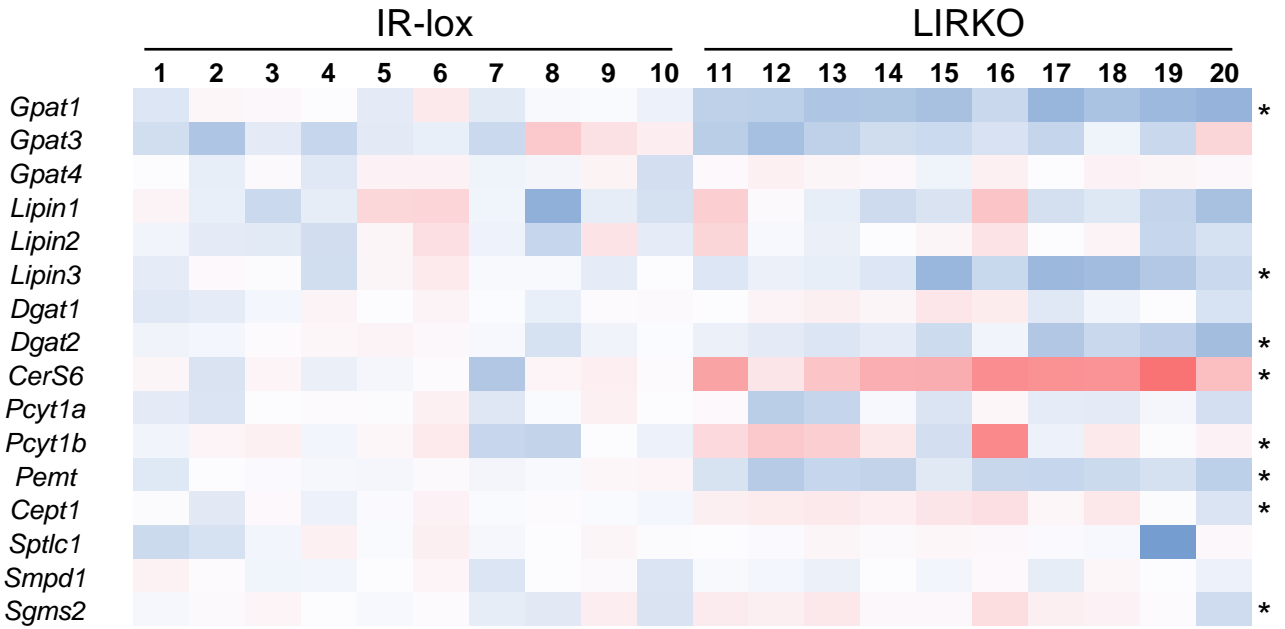
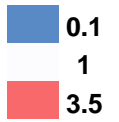


### Supplemental Figure 2: Liver diglyceride levels in LFKO, LIRKO, and LDKO mice.

Diglyceride (DG) abundance in the livers of control (CON), LFKO, LIRKO, and LDKO mice (8-10 weeks old) was measured using LC-MS. Error bars represent SEM; n=5-15; \*p<0.05 versus CON; #p<0.05 LIRKO vs LDKO; \$p<0.05 LFKO vs LDKO.

# Supplemental Figure 3

Fold change



## Supplemental Figure 3: Gene expression in IR-lox and LIRKO livers.

Gene expression was measured by real-time PCR in LIRKO versus IR-lox mice (8-10 weeks old). Each column represents data from a single mouse; n=10; \*p<0.05 versus IR-lox.

### Supplemental Table 1

| Class | Fatty Acid     |
|-------|----------------|
| Cer   | d18:1/17:0     |
| PC    | 17:0/14:1      |
| PE    | 17:0/14:1      |
| TG    | 17:1/17:1/17:1 |
| DG    | 19:0/19:0      |
| SM    | d35:1          |
| LPC   | 17:1           |
| LPI   | 17:1           |

**Supplemental Table 1. Internal lipid standards used in the LC-MS/MS experiment.** Cer, Ceramide; PC, Phosphatidylcholine; PE, Phosphatidylethanolamine; TG, Triglyceride; DG, Diglyceride; SM, Sphingomyelin; LPC, Lysophosphatidylcholine; LPI, Lysophosphatidylinositol.

**Supplemental Table 2**

| Normalized mean $\pm$ SEM | CON             | LFKO            | LIRKO           | LDKO            |
|---------------------------|-----------------|-----------------|-----------------|-----------------|
| Cer(d34:1)                | 1.00 $\pm$ 0.05 | 0.97 $\pm$ 0.05 | 2.42 $\pm$ 0.20 | 1.46 $\pm$ 0.10 |
| Cer(d40:1)                | 1.00 $\pm$ 0.09 | 0.98 $\pm$ 0.11 | 0.61 $\pm$ 0.04 | 0.67 $\pm$ 0.07 |
| Cer(d41:1)                | 1.00 $\pm$ 0.04 | 0.83 $\pm$ 0.05 | 2.51 $\pm$ 0.12 | 1.40 $\pm$ 0.09 |
| DG(34:1)                  | 1.00 $\pm$ 0.06 | 1.60 $\pm$ 0.30 | 0.57 $\pm$ 0.16 | 1.08 $\pm$ 0.28 |
| DG(34:3)                  | 1.00 $\pm$ 0.10 | 1.76 $\pm$ 0.52 | 0.28 $\pm$ 0.13 | 1.32 $\pm$ 0.35 |
| DG(36:4)                  | 1.00 $\pm$ 0.15 | 1.16 $\pm$ 0.33 | 0.45 $\pm$ 0.12 | 1.27 $\pm$ 0.28 |
| DG(40:7)                  | 1.00 $\pm$ 0.12 | 1.34 $\pm$ 0.32 | 0.54 $\pm$ 0.05 | 1.13 $\pm$ 0.22 |
| DG(40:8)                  | 1.00 $\pm$ 0.16 | 1.24 $\pm$ 0.33 | 0.30 $\pm$ 0.03 | 1.22 $\pm$ 0.23 |
| DG(51:0)                  | 1.00 $\pm$ 0.14 | 1.74 $\pm$ 0.51 | 0.35 $\pm$ 0.05 | 1.29 $\pm$ 0.26 |
| DG(53:3)                  | 1.00 $\pm$ 0.17 | 2.58 $\pm$ 1.61 | 0.43 $\pm$ 0.14 | 2.10 $\pm$ 0.99 |
| LPC(15:0)                 | 1.00 $\pm$ 0.06 | 1.10 $\pm$ 0.12 | 1.56 $\pm$ 0.13 | 1.15 $\pm$ 0.16 |
| LPC(16:1)                 | 1.00 $\pm$ 0.10 | 1.34 $\pm$ 0.11 | 0.67 $\pm$ 0.02 | 0.91 $\pm$ 0.07 |
| LPC(18:2)                 | 1.00 $\pm$ 0.07 | 1.05 $\pm$ 0.04 | 0.66 $\pm$ 0.03 | 0.94 $\pm$ 0.07 |
| LPC(18:3)                 | 1.00 $\pm$ 0.06 | 1.09 $\pm$ 0.06 | 0.78 $\pm$ 0.06 | 1.02 $\pm$ 0.10 |
| LPC(19:0)                 | 1.00 $\pm$ 0.12 | 1.13 $\pm$ 0.32 | 0.38 $\pm$ 0.07 | 0.84 $\pm$ 0.23 |
| LPC(20:4)                 | 1.00 $\pm$ 0.10 | 0.95 $\pm$ 0.09 | 0.71 $\pm$ 0.06 | 0.90 $\pm$ 0.09 |
| PE(37:3)                  | 1.00 $\pm$ 0.21 | 0.80 $\pm$ 0.34 | 2.97 $\pm$ 0.68 | 1.76 $\pm$ 0.78 |
| PE(38:1)                  | 1.00 $\pm$ 0.22 | 0.98 $\pm$ 0.37 | 0.20 $\pm$ 0.05 | 0.38 $\pm$ 0.13 |
| PE(40:4)                  | 1.00 $\pm$ 0.27 | 0.94 $\pm$ 0.52 | 0.19 $\pm$ 0.05 | 0.31 $\pm$ 0.13 |
| PE(40:6)                  | 1.00 $\pm$ 0.24 | 0.82 $\pm$ 0.32 | 4.43 $\pm$ 1.03 | 2.17 $\pm$ 0.94 |
| PE(46:1)                  | 1.00 $\pm$ 0.24 | 1.21 $\pm$ 0.24 | 0.39 $\pm$ 0.16 | 3.01 $\pm$ 2.05 |
| PE(48:2)                  | 1.00 $\pm$ 0.19 | 1.28 $\pm$ 0.27 | 0.53 $\pm$ 0.11 | 1.04 $\pm$ 0.36 |
| SM(d36:1)                 | 1.00 $\pm$ 0.15 | 1.02 $\pm$ 0.23 | 1.96 $\pm$ 0.22 | 2.23 $\pm$ 0.51 |
| SM(d36:4)                 | 1.00 $\pm$ 0.08 | 0.81 $\pm$ 0.12 | 1.90 $\pm$ 0.26 | 1.27 $\pm$ 0.12 |
| SM(d39:1)                 | 1.00 $\pm$ 0.10 | 0.76 $\pm$ 0.10 | 0.62 $\pm$ 0.05 | 0.63 $\pm$ 0.07 |
| SM(d40:1)                 | 1.00 $\pm$ 0.11 | 0.84 $\pm$ 0.14 | 0.42 $\pm$ 0.04 | 0.58 $\pm$ 0.08 |
| SM(d40:2)                 | 1.00 $\pm$ 0.09 | 0.88 $\pm$ 0.04 | 0.34 $\pm$ 0.05 | 0.53 $\pm$ 0.06 |
| SM(d41:2)                 | 1.00 $\pm$ 0.07 | 0.77 $\pm$ 0.07 | 0.72 $\pm$ 0.09 | 0.89 $\pm$ 0.06 |
| SM(d42:1)                 | 1.00 $\pm$ 0.08 | 0.77 $\pm$ 0.09 | 0.64 $\pm$ 0.07 | 0.77 $\pm$ 0.07 |
| SM(d42:4)                 | 1.00 $\pm$ 0.11 | 0.84 $\pm$ 0.12 | 0.43 $\pm$ 0.04 | 0.57 $\pm$ 0.08 |
| SM(d43:4)                 | 1.00 $\pm$ 0.08 | 0.69 $\pm$ 0.03 | 1.46 $\pm$ 0.14 | 1.16 $\pm$ 0.08 |
| SM(d44:4)                 | 1.00 $\pm$ 0.08 | 0.76 $\pm$ 0.10 | 0.66 $\pm$ 0.08 | 0.76 $\pm$ 0.07 |

| Normalized mean $\pm$ SEM | CON             | LFKO            | LIRKO           | LDKO            |
|---------------------------|-----------------|-----------------|-----------------|-----------------|
| PC(31:2)                  | 1.00 $\pm$ 0.10 | 1.19 $\pm$ 0.10 | 0.53 $\pm$ 0.05 | 0.84 $\pm$ 0.02 |
| PC(32:0)                  | 1.00 $\pm$ 0.07 | 0.85 $\pm$ 0.03 | 1.38 $\pm$ 0.10 | 1.30 $\pm$ 0.11 |
| PC(33:1)                  | 1.00 $\pm$ 0.06 | 1.22 $\pm$ 0.14 | 0.50 $\pm$ 0.07 | 0.74 $\pm$ 0.13 |
| PC(33:2)                  | 1.00 $\pm$ 0.07 | 0.98 $\pm$ 0.09 | 0.29 $\pm$ 0.08 | 0.69 $\pm$ 0.05 |
| PC(34:0)                  | 1.00 $\pm$ 0.07 | 0.90 $\pm$ 0.05 | 1.59 $\pm$ 0.13 | 1.38 $\pm$ 0.16 |
| PC(34:1)                  | 1.00 $\pm$ 0.06 | 0.98 $\pm$ 0.06 | 1.29 $\pm$ 0.06 | 1.09 $\pm$ 0.08 |
| PC(34:2)                  | 1.00 $\pm$ 0.07 | 0.89 $\pm$ 0.06 | 0.68 $\pm$ 0.04 | 0.90 $\pm$ 0.06 |
| PC(34:3)                  | 1.00 $\pm$ 0.07 | 1.04 $\pm$ 0.05 | 0.50 $\pm$ 0.04 | 0.76 $\pm$ 0.05 |
| PC(34:3)                  | 1.00 $\pm$ 0.08 | 0.90 $\pm$ 0.05 | 0.55 $\pm$ 0.03 | 0.82 $\pm$ 0.04 |
| PC(35:1)                  | 1.00 $\pm$ 0.10 | 0.92 $\pm$ 0.09 | 1.32 $\pm$ 0.10 | 1.14 $\pm$ 0.08 |
| PC(35:2)                  | 1.00 $\pm$ 0.11 | 0.62 $\pm$ 0.07 | 0.51 $\pm$ 0.16 | 1.03 $\pm$ 0.04 |
| PC(35:3)                  | 1.00 $\pm$ 0.07 | 1.00 $\pm$ 0.06 | 0.36 $\pm$ 0.05 | 0.64 $\pm$ 0.06 |
| PC(35:4)                  | 1.00 $\pm$ 0.08 | 0.87 $\pm$ 0.09 | 0.35 $\pm$ 0.02 | 0.73 $\pm$ 0.10 |
| PC(36:1)                  | 1.00 $\pm$ 0.06 | 0.96 $\pm$ 0.04 | 1.53 $\pm$ 0.11 | 1.16 $\pm$ 0.06 |
| PC(36:4)                  | 1.00 $\pm$ 0.08 | 0.79 $\pm$ 0.03 | 0.63 $\pm$ 0.03 | 0.85 $\pm$ 0.07 |
| PC(36:4)                  | 1.00 $\pm$ 0.06 | 0.98 $\pm$ 0.07 | 1.35 $\pm$ 0.08 | 1.14 $\pm$ 0.11 |
| PC(36:4)                  | 1.00 $\pm$ 0.13 | 0.92 $\pm$ 0.10 | 1.45 $\pm$ 0.08 | 1.58 $\pm$ 0.08 |
| PC(36:5)                  | 1.00 $\pm$ 0.05 | 0.94 $\pm$ 0.05 | 0.66 $\pm$ 0.05 | 0.91 $\pm$ 0.06 |
| PC(37:2)                  | 1.00 $\pm$ 0.11 | 0.89 $\pm$ 0.14 | 0.41 $\pm$ 0.11 | 0.65 $\pm$ 0.17 |
| PC(37:3)                  | 1.00 $\pm$ 0.07 | 0.86 $\pm$ 0.08 | 0.66 $\pm$ 0.06 | 0.85 $\pm$ 0.09 |
| PC(37:4)                  | 1.00 $\pm$ 0.16 | 0.59 $\pm$ 0.11 | 0.29 $\pm$ 0.09 | 0.72 $\pm$ 0.15 |
| PC(37:6)                  | 1.00 $\pm$ 0.11 | 0.78 $\pm$ 0.11 | 0.60 $\pm$ 0.10 | 0.55 $\pm$ 0.13 |
| PC(38:2)                  | 1.00 $\pm$ 0.10 | 0.91 $\pm$ 0.10 | 0.37 $\pm$ 0.07 | 0.47 $\pm$ 0.04 |
| PC(38:4)                  | 1.00 $\pm$ 0.07 | 0.87 $\pm$ 0.05 | 1.23 $\pm$ 0.08 | 1.01 $\pm$ 0.04 |
| PC(38:4)                  | 1.00 $\pm$ 0.11 | 0.85 $\pm$ 0.04 | 1.85 $\pm$ 0.11 | 1.50 $\pm$ 0.08 |
| PC(38:4)                  | 1.00 $\pm$ 0.06 | 0.83 $\pm$ 0.08 | 1.37 $\pm$ 0.09 | 1.32 $\pm$ 0.11 |
| PC(38:5)                  | 1.00 $\pm$ 0.12 | 0.68 $\pm$ 0.06 | 0.64 $\pm$ 0.04 | 0.71 $\pm$ 0.05 |
| PC(38:7)                  | 1.00 $\pm$ 0.09 | 0.82 $\pm$ 0.11 | 0.59 $\pm$ 0.04 | 0.70 $\pm$ 0.08 |
| PC(38:8)                  | 1.00 $\pm$ 0.11 | 0.83 $\pm$ 0.23 | 0.36 $\pm$ 0.08 | 0.59 $\pm$ 0.20 |
| PC(39:4)                  | 1.00 $\pm$ 0.10 | 0.86 $\pm$ 0.16 | 0.34 $\pm$ 0.10 | 0.83 $\pm$ 0.24 |
| PC(39:7)                  | 1.00 $\pm$ 0.11 | 0.79 $\pm$ 0.15 | 0.46 $\pm$ 0.03 | 0.52 $\pm$ 0.11 |
| PC(40:4)                  | 1.00 $\pm$ 0.12 | 1.14 $\pm$ 0.35 | 0.54 $\pm$ 0.11 | 0.64 $\pm$ 0.11 |
| PC(40:6)                  | 1.00 $\pm$ 0.10 | 0.69 $\pm$ 0.04 | 1.40 $\pm$ 0.14 | 0.95 $\pm$ 0.06 |
| PC(40:8)                  | 1.00 $\pm$ 0.10 | 0.73 $\pm$ 0.09 | 0.60 $\pm$ 0.05 | 0.59 $\pm$ 0.12 |
| PC(41:6)                  | 1.00 $\pm$ 0.13 | 0.75 $\pm$ 0.10 | 0.37 $\pm$ 0.14 | 0.58 $\pm$ 0.15 |
| PC(42:10)                 | 1.00 $\pm$ 0.20 | 0.66 $\pm$ 0.13 | 0.48 $\pm$ 0.10 | 0.46 $\pm$ 0.15 |
| PC(42:6)                  | 1.00 $\pm$ 0.09 | 0.63 $\pm$ 0.16 | 0.07 $\pm$ 0.00 | 0.25 $\pm$ 0.06 |
| PC(42:7)                  | 1.00 $\pm$ 0.13 | 0.83 $\pm$ 0.25 | 0.31 $\pm$ 0.03 | 0.50 $\pm$ 0.09 |

| Normalized mean $\pm$ SEM | CON             | LFKO            | LIRKO           | LDKO            |
|---------------------------|-----------------|-----------------|-----------------|-----------------|
| TG(40:0)                  | 1.00 $\pm$ 0.17 | 1.82 $\pm$ 0.40 | 0.53 $\pm$ 0.11 | 0.89 $\pm$ 0.20 |
| TG(46:9)                  | 1.00 $\pm$ 0.08 | 1.19 $\pm$ 0.11 | 0.67 $\pm$ 0.10 | 1.05 $\pm$ 0.06 |
| TG(51:4)                  | 1.00 $\pm$ 0.14 | 2.27 $\pm$ 0.49 | 0.50 $\pm$ 0.07 | 0.75 $\pm$ 0.08 |
| TG(52:1)                  | 1.00 $\pm$ 0.12 | 1.71 $\pm$ 0.55 | 3.27 $\pm$ 0.65 | 3.30 $\pm$ 0.21 |
| TG(52:4)                  | 1.00 $\pm$ 0.08 | 1.60 $\pm$ 0.46 | 1.64 $\pm$ 0.22 | 2.08 $\pm$ 0.28 |
| TG(52:5)                  | 1.00 $\pm$ 0.09 | 2.43 $\pm$ 1.08 | 0.42 $\pm$ 0.09 | 1.48 $\pm$ 0.26 |
| TG(52:6)                  | 1.00 $\pm$ 0.10 | 2.15 $\pm$ 0.51 | 0.68 $\pm$ 0.09 | 1.70 $\pm$ 0.42 |
| TG(52:7)                  | 1.00 $\pm$ 0.14 | 2.11 $\pm$ 0.92 | 0.34 $\pm$ 0.12 | 2.18 $\pm$ 0.81 |
| TG(54:2)                  | 1.00 $\pm$ 0.09 | 2.18 $\pm$ 0.97 | 2.26 $\pm$ 0.38 | 2.38 $\pm$ 0.33 |
| TG(54:4)                  | 1.00 $\pm$ 0.10 | 2.52 $\pm$ 1.30 | 1.61 $\pm$ 0.22 | 1.95 $\pm$ 0.24 |
| TG(54:6)                  | 1.00 $\pm$ 0.08 | 1.61 $\pm$ 0.19 | 0.72 $\pm$ 0.08 | 1.22 $\pm$ 0.14 |
| TG(54:6)                  | 1.00 $\pm$ 0.12 | 1.83 $\pm$ 0.76 | 0.44 $\pm$ 0.05 | 1.88 $\pm$ 0.49 |
| TG(54:6)                  | 1.00 $\pm$ 0.11 | 3.06 $\pm$ 1.22 | 0.67 $\pm$ 0.08 | 1.17 $\pm$ 0.18 |
| TG(54:7)                  | 1.00 $\pm$ 0.18 | 2.56 $\pm$ 0.88 | 0.43 $\pm$ 0.07 | 0.97 $\pm$ 0.21 |
| TG(54:8)                  | 1.00 $\pm$ 0.11 | 2.29 $\pm$ 0.69 | 0.51 $\pm$ 0.06 | 1.37 $\pm$ 0.19 |
| TG(54:8)                  | 1.00 $\pm$ 0.13 | 1.66 $\pm$ 0.69 | 0.48 $\pm$ 0.08 | 1.14 $\pm$ 0.23 |
| TG(55:2)                  | 1.00 $\pm$ 0.14 | 1.98 $\pm$ 1.00 | 0.66 $\pm$ 0.06 | 1.52 $\pm$ 0.29 |
| TG(55:3)                  | 1.00 $\pm$ 0.30 | 1.97 $\pm$ 0.23 | 0.18 $\pm$ 0.12 | 0.53 $\pm$ 0.29 |
| TG(55:6)                  | 1.00 $\pm$ 0.23 | 0.54 $\pm$ 0.21 | 0.36 $\pm$ 0.13 | 1.26 $\pm$ 0.45 |
| TG(55:8)                  | 1.00 $\pm$ 0.16 | 1.73 $\pm$ 0.43 | 0.19 $\pm$ 0.05 | 0.89 $\pm$ 0.16 |
| TG(56:10)                 | 1.00 $\pm$ 0.15 | 1.91 $\pm$ 0.89 | 0.44 $\pm$ 0.07 | 1.25 $\pm$ 0.30 |
| TG(56:2)                  | 1.00 $\pm$ 0.10 | 1.98 $\pm$ 0.44 | 0.64 $\pm$ 0.10 | 0.92 $\pm$ 0.10 |
| TG(56:5)                  | 1.00 $\pm$ 0.11 | 1.93 $\pm$ 0.60 | 0.60 $\pm$ 0.07 | 1.52 $\pm$ 0.20 |
| TG(56:6)                  | 1.00 $\pm$ 0.14 | 2.05 $\pm$ 0.81 | 0.65 $\pm$ 0.06 | 1.31 $\pm$ 0.31 |
| TG(56:7)                  | 1.00 $\pm$ 0.13 | 1.71 $\pm$ 0.53 | 0.43 $\pm$ 0.07 | 1.30 $\pm$ 0.20 |
| TG(56:9)                  | 1.00 $\pm$ 0.13 | 1.76 $\pm$ 0.50 | 0.48 $\pm$ 0.10 | 1.56 $\pm$ 0.29 |
| TG(56:9)                  | 1.00 $\pm$ 0.12 | 2.06 $\pm$ 0.56 | 0.55 $\pm$ 0.07 | 1.18 $\pm$ 0.22 |
| TG(56:9)                  | 1.00 $\pm$ 0.25 | 1.05 $\pm$ 0.36 | 0.33 $\pm$ 0.06 | 0.87 $\pm$ 0.23 |
| TG(57:8)                  | 1.00 $\pm$ 0.12 | 2.09 $\pm$ 0.98 | 0.29 $\pm$ 0.05 | 1.05 $\pm$ 0.21 |
| TG(58:10)                 | 1.00 $\pm$ 0.16 | 1.29 $\pm$ 0.25 | 0.36 $\pm$ 0.04 | 1.65 $\pm$ 0.25 |
| TG(58:11)                 | 1.00 $\pm$ 0.23 | 1.46 $\pm$ 0.62 | 0.35 $\pm$ 0.07 | 1.51 $\pm$ 0.45 |
| TG(58:12)                 | 1.00 $\pm$ 0.15 | 1.76 $\pm$ 0.77 | 0.27 $\pm$ 0.04 | 0.77 $\pm$ 0.17 |
| TG(58:3)                  | 1.00 $\pm$ 0.15 | 2.18 $\pm$ 0.76 | 0.59 $\pm$ 0.12 | 0.84 $\pm$ 0.18 |
| TG(58:6)                  | 1.00 $\pm$ 0.14 | 2.62 $\pm$ 0.88 | 0.57 $\pm$ 0.12 | 0.87 $\pm$ 0.10 |
| TG(58:7)                  | 1.00 $\pm$ 0.12 | 1.94 $\pm$ 0.65 | 0.68 $\pm$ 0.06 | 1.89 $\pm$ 0.42 |
| TG(58:7)                  | 1.00 $\pm$ 0.11 | 1.51 $\pm$ 0.38 | 2.00 $\pm$ 0.07 | 2.31 $\pm$ 0.31 |
| TG(58:8)                  | 1.00 $\pm$ 0.09 | 1.34 $\pm$ 0.15 | 1.63 $\pm$ 0.10 | 1.51 $\pm$ 0.13 |
| TG(58:8)                  | 1.00 $\pm$ 0.19 | 1.68 $\pm$ 0.72 | 0.50 $\pm$ 0.07 | 1.64 $\pm$ 0.39 |
| TG(58:9)                  | 1.00 $\pm$ 0.17 | 1.94 $\pm$ 0.56 | 0.30 $\pm$ 0.02 | 1.35 $\pm$ 0.24 |
| TG(58:9)                  | 1.00 $\pm$ 0.16 | 1.76 $\pm$ 0.66 | 0.40 $\pm$ 0.11 | 1.93 $\pm$ 0.29 |
| TG(60:11)                 | 1.00 $\pm$ 0.11 | 1.55 $\pm$ 0.29 | 0.58 $\pm$ 0.05 | 1.54 $\pm$ 0.22 |
| TG(60:12)                 | 1.00 $\pm$ 0.20 | 1.06 $\pm$ 0.46 | 1.82 $\pm$ 0.27 | 1.75 $\pm$ 0.29 |
| TG(62:16)                 | 1.00 $\pm$ 0.25 | 1.15 $\pm$ 0.43 | 0.34 $\pm$ 0.08 | 1.29 $\pm$ 0.41 |



**Supplemental Table 2. Changes in lipid species abundance in LIRKO, LDKO, and LFKO versus control livers.** Fold changes for each lipid species in LIRKO, LDKO, and LFKO livers relative to controls (8-10 weeks old male mice). Only species that were significantly different in LIRKO versus controls are shown ( $p < 0.05$ ). Species that are also significantly different in LFKO or LDKO versus controls are highlighted in red;  $n=5-15$ . Cer – Ceramide; LPC – Lysophosphatidylcholine; PC – Phosphatidylcholine; PE – Phosphatidylethanolamine; SM – Sphingomyelin; TG – Triglyceride; DG – Diglyceride.