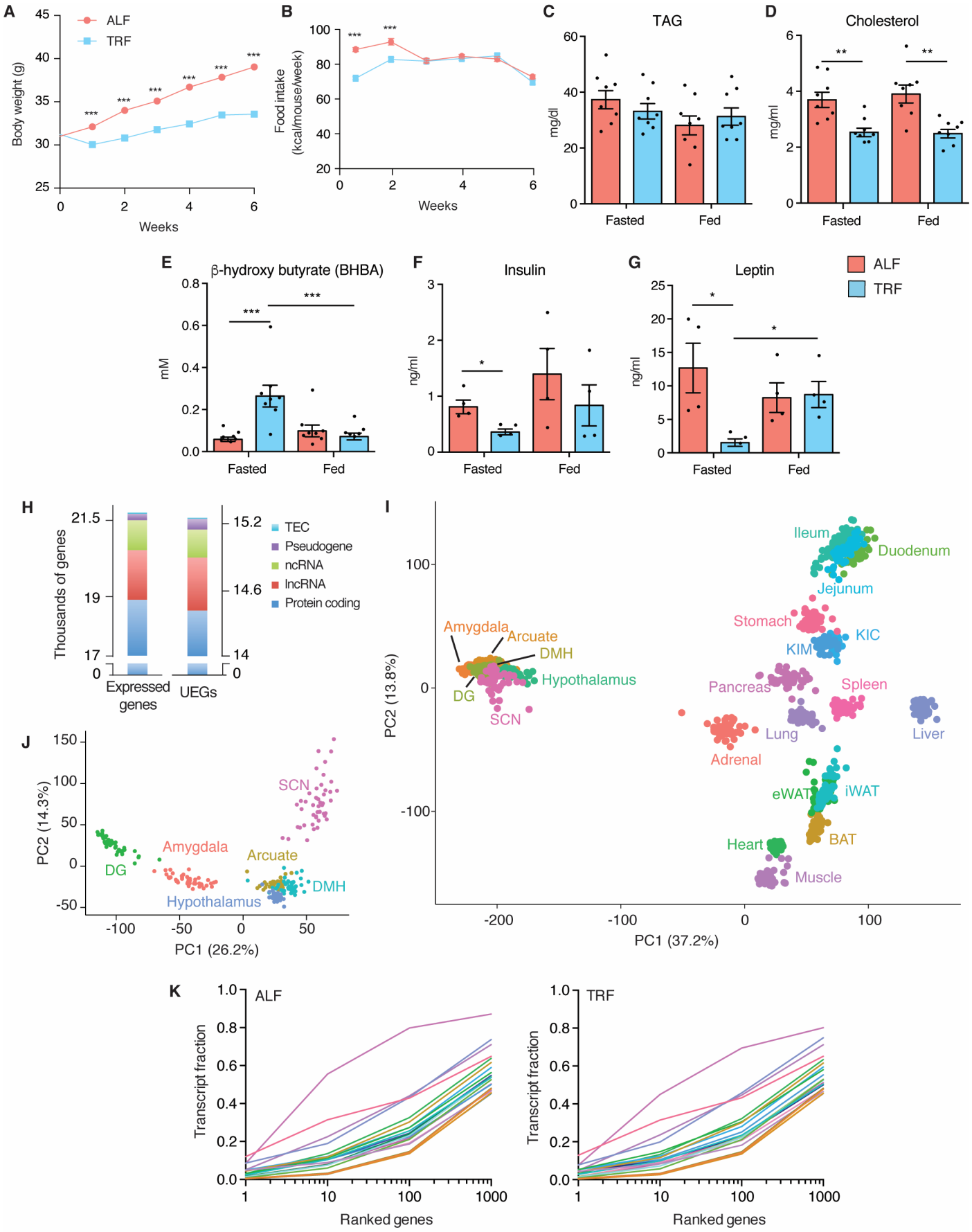
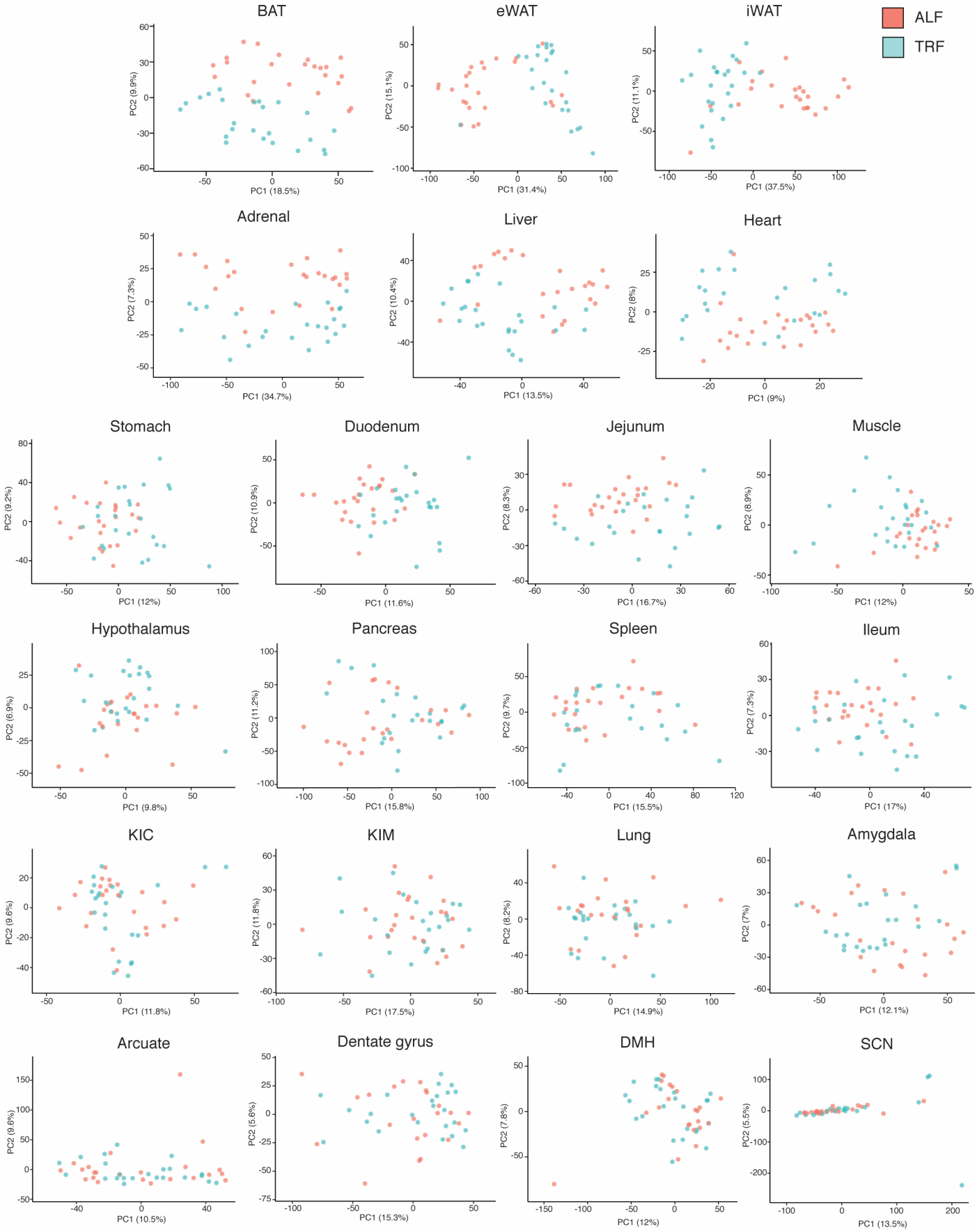
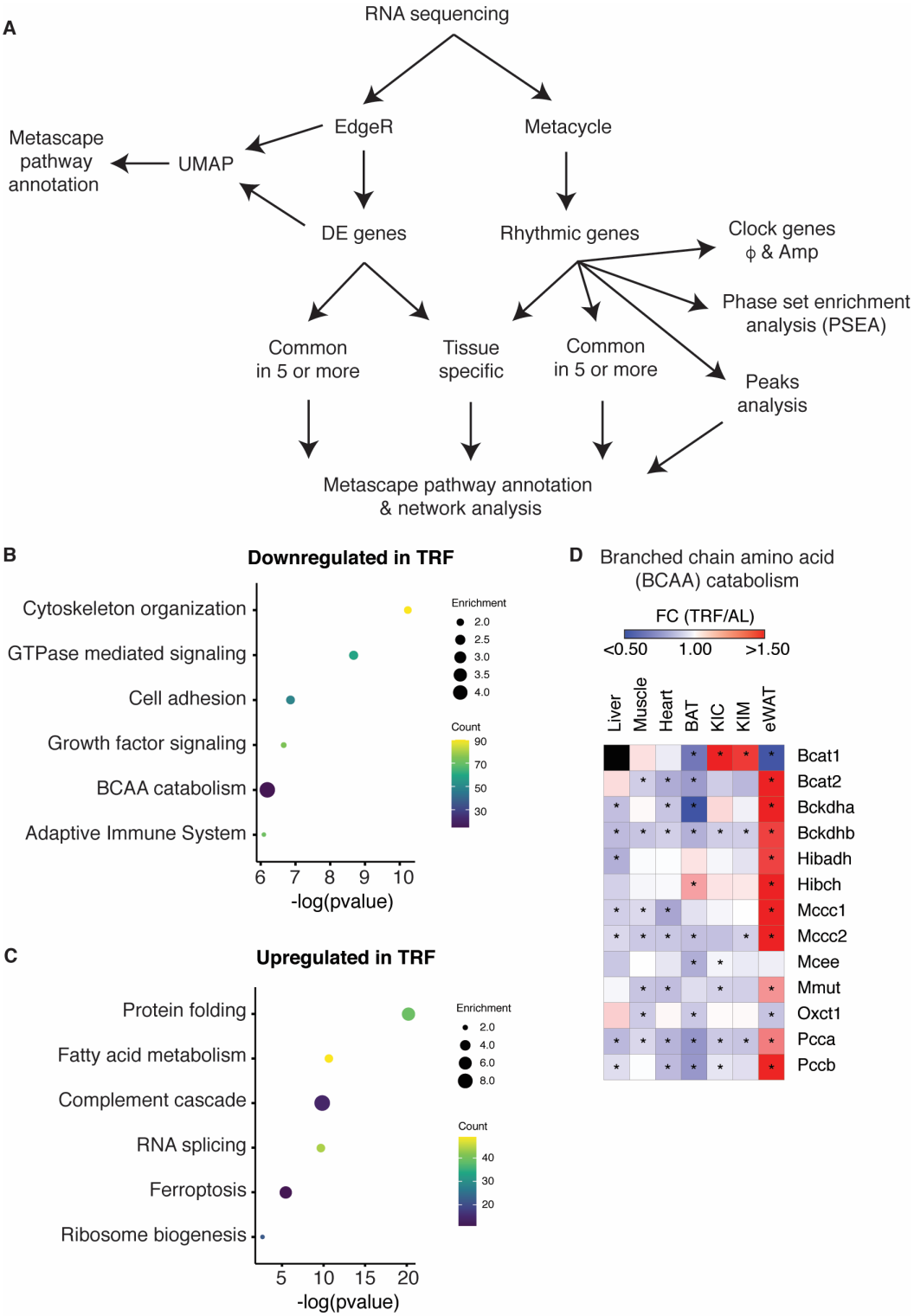


Supplementary figure 1. Effect of short term TRF on physiology and gene expression. Related to Figure 1. (A, B) Evolution of (A) Body weight and (B) Weekly food consumption during the TRF intervention period is shown. (C-G) Serum analysis of the indicated metabolites (C-E) and hormones (F, G) in the subjective fasted (ZT10-ZT12) and fed (ZT18-ZT20) phases in ALF or TRF paradigm. (H) Number of genes expressed in at least one of the 22 tissues

(21,791, left) or present in all the tissues sampled – Ubiquitously expressed genes (UEG) (15,253, right). (I) Principal component analysis performed on the 12 time points of ALF and TRF samples from 22 tissues shows clustering of similar tissues based on gene expression profiles. The 6 brain tissues are clustered very tightly apart from the peripheral organs. (J) Principal component analysis performed on the 12 time points of ALF and TRF samples from 6 brain tissues shows clustering of similar region tissues Arcuate, DMH and hypothalamus, while Amygdala, DG and SCN cluster separately. (K) Cumulative distribution of the average fraction of total transcriptome contributed by genes when sorted from most to least expressed in each tissue (x-axis). Each tissue is color-coded as represented in (I).

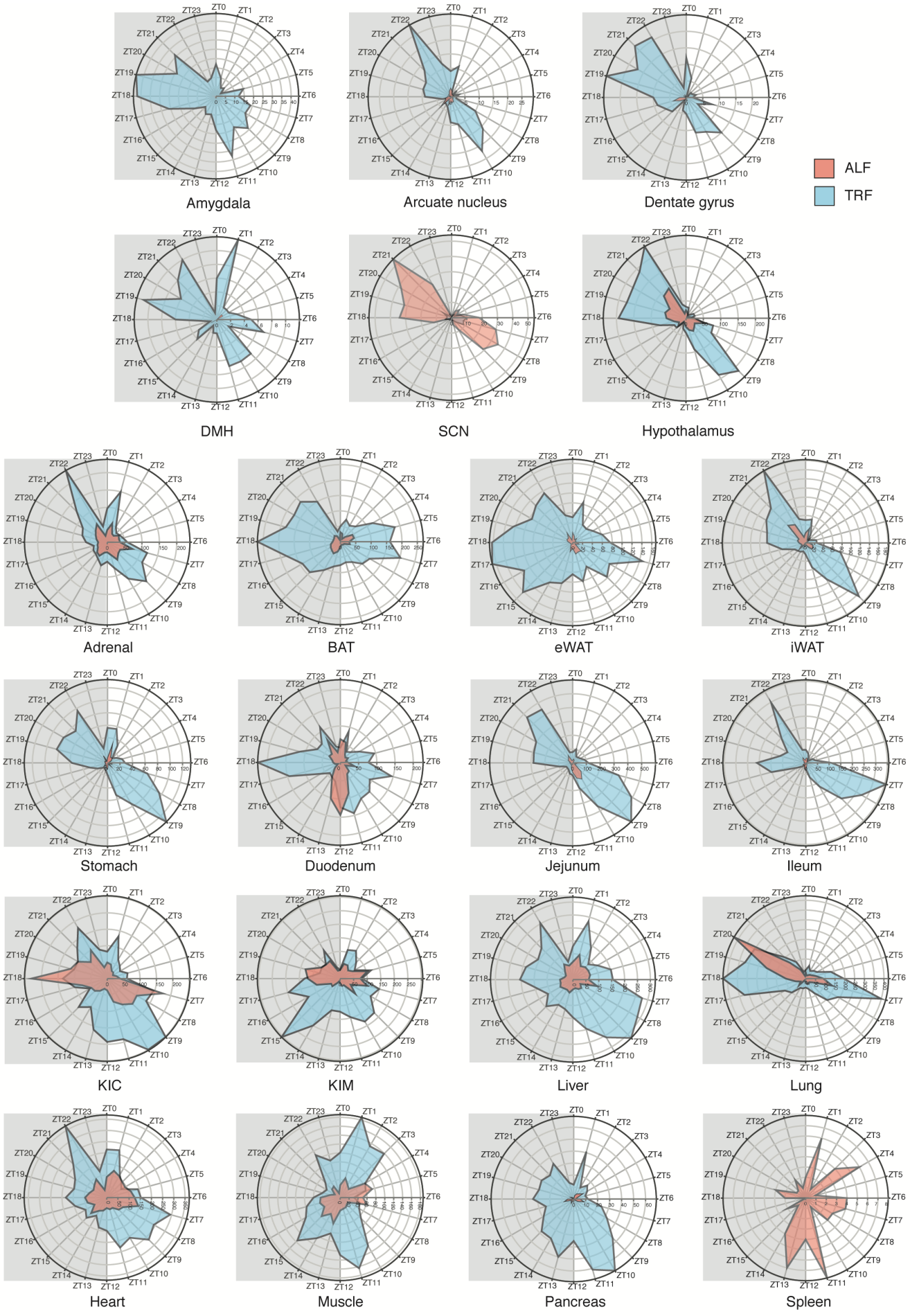


Supplementary figure 2. TRF leads to a tissue-specific transcriptional response. Related to Figures 1 and 2. Principal component analysis performed on the 12 time points of indicated 22 tissues shows tissue specific clustering or separation of ALF and TRF samples.

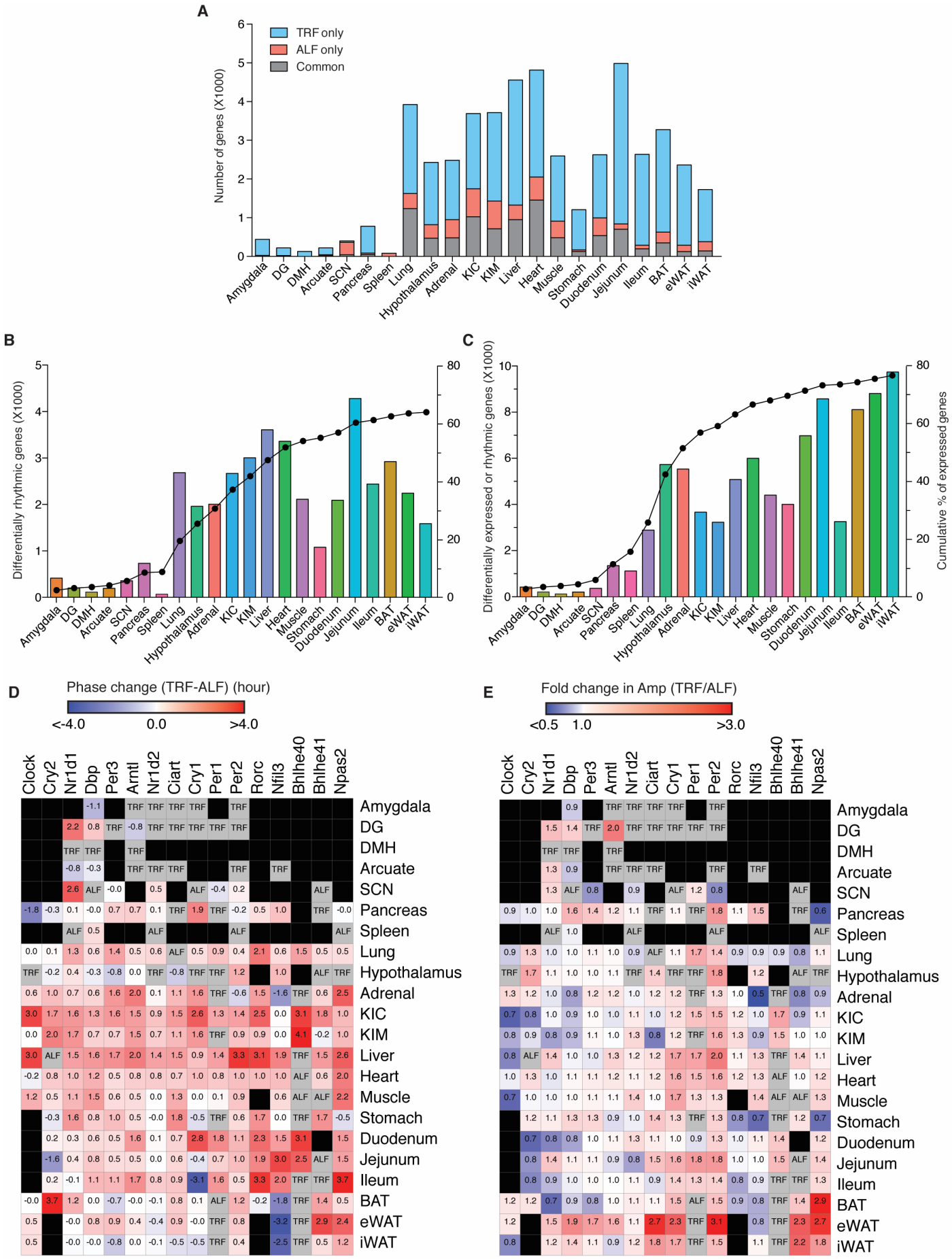


Supplementary figure 3. TRF leads to both tissue-specific and multi-tissue responses. Related to Figure 2. (A) Flow chart depicting the different analyses performed in this article. (B, C) Overrepresentation analysis using KEGG pathway and GO BP for common differentially expressed genes in 5 or more tissues that are (B) Downregulated in TRF or (C) Upregulated in TRF. (D) Heatmap of fold change (FC-TRF/AL) in expression of genes involved in branched chain amino acid (BCAA) catabolism in the indicated tissues. Genes not detected in a particular tissue are indicated in black.

Statistics: * indicates P<0.05 using multiple t-test comparison.

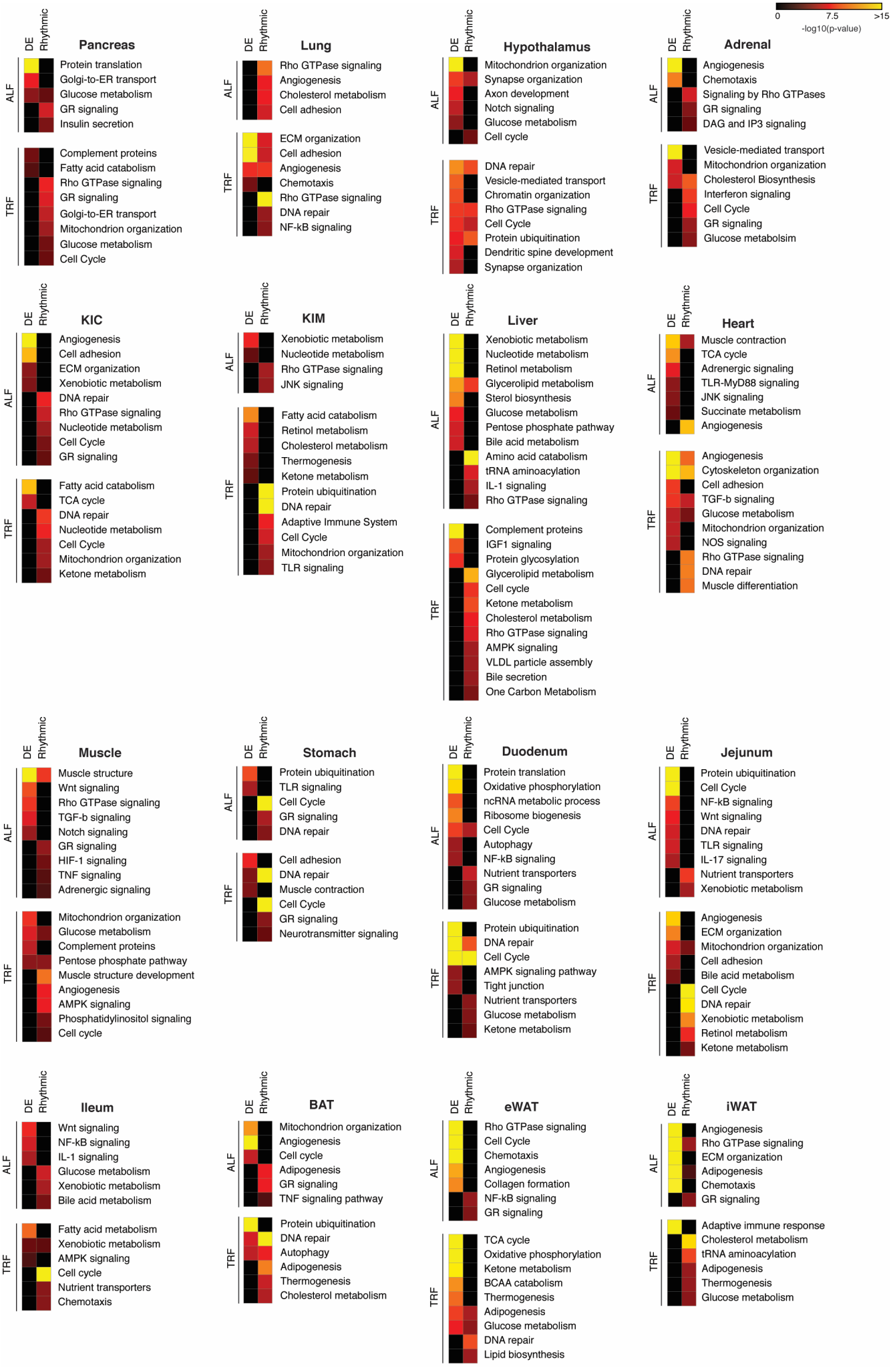


Supplementary figure 4. Phase plots for all rhythmic genes in ALF and TRF in each tissue. Related to Figure 3. Radial plots of the distribution of peak phases of expression of significant cycling genes in ALF or TRF paradigm in each tissue. Gray indicates dark phase (ZT12-ZT24/ZT0), and the number of cycling genes are listed in black.

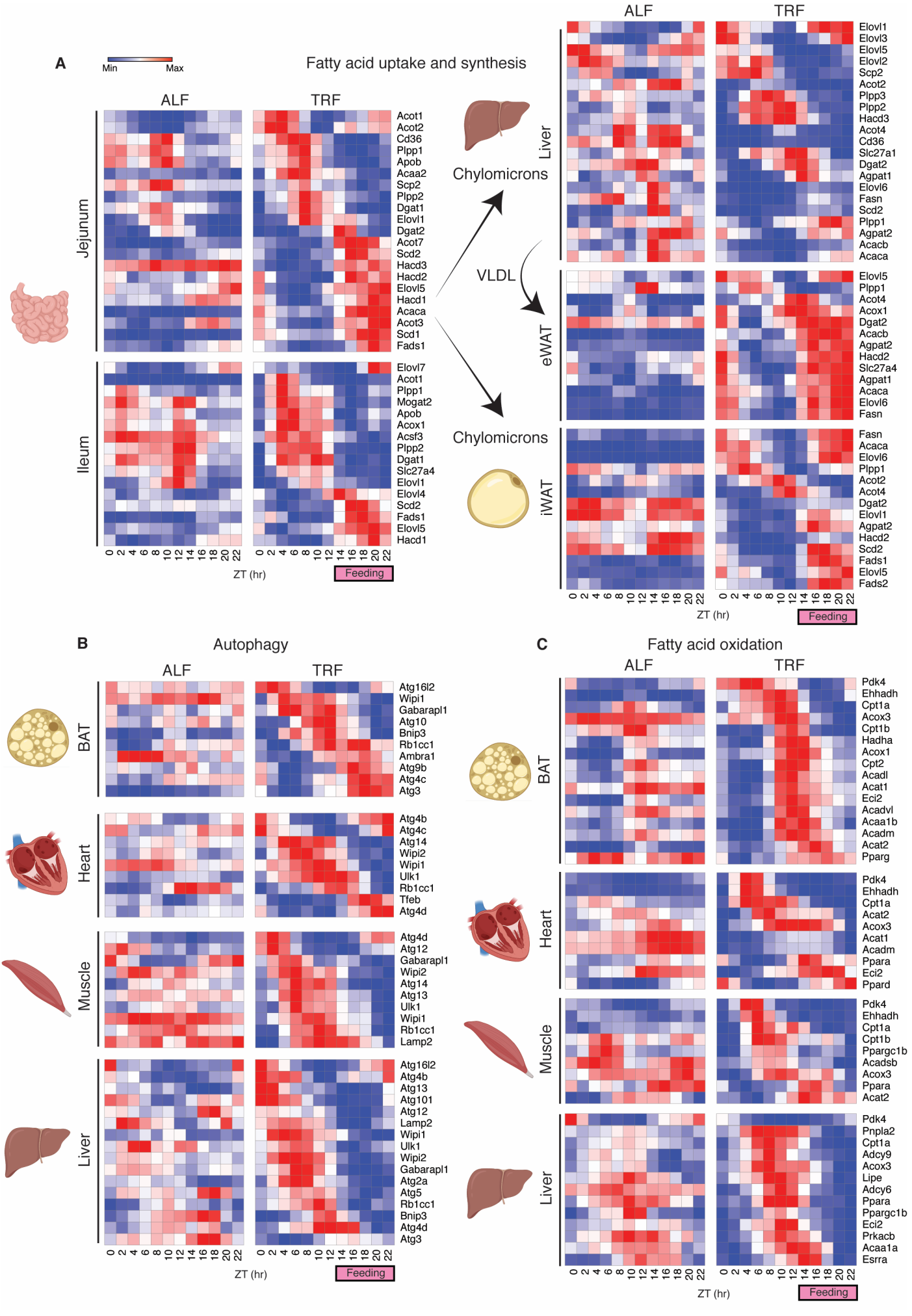


Supplementary figure 5. TRF leads to tissue-specific changes in rhythmic genes. Related to Figures 4 and 6. (A) Stacked bar plot indicating the number of common rhythmic genes, genes rhythmic only in ALF condition and genes rhythmic only in TRF condition in each tissue. (B) Number of differentially rhythmic (DR) genes per tissue (bar) and

their cumulative contribution to the total percent of DR genes (line). (C) Number of differentially expressed (DE) or differentially rhythmic (DR) genes per tissue (bar) and their cumulative contribution to the total percent of DE+DR genes (line). (D) Phase change (TRF-AL) in the peak phase of expression (in hour) of clock genes in the tissues where they are detected as cycling in ALF and TRF. Genes detected as cycling in only ALF or TRF are indicated in grey and genes not detected as significantly cycling in a particular tissue are indicated in black. Positive phase change indicates phase delay and negative phase change indicates phase advance under TRF. (E) Fold change (FC-TRF/AL) in the amplitudes of clock genes in the tissues where they are detected as cycling in ALF and TRF. Genes detected as cycling in only ALF or TRF are indicated in grey and genes not detected as significantly cycling in a particular tissue are indicated in black.


0
7.5
>15
-log10(p-value)
Pancreas
DE
Rhythmic
ALF
Protein translation
Golgi-to-ER transport
Glucose metabolism
GR signaling
Insulin secretion
TRF
Complement proteins
Fatty acid catabolism
Rho GTPase signaling
GR signaling
Golgi-to-ER transport
Mitochondrion organization
Glucose metabolism
Cell Cycle
Lung
ALF
Rho GTPase signaling
Angiogenesis
Cholesterol metabolism
Cell adhesion
TRF
ECM organization
Cell adhesion
Angiogenesis
Chemotaxis
Rho GTPase signaling
DNA repair
NF-kB signaling
Hypothalamus
ALF
Mitochondrion organization
Synapse organization
Axon development
Notch signaling
Glucose metabolism
Cell cycle
TRF
DNA repair
Vesicle-mediated transport
Chromatin organization
Rho GTPase signaling
Cell Cycle
Protein ubiquitination
Dendritic spine development
Synapse organization
Adrenal
ALF
Angiogenesis
Chemotaxis
Signaling by Rho GTPases
GR signaling
DAG and IP3 signaling
TRF
Vesicle-mediated transport
Mitochondrion organization
Cholesterol Biosynthesis
Interferon signaling
Cell Cycle
GR signaling
Glucose metabolsim
KIC
ALF
Angiogenesis
Cell adhesion
ECM organization
Xenobiotic metabolism
DNA repair
Rho GTPase signaling
Nucleotide metabolism
Cell Cycle
GR signaling
TRF
Fatty acid catabolism
TCA cycle
DNA repair
Nucleotide metabolism
Cell Cycle
Mitochondrion organization
Ketone metabolism
KIM
ALF
Xenobiotic metabolism
Nucleotide metabolism
Rho GTPase signaling
JNK signaling
TRF
Fatty acid catabolism
Retinol metabolism
Cholesterol metabolism
Thermogenesis
Ketone metabolism
Protein ubiquitination
DNA repair
Adaptive Immune System
Cell Cycle
Mitochondrion organization
TLR signaling
Liver
ALF
Xenobiotic metabolism
Nucleotide metabolism
Retinol metabolism
Glycerolipid metabolism
Sterol biosynthesis
Glucose metabolism
Pentose phosphate pathway
Bile acid metabolism
Amino acid catabolism
tRNA aminoacylation
IL-1 signaling
Rho GTPase signaling
TRF
Complement proteins
IGF1 signaling
Protein glycosylation
Glycerolipid metabolism
Cell cycle
Ketone metabolism
Cholesterol metabolism
Rho GTPase signaling
AMPK signaling
VLDL particle assembly
Bile secretion
One Carbon Metabolism
Heart
ALF
Muscle contraction
TCA cycle
Adrenergic signaling
TLR-MyD88 signaling
JNK signaling
Succinate metabolism
Angiogenesis
TRF
Angiogenesis
Cytoskeleton organization
Cell adhesion
TGF-b signaling
Glucose metabolism
Mitochondrion organization
NOS signaling
Rho GTPase signaling
DNA repair
Muscle differentiation
Muscle
ALF
Muscle structure
Wnt signaling
Rho GTPase signaling
TGF-b signaling
Notch signaling
GR signaling
HIF-1 signaling
TNF signaling
Adrenergic signaling
TRF
Mitochondrion organization
Glucose metabolism
Complement proteins
Pentose phosphate pathway
Muscle structure development
Angiogenesis
AMPK signaling
Phosphatidylinositol signaling
Cell cycle
Stomach
ALF
Protein ubiquitination
TLR signaling
Cell Cycle
GR signaling
DNA repair
TRF
Cell adhesion
DNA repair
Muscle contraction
Cell Cycle
GR signaling
Neurotransmitter signaling
Duodenum
ALF
Protein translation
Oxidative phosphorylation
ncRNA metabolic process
Ribosome biogenesis
Cell Cycle
Autophagy
NF-kB signaling
Nutrient transporters
GR signaling
Glucose metabolism
TRF
Protein ubiquitination
DNA repair
Cell Cycle
AMPK signaling pathway
Tight junction
Nutrient transporters
Glucose metabolism
Ketone metabolism
Jejunum
ALF
Protein ubiquitination
Cell Cycle
NF-kB signaling
Wnt signaling
DNA repair
TLR signaling
IL-17 signaling
Nutrient transporters
Xenobiotic metabolism
TRF
Angiogenesis
ECM organization
Mitochondrion organization
Cell adhesion
Bile acid metabolism
Cell Cycle
DNA repair
Xenobiotic metabolism
Retinol metabolism
Ketone metabolism
Ileum
ALF
Wnt signaling
NF-kB signaling
IL-1 signaling
Glucose metabolism
Xenobiotic metabolism
Bile acid metabolism
TRF
Fatty acid metabolism
Xenobiotic metabolism
AMPK signaling
Cell cycle
Nutrient transporters
Chemotaxis
BAT
ALF
Mitochondrion organization
Angiogenesis
Cell cycle
Adipogenesis
GR signaling
TNF signaling pathway
TRF
Protein ubiquitination
DNA repair
Autophagy
Adipogenesis
Thermogenesis
Cholesterol metabolism
eWAT
ALF
Rho GTPase signaling
Cell Cycle
Chemotaxis
Angiogenesis
Collagen formation
NF-kB signaling
GR signaling
TRF
TCA cycle
Oxidative phosphorylation
Ketone metabolism
BCAA catabolism
Thermogenesis
Adipogenesis
Glucose metabolism
DNA repair
Lipid biosynthesis
iWAT
ALF
Angiogenesis
Rho GTPase signaling
ECM organization
Adipogenesis
Chemotaxis
GR signaling
TRF
Adaptive immune response
Cholesterol metabolism
tRNA aminoacylation
Adipogenesis
Thermogenesis
Glucose metabolism

Supplementary figure 6. Tissue-specific pathways changing in expression or rhythmicity upon TRF intervention. Related to Figures 2 and 4. Heatmaps of tissue specific Metascape annotated pathways for genes upregulated or rhythmic in ALF or TRF are shown. Pathways significantly enriched by overrepresentation analysis (ORA) ($P<0.05$) and not already represented in Fig. 2D and Fig. 4C are indicated here. Insignificantly enriched pathways are represented in black.


A
Min
Max
Fatty acid uptake and synthesis
ALF
TRF
Jejunum
Acot1
Acot2
Cd36
Plpp1
Apob
Acaa2
Scp2
Plpp2
Dgat1
Elovl1
Dgat2
Acot7
Scd2
Hacd3
Hacd2
Elovl5
Hacd1
Acaca
Acot3
Scd1
Fads1
Ileum
Elovl7
Acot1
Plpp1
Mogat2
Apob
Acox1
Acsf3
Plpp2
Dgat1
Slc27a4
Elovl1
Elovl4
Scd2
Fads1
Elovl5
Hacd1
ZT (hr)
Feeding
Chylomicrons
VLDL
Chylomicrons
Liver
Elovl1
Elovl3
Elovl5
Elovl2
Scp2
Acot2
Plpp3
Plpp2
Hacd3
Acot4
Cd36
Slc27a1
Dgat2
Agpat1
Elovl6
Fasn
Scd2
Plpp1
Agpat2
Acacb
Acaca
eWAT
Elovl5
Plpp1
Acot4
Acox1
Dgat2
Acacb
Agpat2
Hacd2
Slc27a4
Agpat1
Acaca
Elovl6
Fasn
iWAT
Fasn
Acaca
Elovl6
Plpp1
Acot2
Acot4
Dgat2
Elovl1
Agpat2
Hacd2
Scd2
Fads1
Elovl5
Fads2
B
Autophagy
BAT
Atg16l2
Wipi1
Gabarapl1
Atg10
Bnip3
Rb1cc1
Ambra1
Atg9b
Atg4c
Atg3
Heart
Atg4b
Atg4c
Atg14
Wipi2
Wipi1
Ulk1
Rb1cc1
Tfeb
Atg4d
Muscle
Atg4d
Atg12
Gabarapl1
Wipi2
Atg14
Atg13
Ulk1
Wipi1
Rb1cc1
Lamp2
Liver
Atg16l2
Atg4b
Atg13
Atg101
Atg12
Lamp2
Wipi1
Ulk1
Wipi2
Gabarapl1
Atg2a
Atg5
Rb1cc1
Bnip3
Atg4d
Atg3
C
Fatty acid oxidation
BAT
Pdk4
Ehhadh
Cpt1a
Acox3
Cpt1b
Hadha
Acox1
Cpt2
Acadl
Acat1
Eci2
Acadvl
Acaa1b
Acadm
Acat2
Pparg
Heart
Pdk4
Ehhadh
Cpt1a
Acat2
Acox3
Acat1
Acadm
Ppara
Eci2
Ppard
Muscle
Pdk4
Ehhadh
Cpt1a
Cpt1b
Ppargc1b
Acadsb
Acox3
Ppara
Acat2
Liver
Pdk4
Pnpla2
Cpt1a
Adcy9
Acox3
Lipe
Adcy6
Ppara
Ppargc1b
Eci2
Prkacb
Acaa1a
Esrra

Supplementary figure 7. TRF increases the expression and rhythmicity of genes involved in autophagy and fatty acid metabolism. Related to Figures 4 and 7. (A-C) Heatmap of relative expression of genes involved in (A) Fatty acid uptake and synthesis, (B) Autophagy and (C) Fatty acid oxidation that are significantly cycling in TRF (FDR<0.05) in the indicated tissues and represented as a running average (k=2) across 12 time points. The TRF feeding window from ZT13-ZT22 is indicated.