

Supplementary Material

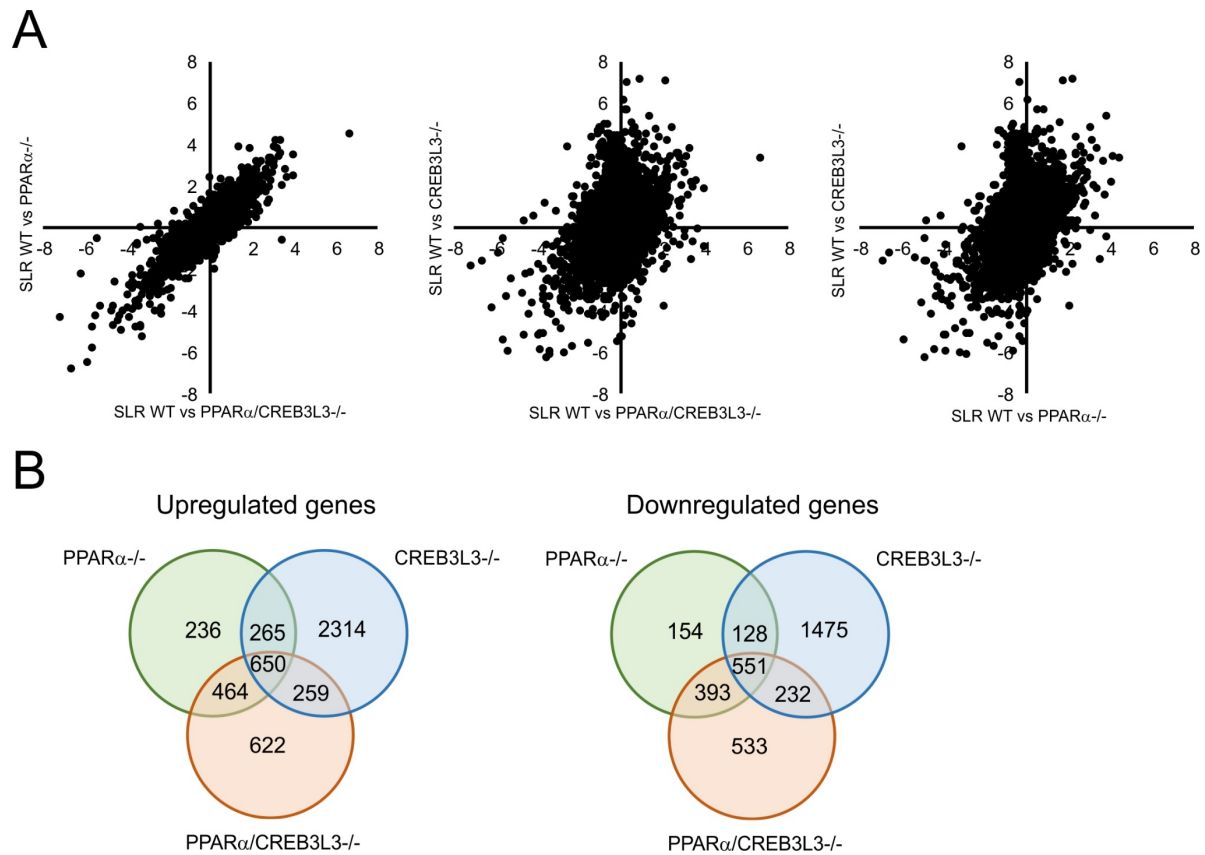
Supplemental Table 1. List of 34 genes that were commonly downregulated in livers of PPAR α ^{-/-}, CREB3L3^{-/-}, and PPAR α /CREB3L3^{-/-} mice in the fasted state (IBMT P-value<0.001).

<i>Mfsd2a</i>	Major Facilitator Superfamily Domain Containing 2A
<i>Mtnr1a</i>	Melatonin Receptor 1A
<i>Fgf21</i>	Fibroblast Growth Factor 21
<i>Lamb3</i>	Laminin Subunit Beta 3
<i>Sema5b</i>	Semaphorin 5B
<i>Xrcc3</i>	X-Ray Repair Cross Complementing 3
<i>D630045J12Rik</i>	RIKEN cDNA D630045J12 gene
<i>Crip2</i>	Cysteine Rich Protein 2
<i>Tlr12</i>	Toll-like Receptor 12
<i>Srebf1</i>	Sterol Regulatory Element Binding Transcription Factor 1
<i>Kcnk1</i>	Potassium Two Pore Domain Channel Subfamily K Member 1
<i>Tmem28</i>	Transmembrane Protein 28
<i>Rtfdc1</i>	Replication Termination Factor 2
<i>Dpy19l3</i>	Dpy-19 Like C-Mannosyltransferase 3
<i>Hsd17b10</i>	Hydroxysteroid 17-Beta Dehydrogenase 10
<i>Gm10851</i>	Predicted gene 10851
<i>Sntg2</i>	Syntrophin Gamma 2
<i>Tram2</i>	Translocation Associated Membrane Protein 2
<i>Tmem134</i>	Transmembrane Protein 134
<i>Succl1</i>	Succinate-CoA Ligase Alpha Subunit
<i>Sulf2</i>	Sulfatase 2
<i>Fam73b</i>	Mitoguardin 2
<i>Nat1</i>	N-acetyl transferase 1
<i>Tmem184a</i>	Transmembrane protein 184a
<i>Sun2</i>	Sad1 and UNC84 domain containing 2
<i>Sel1l3</i>	Sel-1 suppressor of lin-12-like 3 (C. elegans)
<i>Cog4</i>	Component Of Oligomeric Golgi Complex 4
<i>Rtn4ip1</i>	Reticulon 4 Interacting Protein 1
<i>Rmdn3</i>	Regulator Of Microtubule Dynamics 3
<i>Nsmf</i>	NMDA Receptor Synaptonuclear Signaling And Neuronal Migration Factor
<i>Ldha</i>	Lactate dehydrogenase A
<i>Ak2</i>	Adenylate kinase 2
<i>St3gal3</i>	ST3 beta-galactoside alpha-2,3-sialyltransferase 3
<i>Oard1</i>	O-acyl-ADP-ribose deacylase 1

Supplemental Table 2. Specific functions of the genes connected to cell cycle illustrated in figures 10B and C.

Cenpe, Centrosome-associated protein E	required for stable spindle microtubule capture at kinetochores	Promoting cell cycle progression
Mastl, microtubule-associated serine/threonine kinase		Possibly Pro
Nuf2, NDC80 kinetochore complex component NUF2	Yeast Nuf2 disappears from the centromere during meiotic prophase when centromeres lose their connection to the spindle pole body, and plays a regulatory role in chromosome segregation	Likely pro
Rrm2	catalyzes the formation of deoxyribonucleotides from ribonucleotides	Pro
Bub1, BUB1 mitotic checkpoint serine/threonine kinase	The encoded protein functions in part by phosphorylating members of the mitotic checkpoint complex and activating the spindle checkpoint	Pro
Ncapg, non-SMC condensin I complex subunit G	subunit of condensin complex, which is involved in condensation and stabilization of chromosomes during mitosis	Likely pro
Kif2c, Kinesin family member 2c	depolymerize microtubules at the plus end, thereby promoting mitotic chromosome segregation	Pro
Birc5, baculoviral IAP repeat containing 5	inhibitor of apoptosis (IAP) gene family, which encode negative regulatory proteins that prevent apoptotic cell death	Possibly Pro
Incep, inner centromere protein		Pro
Cdk1		Pro
Aurka, aurora kinase A	involved in microtubule formation and/or stabilization at the spindle pole during chromosome segregation	Pro
Aurkb, same as Aurka		Pro
Kntc1, kinetochore associated 1	involved in mechanisms to ensure proper chromosome segregation	Pro
Kif23, kinesin family member 23	This protein has been shown to cross-bridge antiparallel microtubules and drive microtubule movement in vitro	Pro
Top2a, DNA topoisomerase II alpha		Pro
Cenpf, centromere protein F		Pro
Zwilch, zwilch kinetochore protein		Likely Pro
Casc5, kinetochore scaffold	interacts with at least 5 different kinetochore proteins and two checkpoint kinases	Likely Pro
Cdca8, cell division cycle associated 8	Spindle formation	Pro
Cdca5 – same as Cdca8		Pro
Ube2c, ubiquitin conjugating enzyme E2 C	The encoded protein is required for the destruction of mitotic cyclins and for cell cycle progression	Pro
Prcl, protein regulator of cytokinesis 1	present at high levels during the S and G2/M phases of mitosis but its levels drop dramatically when the cell exits mitosis and enters the G1 phase. It is located in the nucleus during interphase, becomes associated with mitotic spindles in a highly dynamic manner during mitosis, and localizes to the cell mid-body during cytokinesis. This protein has been shown to be a substrate of several cyclin-dependent kinases (CDKs). It is necessary for polarizing parallel microtubules and concentrating the factors responsible for contractile ring assembly	Pro
Anln, anillin actin binding protein	This gene encodes an actin-binding protein that plays a role in cell growth and migration, and in cytokinesis	Likely Pro

Ccna2, cyclin A2	his protein binds and activates cyclin-dependent kinase 2 and thus promotes transition through G1/S and G2/M	Pro
Mki67, marker of proliferation Ki-67	"necessary for cellular proliferation"	Possibly Pro
Plk1, polo like kinase 1	Depletion of this protein in cancer cells dramatically inhibited cell proliferation and induced apoptosis	Pro
Tpx2, microtubule nucleation factor	controls spindle integrity, genome stability	Likely Pro
Foxm1, forkhead box M1	The encoded protein is phosphorylated in M phase and regulates the expression of several cell cycle genes, such as cyclin B1 and cyclin D1	Pro
S100a11, S100 calcium binding protein A11	involved in the regulation of a number of cellular processes such as cell cycle progression and differentiation	Possibly Pro
Ccnb2, cyclin B2	essential components of the cell cycle regulatory machinery	Likely pro
Cep55, centrosomal protein 55		Possibly Pro
Emp1, epithelial membrane protein 1		?
Racgap1, Rac GTPase activating protein	This protein plays a regulatory role in cytokinesis, cell growth, and differentiation	Possibly Pro



Supplemental figure 2. Similar effects of PPAR α and combined PPAR α /CREB3L3 ablation on hepatic gene expression. A) Correlation plot showing comparative hepatic gene expression changes in PPAR α -/-, CREB3L3-/-, and combined PPAR α /CREB3L3-/- mice in relation to wildtype mice after a 4 day ketogenic diet (expressed as signal log ratio, SLR). B) Venn diagram showing overlap in upregulated genes (left panel) and downregulated genes (right panel) in PPAR α -/-, CREB3L3-/-, and combined PPAR α /CREB3L3-/- mice, in comparison with wildtype mice (IBMT P value<0.001).