Supplemental Data

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Genome-wide Coactivation Analysis of PGC-1α Identifies BAF60a as a Regulator of Hepatic Lipid Metabolism

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Supplemental Tables

Table S2. Transcription Factor and Cofactor Families in the Human Genome and TFORC.

Category	hTF	TFORC	Coverage
b-ZIP	51	31	60.8%
HLH	103	47	45.6%
HMG-box	52	26	50.0%
Homeobox	207	72	34.8%
Nuclear receptor	48	30	62.5%
Zinc-finger	777	347	44.7%
Other DNA-binding	265	137	51.7%
Basal transcription	70	45	64.3%
Cofactor	211	117	55.5%
Others	601	294	48.9%
TOTAL	2385	1146	48.1%

Table S3. List of genes used in clustering analysis.

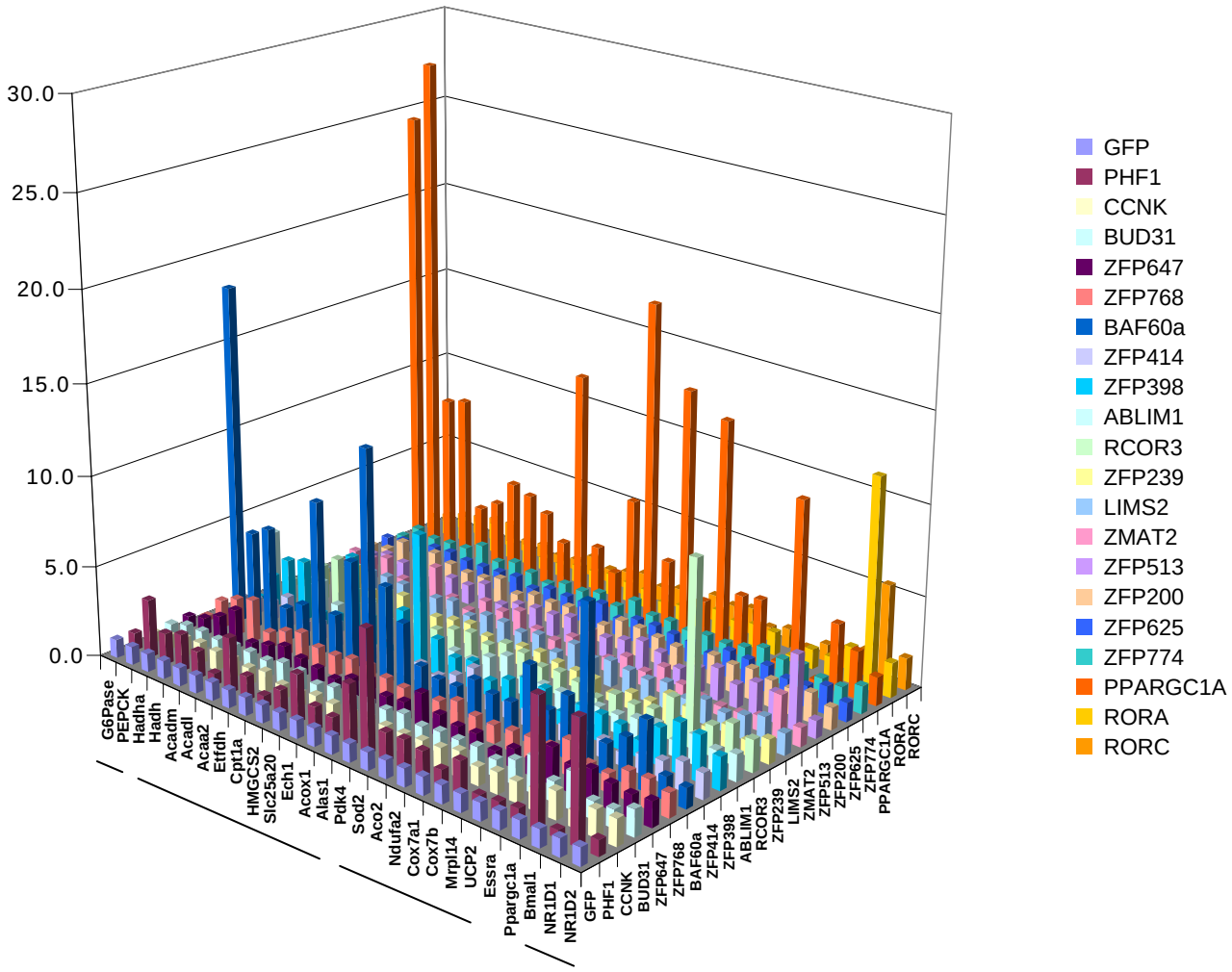
Symbol	Pathway	Gene Name
G6Pase	Gluconeogenesis	glucose-6-phosphatase, catalytic
PEPCK	Gluconeogenesis	phosphoenolpyruvate carboxykinase 1, cytosolic
Hadha	Fatty acid β-oxidation	mitochondrial trifunctional protein, alpha subunit
Hadh	Fatty acid β-oxidation	hydroxyacyl-Coenzyme A dehydrogenase
Acadm	Fatty acid β-oxidation	acyl-Coenzyme A dehydrogenase, medium chain
Acadl	Fatty acid β-oxidation	acyl-Coenzyme A dehydrogenase, long chain
Acaa2	Fatty acid β-oxidation	mitochondrial 3-oxoacyl-Coenzyme A thiolase
Etfdh	Fatty acid β-oxidation	electron-transferring-flavoprotein dehydrogenase
Cpt1a	Fatty acid β-oxidation	carnitine palmitoyltransferase 1A (liver)
HMGCS2	Fatty acid β-oxidation	3-hydroxy-3-methylglutaryl-Coenzyme A synthase 2 (mitochondrial)
Slc25a20	Fatty acid β-oxidation	solute carrier family 25 (carnitine/acylcarnitine translocase), member 20
Ech1	Fatty acid β-oxidation	enoyl Coenzyme A hydratase 1, peroxisomal
Acox1	Fatty acid β-oxidation	acyl-Coenzyme A oxidase 1, palmitoyl
Alas1	Heme biosynthesis	aminolevulinic acid synthase 1
Pdk4	Glucose metabolism	pyruvate dehydrogenase kinase, isoenzyme 4
Sod2	ROS metabolism	superoxide dismutase 2, mitochondrial
Aco2	Mitochondrial OXPHOS	aconitase 2, mitochondrial
Ndufa2	Mitochondrial OXPHOS	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 2
Cox7a1	Mitochondrial OXPHOS	cytochrome c oxidase, subunit VIIa 1
Cox7b	Mitochondrial OXPHOS	cytochrome c oxidase, subunit VIIb
Mrpl14	Mitochondrial OXPHOS	mitochondrial ribosomal protein L14
UCP2	ROS metabolism	uncoupling protein 2 (mitochondrial, proton carrier)
Essra	Transcriptional regulation	estrogen-related receptor alpha
Ppargc1a	Transcriptional regulation	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha
Bmal1	Circadian clock	aryl hydrocarbon receptor nuclear translocator-like
NR1D1	Circadian clock	nuclear receptor subfamily 1, group D, member 1
NR1D2	Circadian clock	nuclear receptor subfamily 1, group D, member 2

Table S4. Regulation of fatty acid oxidation genes by PPARα and BAF60a.

Probeset ID	Gene ID	Fold Wy14643	Fold BAF60a	Gene Symbol
1416409_at	11430	1.6	2.4	Acox1
1416772_at	12896	2.3	2.5	Cpt2
1416946_a_at	113868 /// 235674	1.7	3.7	Acaa1a /// Acaa1b
1416947_s_at	113868 /// 235674	1.7	3.1	Acaa1a /// Acaa1b
1417556_at	14080	4.2	0.9	Fabp1
1417956_at	12683	2.4	6.8	Cidea
1418321_at	13177	2.3	1.0	Dci
1419365_at	18631	2.4	1.8	Pex11a
1419367_at	67460	2.5	2.6	Decr1
1419395_at	74156	2.1	1.0	Acot12
1422526_at	14081	5.8	2.2	Acsl1
1422780_at	59038	2.2	1.5	Pxmp4
1422996_at	171210	21.7	0.8	Acot2
1422997_s_at	171210 /// 26897	35.2	5.4	Acot1 /// Acot2
1423108_at	57279	2.3	3.5	Slc25a20
1423109_s_at	57279	2.6	3.7	Slc25a20
1423858_a_at	15360	14.5	6.6	Hmgcs2
1423883_at	14081	4.0	2.4	Acsl1
1424183_at	110446	1.7	1.2	Acat1
1424451_at	235674	3.7	4.7	Acaa1b
1425195_a_at	110460 /// 224530	1.0	2.4	Acat2 /// Acat3
1426522_at	231086 /// 623031	2.4	2.2	Hadhb /// LOC623031
1426785_s_at	23945	3.0	3.3	Mgll
1427052_at	100705	2.0	0.9	Acacb
1428145_at	52538	1.6	4.2	Acaa2
1428146_s_at	52538	1.4	5.3	Acaa2
1431012_a_at	23986	2.9	3.4	Peci
1431833_a_at	15360	3.1	2.6	Hmgcs2
1433443_a_at	208715	0.9	3.4	Hmgcs1
1433446_at	208715	0.9	3.4	Hmgcs1
1433545_s_at	102632	1.7	2.8	Acad11
1437172_x_at	231086	2.2	1.9	Hadhb
1439478_at	171210	13.6	0.8	Acot2
1448188_at	22228	1.8	1.3	Ucp2
1448382_at	74147	18.1	7.3	Ehhadh
1448491_at	51798	3.3	2.1	Ech1
1448764_a_at	14080	3.8	1.1	Fabp1
1448987_at	11363	1.7	2.7	Acadl
1449065_at	26897	99.6	1.4	Acot1
1449442_at	18631	2.0	1.8	Pex11a
1449457_at	74156	1.7	1.0	Acot12
1449749_s_at	224481	5.3	1.4	Tfb1m
1449964_a_at	56690	2.1	1.0	Mlycd
1450391_a_at	23945	3.1	2.9	Mgll
1450504_a_at	28169	1.6	1.6	Agpat3
1450643_s_at	14081	4.6	2.4	Acsl1
1450966_at	74114	2.2	2.1	Crot
1451084_at	66841	2.0	2.1	Etfdh
1451271_a_at	110446	2.2	2.1	Acat1
1452173_at	97212	2.0	2.0	Hadha
1452260_at	14311	2.1	1.5	Cidec
1453836_a_at	23945	4.0	3.1	Mgll
1454647_at	102632	1.6	2.1	Acad11
1455061_a_at	52538	1.5	7.0	Acaa2
1455438_at	59038	2.0	1.5	Pxmp4
1455972_x_at	15107	1.1	2.4	Hadhsc
1460184_at	15107	1.4	2.1	Hadhsc
1460409_at	12894	2.6	2.8	Cpt1a

Table S5. List of qPCR and ChIP PCR primers.

	Gene	Forward primer	Reverse primer
qPCR	Acaa1b	ATGCTTCCATGCTGAGATTGT	TCCATCCTTGAAGGCAGGCTT
	Acaa2	GATCTCAAGCTGGAAGATAC	ACCTCTGCTGAGACTGCAAG
	Acox1	GCCTGCTGTGTGGGTATGTCATT	GTCATGGGCGGGTGCAT
	Ech1	AAGATAAGGACGCCATGCTGAA	TCCAGGTGGCCATGTAGTCA
	Ehhadh	CAGATGAAGCACTCAAGCTTG	ACCTTGGCAATGGCTTCTGCA
	Hadha	TGCTCCTCGACCACGCTAAC	GCCTTGGTCTTTTTCCTGCTT
	Etfdh	GGAAGGCGGGAAGAGGATAG	GCCGTGTGGGTACCTTTGAT
	Slc25a20	GTTCACCACAGGAATCATGAC	GTGAGCACAGTCCCTTTGTAG
	Cox7a1	GTCTCCCAGGCTCTGGTCCG	CTGTACAGGACGTTGTCCATTC
	BAF60a	TGGACCCAAATGACCAGAAAA	TCTTGTTGTCTAGAGTGGCGATCT
ChIP	Acaa1b	GCACTGATGAGGGCATCTC	CTAAGCTGGATGCTTGAGTAC
	Acox1	TCTAACGTCAGTCAAGTCGG	GAAAGCTGTTGATTTTACTGG
	Hadha	TCAATTAAATGCCAGGGGAG	GATACTAGTTACTTCCCAGAC



Supplemental Figures

Figure S1. Effects of Individual Factors on the Expression of PGC-1α Target Genes

qPCR analysis of mRNA expression in primary hepatocytes transduced with recombinant adenoviruses expressing GFP, PGC-1α or individual PGC-1α partners. The expression of PGC-1α target genes involved in hepatic gluconeogenesis, fatty acid β-oxidation, mitochondrial OXPHOS and circadian clock function were normalized to the GFP control. Note that BAF60a (blue bars) and PGC-1α induce the expression of a common set of genes (orange bars).

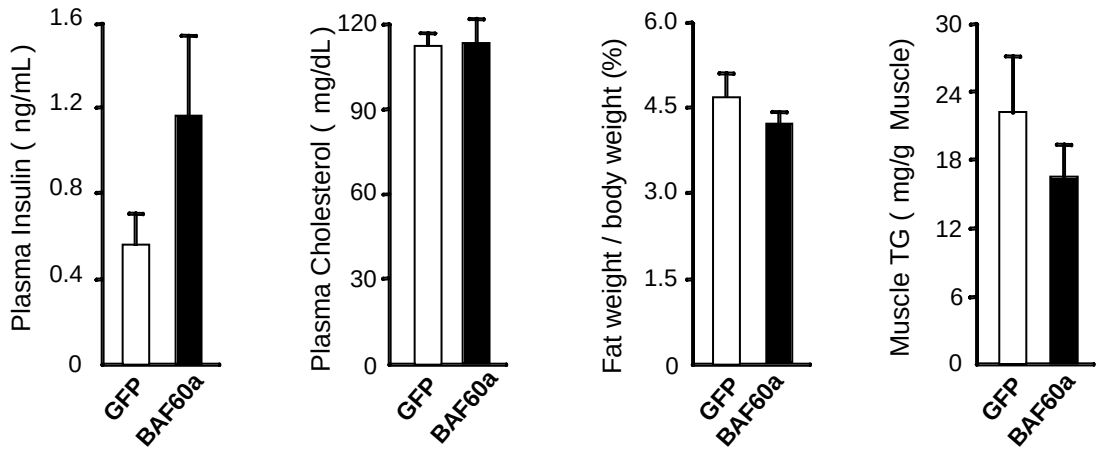


Figure S2. Metabolic characteristics of mice transduced with GFP or BAF60a adenoviruses

Plasma insulin and total cholesterol concentrations, percent gonadal fat weight, and muscle TG content in mice transduced with adenoviruses expressing GFP (open circle) or BAF60a (filled circle). Data represent mean ± SEM, n=5. No statistical difference was observed between two groups.

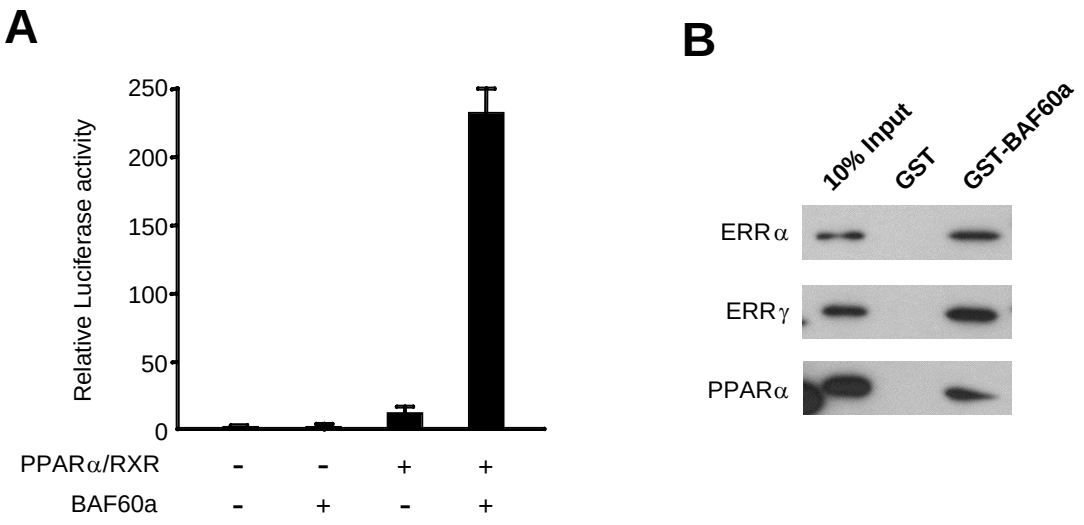


Figure S3. Interaction of BAF60a with nuclear receptors

(A) DR-1 luciferase reporter was transiently transfected into BOSC cells with PPARα/RXR in the presence or absence of BAF60a. Data represent mean ± stdev.

(B) Immunoblots of Flag-tagged ERRα, ERRγ and PPARα. GST and GST-BAF60a fusion proteins were incubated with *in vitro* transcribed and translated Flag-ERRα, Flag-ERRγ or Flag-PPARα followed by immunoblotting analysis using Flag antibody.

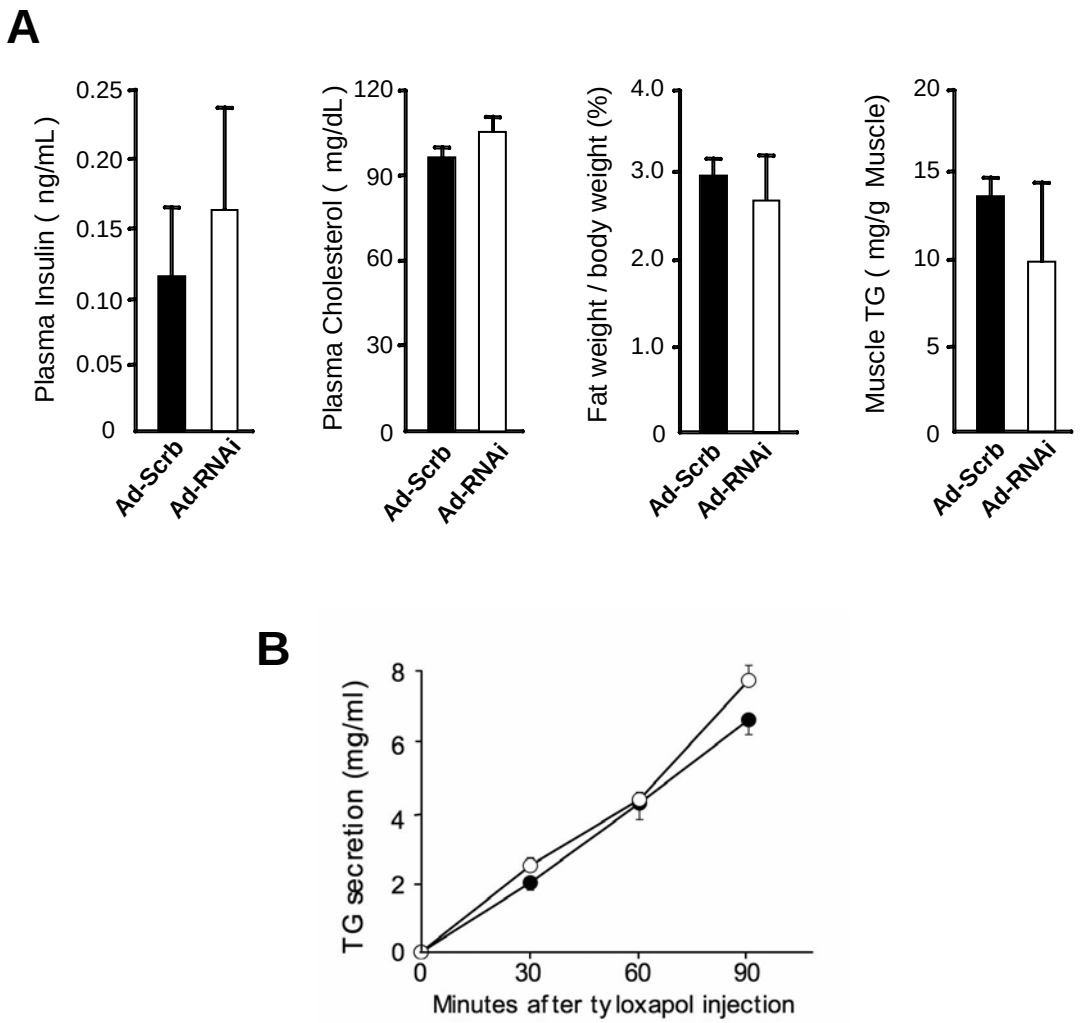


Figure S4. Metabolic characteristics of mice transduced with control or BAF60a RNAi adenoviruses

(A) Plasma insulin and total cholesterol concentrations, percent gonadal fat weight, and muscle TG content in mice transduced with control (filled) or BAF60a RNAi (open) adenoviruses.

(B) Increase in plasma TG following intravenous injection of tyloxapol (500 mg/kg) in mice transduced with control (filled) or BAF60a RNAi (open) adenoviruses. Data represent mean ± SEM, n=5. No statistical difference was observed between two groups.