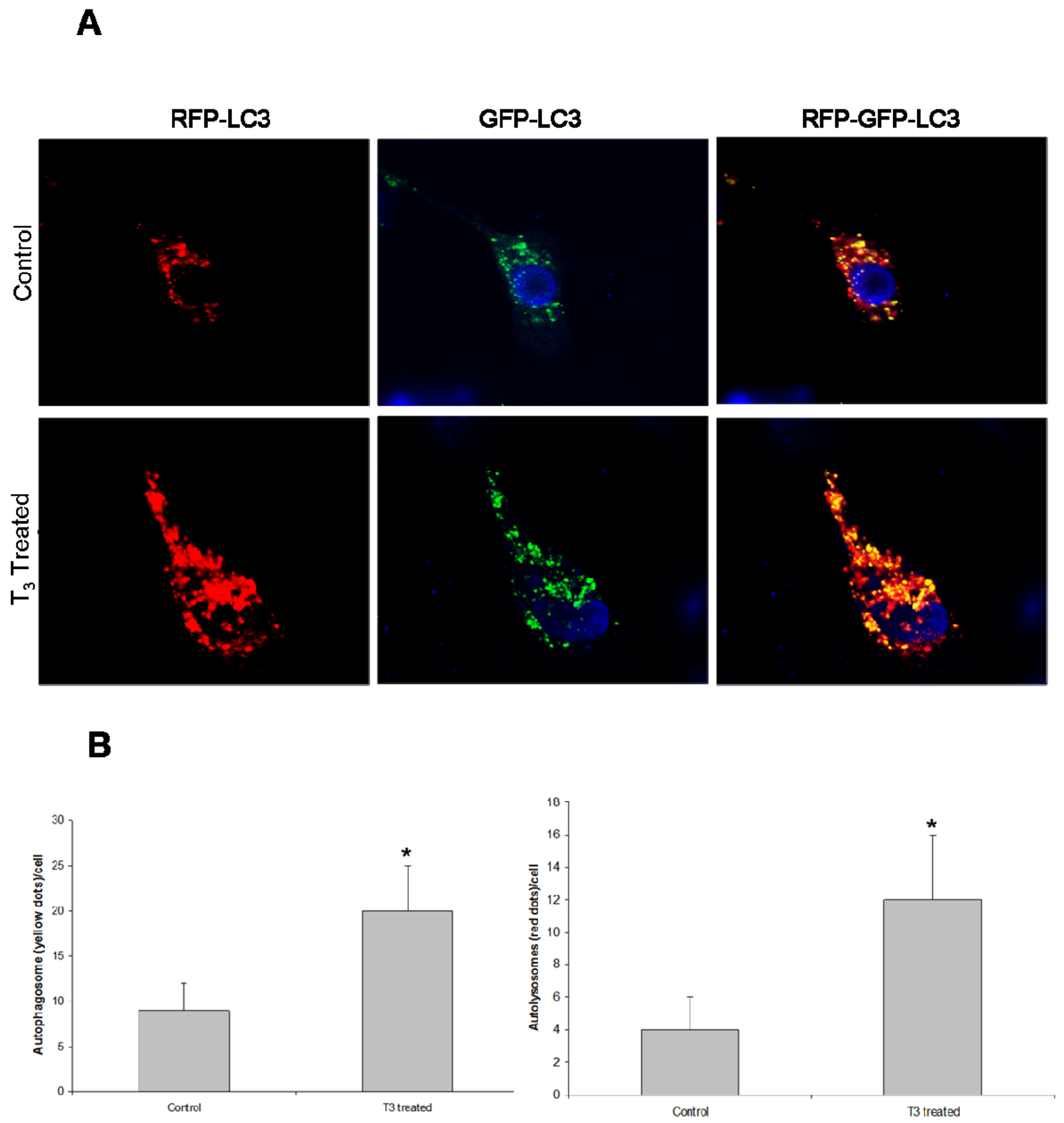
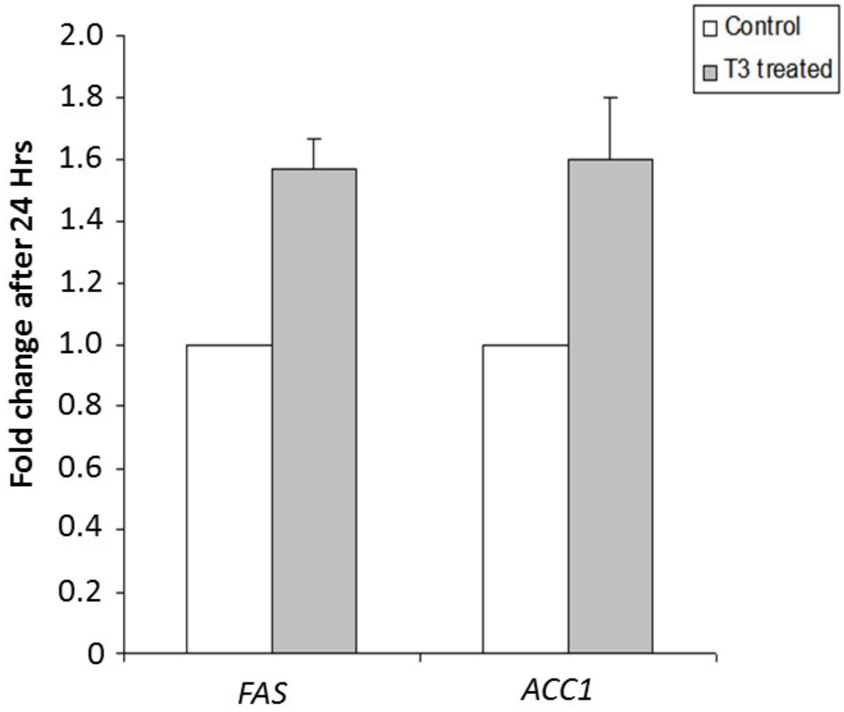


Suppl. Figure 1. T_3 induces autophagic flux in hepatic cells. **(A)** RFP-GFP-LC3 transfected HepG2/TRα cells were visualized and cells were quantified for RFP-LC3–puncta (red dots) representing both autolysosomes and autophagosomes (far left panels). GFP-LC3 (green dots) puncta denote autophagosomes (middle panels). When middle panels are overlaid with left panels, yellow dots represent autophagosomes and red dots are autolysosomes (far right panels) since acidification abolishes green fluorescence. **(B)** The number of autophagosomes (yellow dots) and autolysosomes (red dots) in the overlay (far right panels) were quantitated. Images were performed by confocal microscopy (40X magnification) after 48 hrs T_3 treatment. The p values for assessing the number of LC3-II-positive autophagosomes and autolysosomes using ImageJ were determined using Student's t-test ($n=3$; $p<0.05$).



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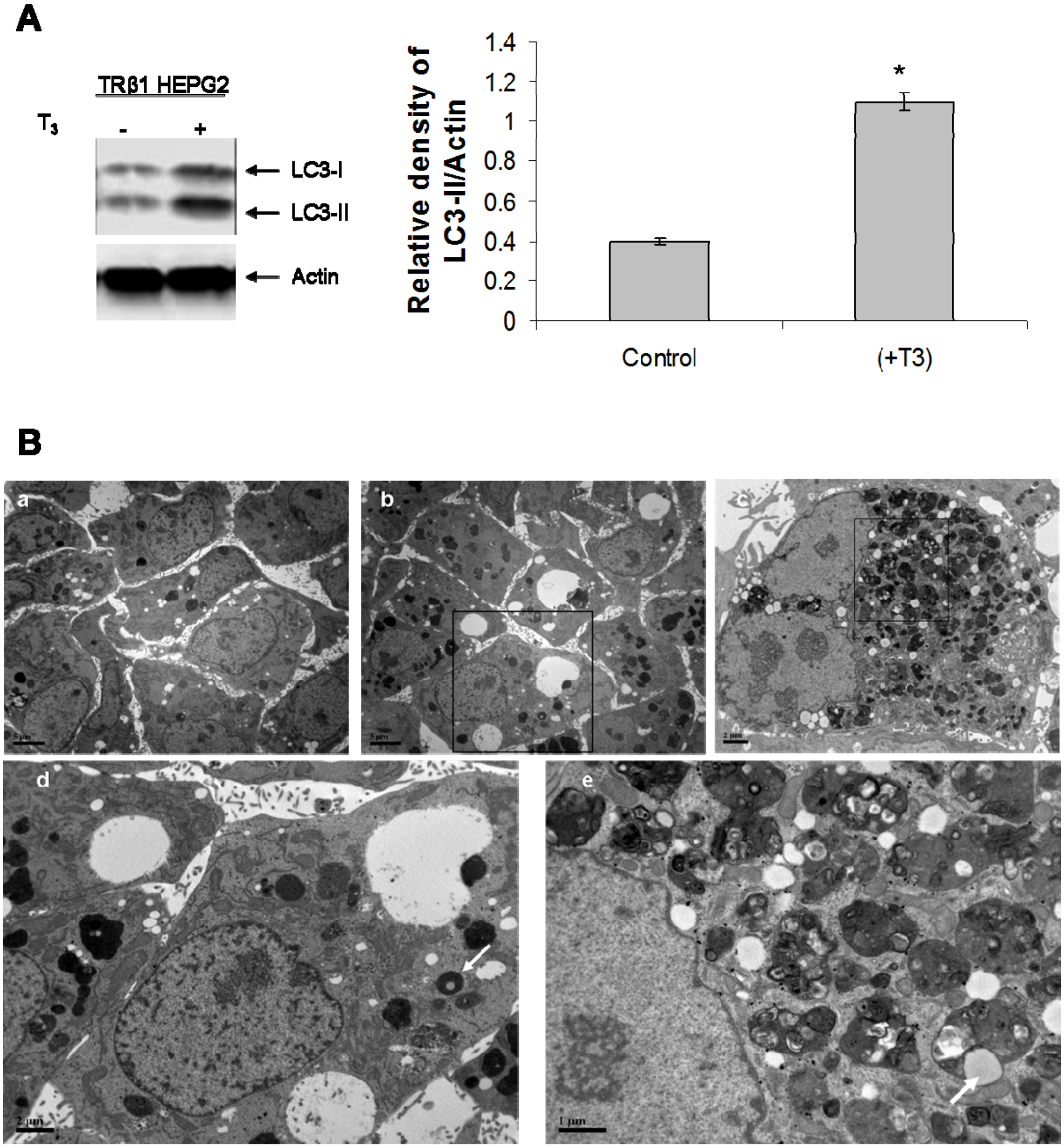
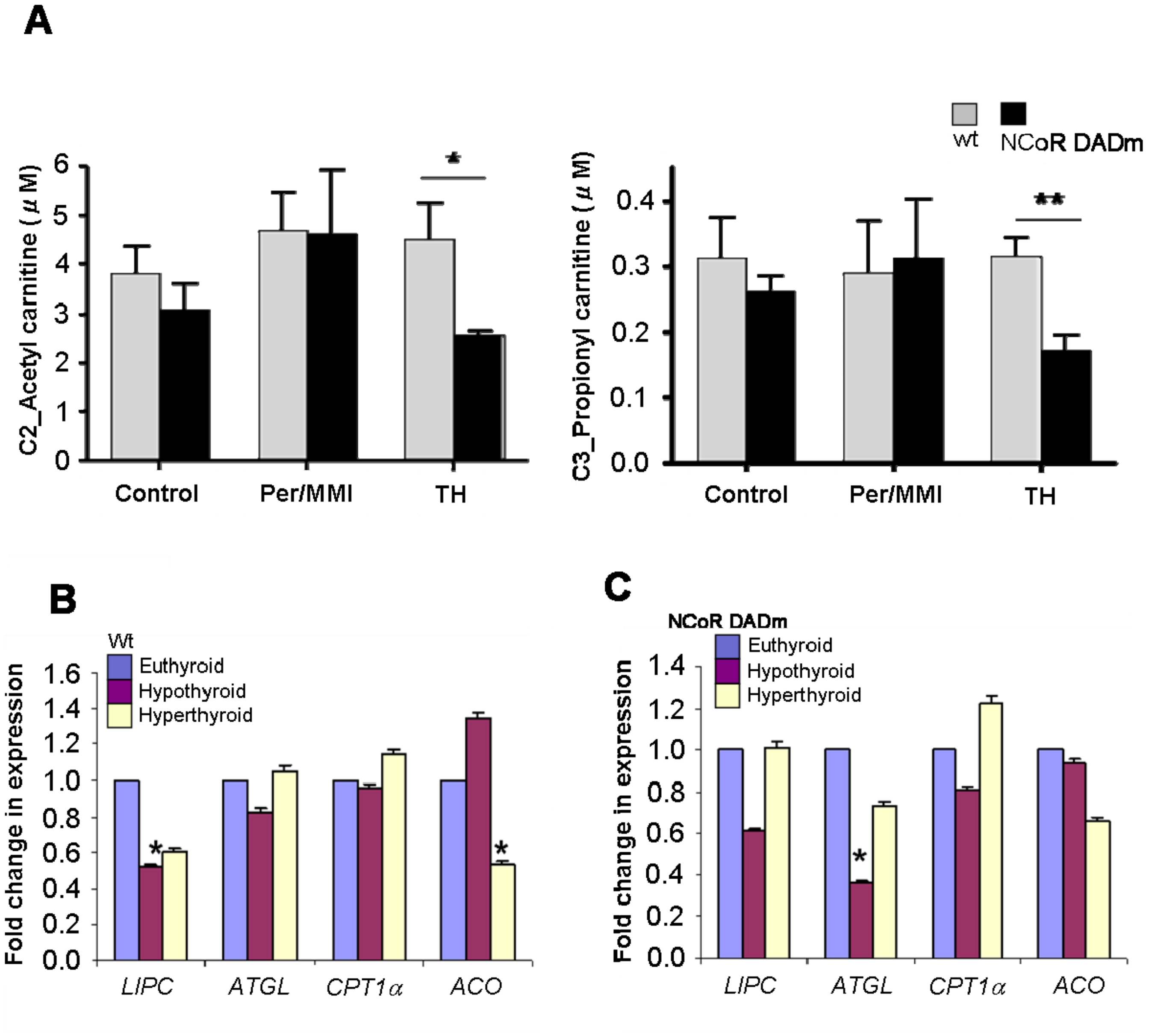
Suppl. Figure 2. Real-Time PCR analysis of *FAS* & *ACC1* mRNA in HepG2/TRα cells (*p<0.05, n=3).



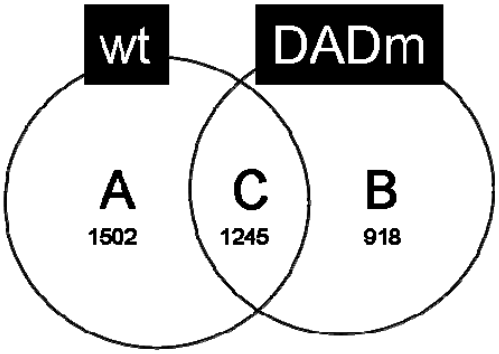
Suppl. Figure 3. T_3 induces autophagy in HepG2/TRβ cells. **(A)** Immunoblot and densitometric analysis of LC-3-II accumulation upon T_3 treatment in HepG2/TRβ cells (n=3, *p<0.05). Electron micrographs and immunoblot of untreated control **(B)** and T_3-treated **(C-F)** HepG2/TRβ cells show increased autophagy. Panel **E** and **F** are magnified images of boxed area in **C** and **D** respectively. White arrows in **E & F** indicate autolysosomes laden with lipid cargo. Scale Bars in (**B,C**) are 5µm, (**D,E**) are 2µm and in (**F**) is 1µm.



Suppl. Figure 4. Metabolomic, and lipolytic target gene regulation of wt and NCoR DADm mice. **(A)** Metabolomic analysis of short chain acyl carnitines in wt and NCoR DADm mice Fresh drinking water was provided daily containing 1% perchlorate and 0.05% methimazole for 2 wk (hypothyroid group). Fourteen hours before they were killed, all animals were given a sc injection of vehicle (0.9% saline in 100 µl volume) for control and hypothyroid group or 40.0µg/100 g T_4 with 4.0µg/100 g T_3 for hyperthyroid group (*p<0.05, n=5). Real-Time PCR analysis of *LIPC*, *ATGL*, *CPT-1*α and *ACO* in **(B)** Wild-type (wt) and **(C)** NCoR DADm mice, (*p<0.05, n=3).

A

	Genotype	
	Wt	DADm
Treatment	HypoTH	HypoTH
	EuTH	EuTH
	HyperTH	HyperTH



A+C: gene changes by thyroid hormone in wt mouse (2747)
B+C: gene changes by thyroid hormone in DADm mouse (2163)
A: gene changes by thyroid hormone but ONLY in wt mouse(1502)
B: gene changes by thyroid hormone but ONLY in DADm mouse (918)
C: COMMON gene changes by thyroid hormone in BOTH wt AND DADm mouse (1245)

B

A: gene changes by thyroid hormone but ONLY in wt mouse(1502)	**B: gene changes by thyroid hormone but ONLY in DADm mouse(918)**
oxidation reduction	generation of precursor metabolites and energy
translation	oxidative phosphorylation
cofactor metabolic process	electron transport chain
coenzyme metabolic process	proton transport
nitrogen compound biosynthetic process	hydrogen transport
organic acid catabolic process	ATP synthesis coupled proton transport
carboxylic acid catabolic process	energy coupled proton transport, down electrochemical gradient
cofactor biosynthetic process	ion transmembrane transport
hexose metabolic process	oxidation reduction
monosaccharide metabolic process	mitochondrion organization
antigen processing and presentation of peptide antigen via MHC class I	translation
glycerolipid metabolic process	phosphorylation
cellular amino acid derivative metabolic process	nucleoside triphosphate metabolic process

amine catabolic process	purine nucleoside triphosphate metabolic process
phospholipid metabolic process	nucleoside triphosphate biosynthetic process
organophosphate metabolic process	phosphorus metabolic process
coenzyme biosynthetic process	phosphate metabolic process
lipid catabolic process	purine nucleoside triphosphate biosynthetic process
alcohol catabolic process	transmembrane transport
cellular lipid catabolic process	ATP biosynthetic process
glycerolipid biosynthetic process	nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process
fatty acid metabolic process	nucleobase, nucleoside and nucleotide biosynthetic process
cellular response to reactive oxygen species	phosphoinositide metabolic process
cellular carbohydrate catabolic process	ATP metabolic process
biogenic amine metabolic process	cellular macromolecule localization
acylglycerol metabolic process	ribonucleoside triphosphate biosynthetic process
cellular amino acid biosynthetic process	purine ribonucleoside triphosphate biosynthetic process
generation of precursor metabolites and energy	mitochondrial transport
triglyceride metabolic process	protein targeting to mitochondrion
cellular amino acid catabolic process	protein localization in mitochondrion

Suppl. Figure 5. (A) Scheme of animal groups used for microarray analysis. **(B)** Pathway analysis of differentially expressed genes in hyperthyroid wt and NCoR DADm (given 40.0µg/100 g T_4 with 4.0µg/100 g T_3 for 14 hrs before sacrifice) mice using DAVID Bioinformatics Resources 6.7. Note the lipid and amino acid catabolic process (red) showing up exclusively in wt mice.

Table 1: **Primer Sequences**

Human	
FAS (sense)	5’- ACAGGGACAACCTGGAGTTCT
FAS (antisense)	5’- CTGTGGTCCCACTTATGAGT
ACC1 (sense)	5’- GTTGCACAAAAGGATTTCAG
ACC1 (antisense)	5’- CGCATTACCATGCTCCGCAC
Actin (sense)	5’- GCACAGAGCCTCGCCTTTGCC
Actin (antisense)	5’- CATGCCCACCATCACGCCCTGG
Mouse	
ACO (sense)	5’- ATATTTACGTCACGTTTACCCCGG
ACO (antisense)	5’- GGCAGGTCATTCAAGTACGACAC
CPT-1α (sense)	5’- CGCACGGAAGGAAAATGG
CPT-1α (antisense)	5’- TGTGCCCAATATTCCTGG
ATGL (sense)	5’- AACACCAGCATCCAGTTCAA
ATGL (antisense)	5’- GGTTCAGTAGGCCATTCCTC
LIPC (sense)	5’- GACGGGAAGAACAAGATTGGAA
LIPC (antisense)	5’- TTGGCATCAGGAGAAAGG
Actin (sense)	5’- GCGAGCACAGCTTCTTTGCA
Actin (antisense)	5’- ACGCAGCTCAGTAACAGTCC