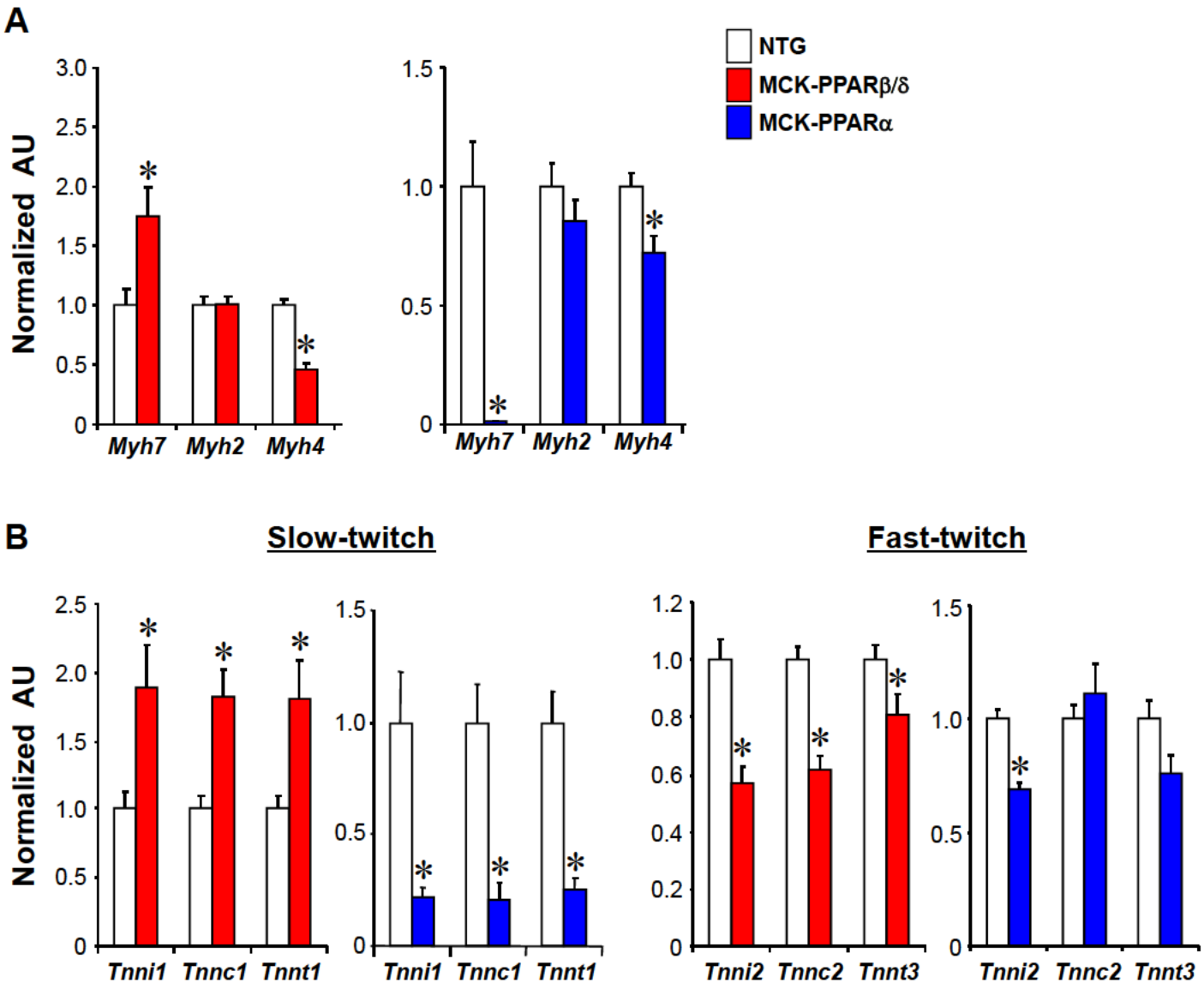
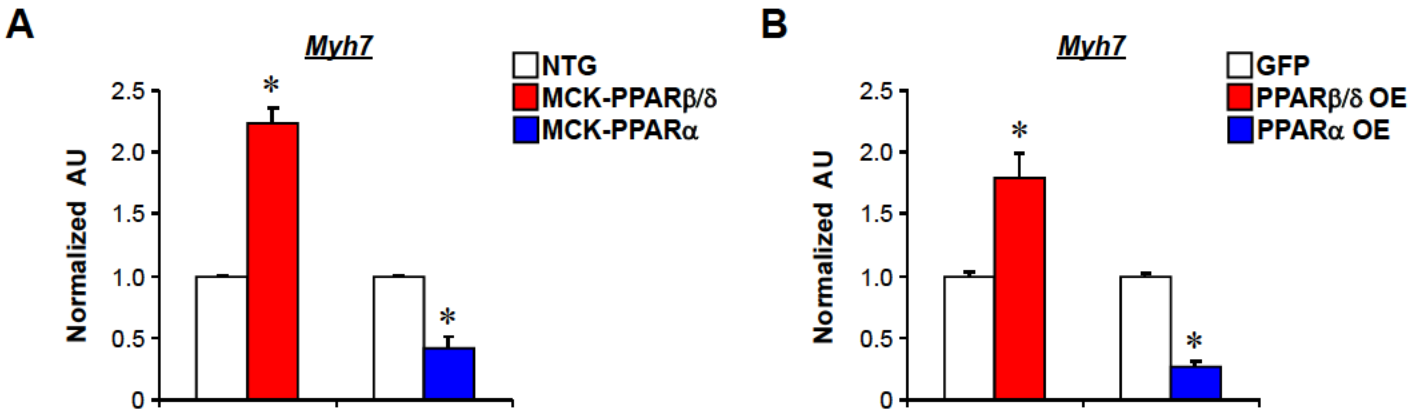
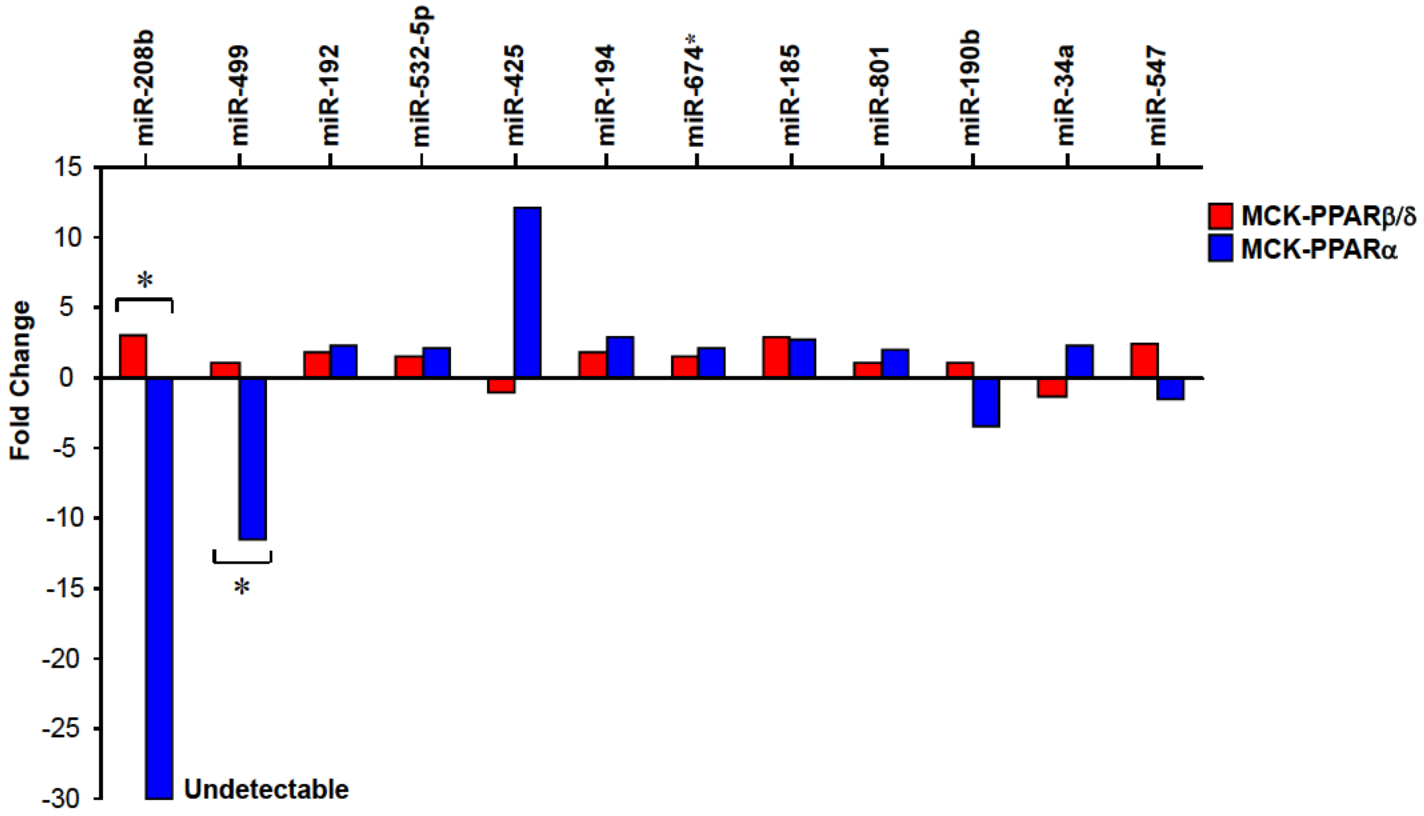


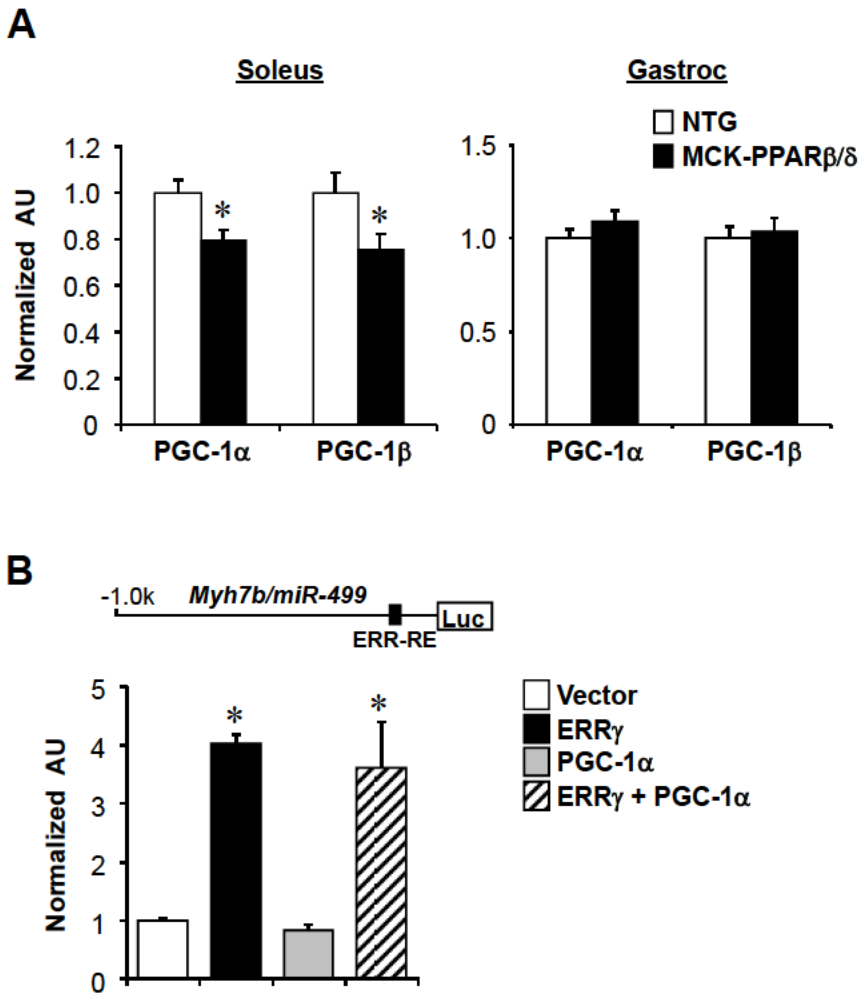
Supplemental Figure 1. PPARβ/δ and PPARα drive opposing muscle fiber type programs in vivo. (A and **B)** Expression of MHC isoforms and representative slow/fast-twitch troponin genes (qRT-PCR) in gastrocnemius muscle from indicated genotypes (n=8-13/group). **P* < 0.05 vs NTG. All values represent mean ± SEM, and shown as arbitrary units (AU) normalized to corresponding controls.



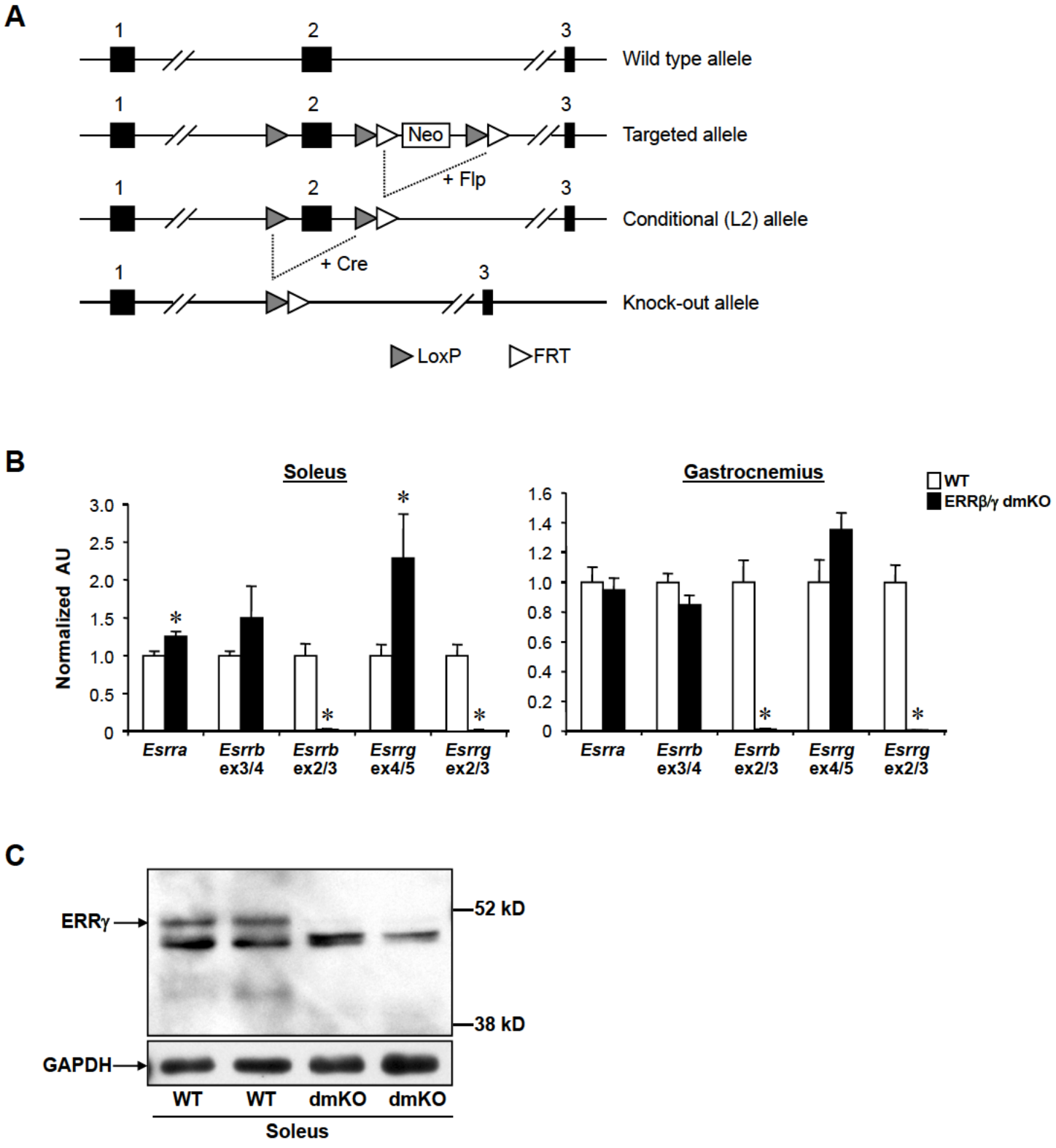
Supplemental Figure 2. PPARβ/δ and PPARα regulate opposing muscle fiber type determination in primary myotubes. (**A**) qRT-PCR analysis of MHC isoforms in primary skeletal myotubes harvested from gastrocnemius of genotypes indicated (n=3). (**B**) Myotubes harvested from WT mice and subjected to adenoviral-based overexpression of PPARβ/δ or PPARα compared to GFP control (n=3). *$P < 0.05$ vs NTG or GFP. All values represent mean ± SEM, and shown as arbitrary units (AU) normalized to corresponding controls.



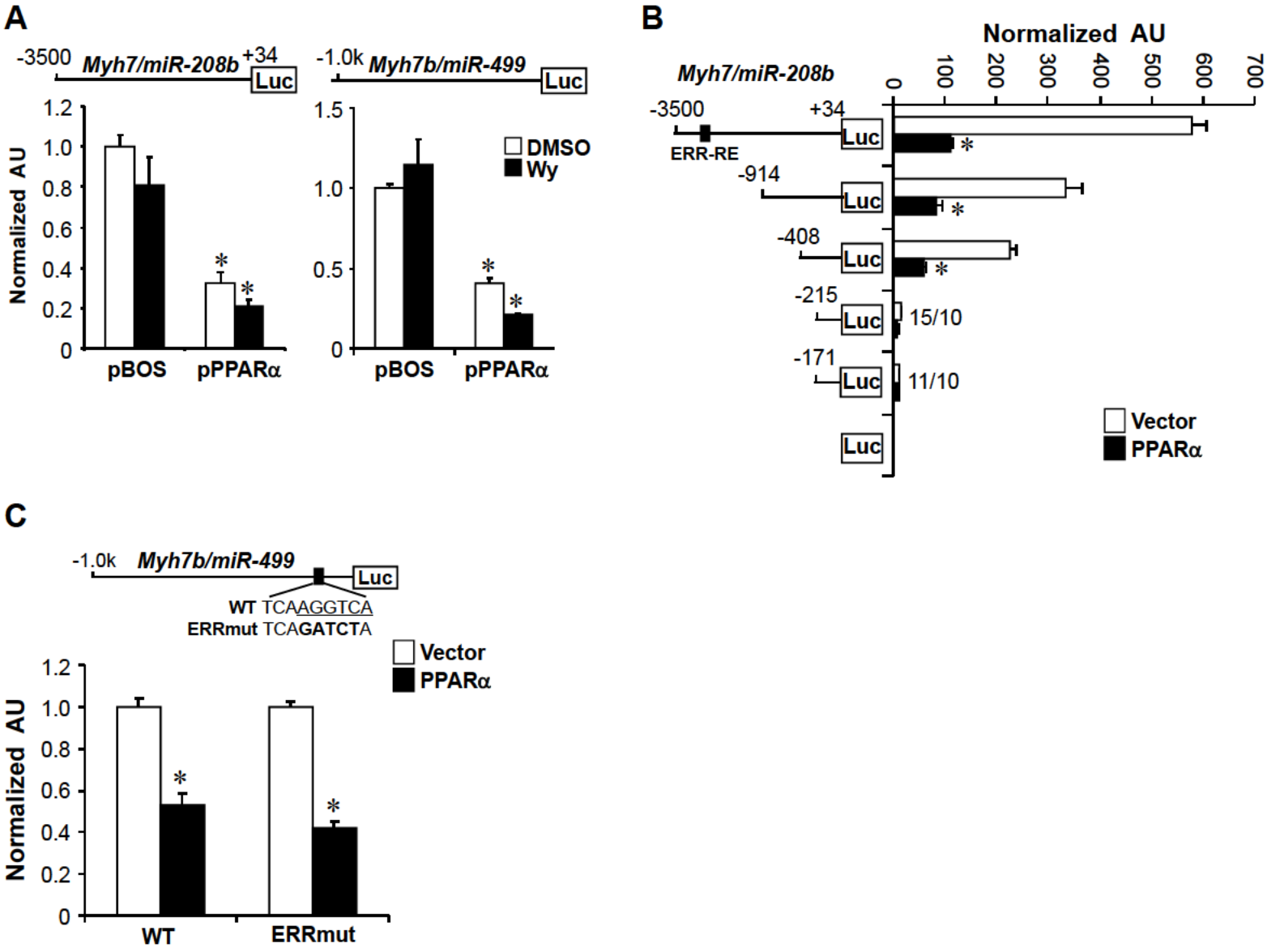
Supplemental Figure 3. PPARβ/δ and PPARα control distinct miRNA sub-networks in skeletal muscle. Bars depict the fold change (upward, upregulated; downward, downregulated) of miRNAs from soleus of 3 month old male MCK-PPARβ/δ (red bars) and MCK-PPARα (blue bars) mice compared to NTG littermate controls. Selected miRNAs from the TLDA Array are shown; criteria for selection was Ct values less than 30, a fold change greater than 2 (either direction) and a significant p value (< 0.01) vs NTG in at least one of the MCK lines. Two differentially regulated miRNAs of interest are denoted with asterisks.



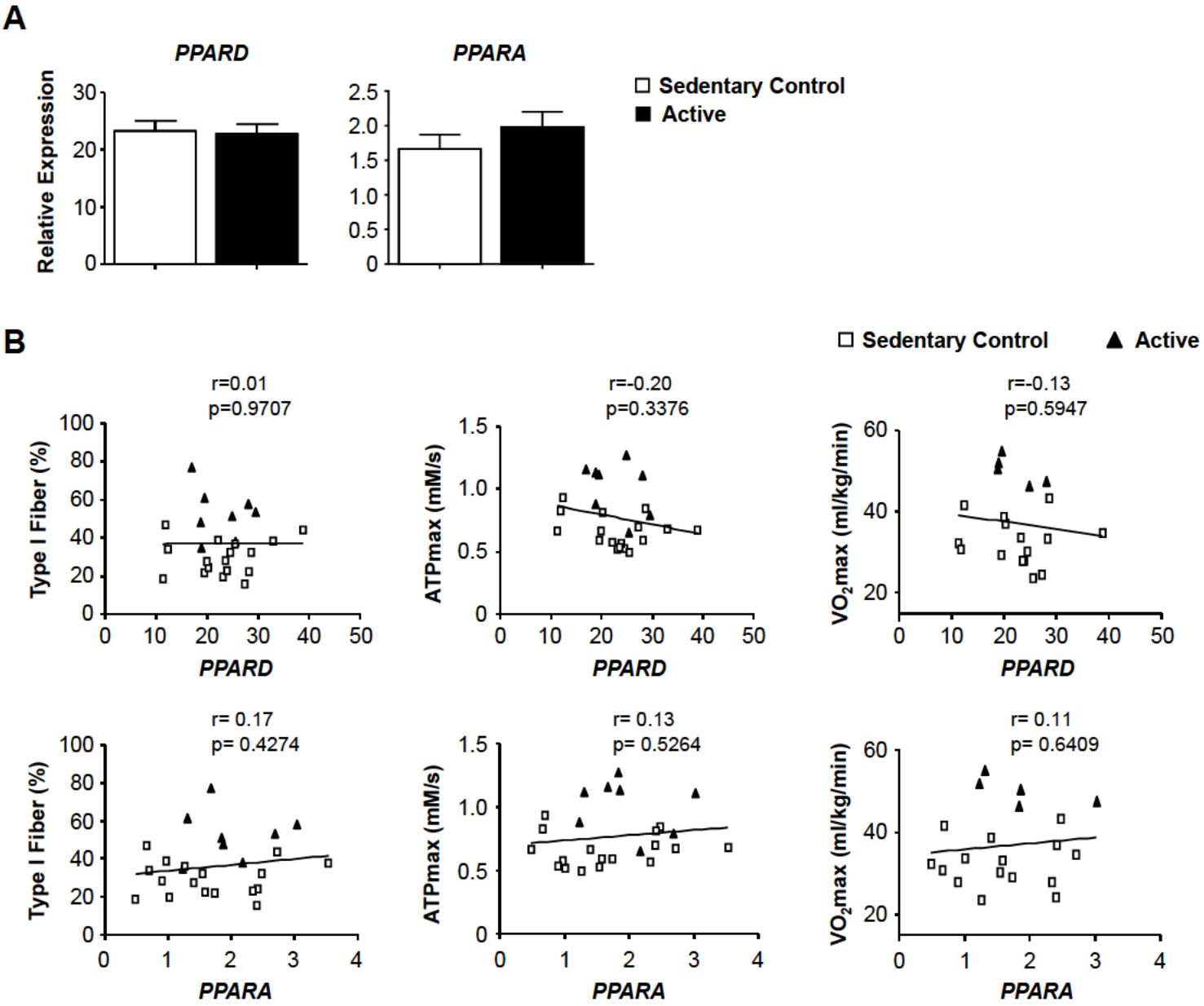
Supplemental Figure 4. PGC-1α-independent activation of the type I fiber program by PPARβ/δ and ERRγ. (**A**) Expression of PGC-1 genes (qRT-PCR) in muscle from indicated genotypes (n=7-12/group). (**B**) The m*Myh7b*.Luc.1K (WT) promoter reporter was cotransfected into C2C12 myotubes in the presence of expression vectors indicated (n=3). **P* < 0.05 vs. corresponding controls. Luciferase assay is shown as arbitrary units (AU), normalized to vector control. All values represent mean ± SEM.



Supplemental Figure 5. Generation of mice with skeletal muscle-specific disruption of the *Esrrg* and *Esrrb* genes. (**A**) Diagram of the wild-type, targeted, conditional (floxed exon 2) and knock-out (deleted exon 2) alleles of *Esrrg* (gene encoding ERRγ). Black boxes depict exons; gray and white triangles depict LoxP and FRT sites, respectively. A similar strategy was used at the *Esrrb* locus to flox and delete exon 2 of the ERRβ encoding gene. (**B** and **C**) qRT-PCR and western blot analysis of ERRβ/ERRγ expression in skeletal muscle from indicated genotypes (n=6/group). *$P < 0.05$ vs WT. All values represent mean ± SEM, and shown as arbitrary units (AU) normalized to corresponding controls.



Supplemental Figure 6. PPARα suppresses *Myh7/miR-208b* and *Myh7b/miR-499* promoter activity through an ERR independent mechanism. (**A**) Rat 3.5 kb *Myh7* and mouse 1.0 kb *Myh7b* promoter reporters were cotransfected into C2C12 myotubes in the presence (PPARα vector) or absence (pBOS vector) of PPARα. 48h post-transfection, cells were treated for 24h with vehicle (DMSO) or 10 μM of the PPARα ligand, Wy14643 (Wy), as indicated (n=3). (**B**) A rat 3.5 kb *Myh7* promoter reporter deletion series was constructed and cotransfected into C2C12 myotubes in the presence or absence of PPARα (n=3). (**C**) (Top) Site-directed mutagenesis was used to abolish the ERR response element. (Bottom) The m*Myh7b*.Luc.1K (WT) or ERRmut.m*Myh7b*.Luc.1K promoter reporters were cotransfected into C2C12 myotubes in the presence or absence of PPARα (n=3). **P* < 0.05 vs. corresponding controls. All values represent mean ± SEM.



Supplemental Figure 7. PPARβ/δ and PPARα are not associated with measures of endurance in human muscle. Samples from 5-8 "active" and 15-17 healthy sedentary controls were used for this analysis. (**A**) mRNA expression levels of *PPARD* and *PPARA* was determined by qRT-PCR. Data represent the mean ± SEM. (**B**) Correlation between the expression of *PPARD* and *PPARA* to the type I fiber %, ATPmax, and VO_2max. Pearson correlation analysis was used to determine the correlation.

Supplemental Table 1. Striated muscle slow-twitch contraction genes are differentially regulated in MCK-PPARβ/δ and MCK-PPARα mice			
		Fold Change	
Gene	**Description**	**MCK-PPARβ/δ**	**MCK-PPARα**
Actc1	actin, alpha, cardiac muscle 1	0.1	0.3
Actn2	actinin alpha 2	1.7	1
Casq2	calsequestrin 2	3.1	1.5
Dmd	dystrophin, muscular dystrophy	3.2	0.8
Myh6	myosin, heavy polypeptide 6, cardiac muscle, alpha	2.5	1.3
Myh7	myosin, heavy polypeptide 7, cardiac muscle, beta	1.7	0.1
Myh8	myosin, heavy polypeptide 8, skeletal muscle, perinatal	2.3	0.6
Myl2	myosin, light polypeptide 2, regulatory, cardiac, slow	2.9	0.7
Tnnc1	troponin C, cardiac/slow skeletal	2.2	0.3
Tnni1	troponin I, skeletal, slow 1	2.2	0.3
Tnni3	troponin I, cardiac 3	4.4	2
Tnnt1	troponin T1, skeletal, slow	2.5	0.4
Tnnt2	troponin T2, cardiac	21.9	0.7
Tpm3	tropomyosin 3, gamma	1	0.1

Genes involved in striated muscle contraction pathway (Gene Ontology) were compared between NTG and MCK-PPAR gastrocnemius. Regulated genes (fold change greater than 1.5 or less than 0.5 in at least one of the MCK lines) are shown. Slow-twitch genes are shaded in pink.

Supplemental Table 2. Human subject characteristics			
	Active n = 8	**Sedentary Control n = 17**	***p* Value**
Age (yr)	23.25 ± 1.28	27.63 ± 1.22	0.0358
Weight (kg)	75.48 ± 3.11	80.24 ± 2.52	0.2753
BMI (kg/m^2)	23.52 ± 1.02	25.69 ± 0.64	0.1045
Fasting Glucose (mg/dl)	88.63 ± 2.05	92.35 ± 2.11	0.2838
ATP_{max} (mM/s)	1.01 ± 0.08	0.66 ± 0.03	<0.0001
Type I Fiber (%)	52.68 ± 4.71	29.37 ± 2.23	<0.0001
VO_{2max} (ml/kg/min)	50.24 ± 1.56	32.41 ± 1.50	<0.0001

Data represent the mean ± SD, differences were analyzed using Two-sample t-test, with a statistically significant difference defined as $P < 0.05$.

Supplemental Table 3. RT-PCR primers		
Mouse Gene	**Forward**	**Reverse**
36b4	5'-ATCCCTGACGCACCGCCGTGA	5'-TGCATCTGCTTGGAGCCCACGT
Esrra	5'-AGGAGTACGTCCTGCTG	5'-CCTCAGCATCTTCAATG
Esrrb	5'-ACGGCTGGATTCGGAGAAC	5'-TCCTGCTCAACCCCTAGTAGATTC
Esrrg	5'-TGACTTGGCTGACCGAG	5'-CCGAGGATCAGAATCTCC
Myh7 (MHC1)	5'-GCCAACTATGCTGGAGCTGATGCCC	5'-GGTGCGTGGAGCGCAAGTTTGTCATAAG
Myh2 (MHC2a)	5'-GGCACAAACTGCTGAAGCAGAGGC	5'-GGTGCTCCTGAGGTTGGTCATCAGC
Myh1 (MHC2x)	5'-GGCAGCAGCAGCTGCGGAAGCAGAGTCTGG	5'-GAGTGCTCCTCAGATTGGTCATTAGC
Myh4 (MHC2b)	5'-GAGCTACTGGATGCCAGTGAGCGC	5'-CTGGACGATGTCTTCCATCTCTCC
Myh7b	5'-GCCTCTGCGGACATTGATAG	5'-GGGCAGCTGGAAGATCACT
Tnni1	5'-TGAAGCCAAATGCCTCCACAACAC	5'-ACACCTTGTGCTTAGAGCCCAGTA
Tnnc1	5'-AGCTCATGAAGGACGGTGACAAGA	5'-AACCGTGCAAGACCAGCATCTACT
Tnnt1	5'-TGGATCCACCAGCTGGAATCAGAA	5'-GCTGATGCGGTTGTAGAGCACATT
Tnni2	5'-AGCAGCAAGGAGCTGGAAGA	5'-ATGGCGTCGGCAGACATAC
Tnnc2	5'-CCATCATCGAGGAGGTGGAC	5'-CTTCCCCTTCGCATCCTCTT
Tnnt3	5'-AACTGGAGACTGACAAATTCGAGT	5'-GCTGTGCTTCTGGGTTTGGT
PGC-1a	5'-CGGAAATCATATCCAACCAG	5'-TGAGAACCGCTAGCAAGTTTG
PGC-1b	5'-TCCAGAAGTCAGCGGCCT	5'-CTGAGCCCGCAGTGTGG
Esrrb ex3/4	5'-CCGGCCACCAATGAATGT	5'-ATCCAGCCGTCGCTTGTACT
Esrrb ex2/3	5'-ACATTGCCTCTGGCTACCAC	5'-CCCACTTTGAGGCATTTCAT
Esrrg ex4/5	5'-TCCCCGACAGTGACATCAAA	5'-GTGTGGAGAAGCCTGGAATA
Esrrg ex2/3	5'-ATGCCCAAGAGACTGTGCTT	5'-CTTCTTTCAGCATGCCCACT
Human Gene	**Forward**	**Reverse**
GAPDH	5'-AGCCACATCGCTCAGACAC	5'-GCCCAATACGACCAAATCC
ESRRG	5'-AGTGGGCATGCTGAAAGAAG	5'-GCTGTTCTCCGCATCTATCC
PPARD	5'-GGG AAAAGTTTTGGCAGGAG	5'-TGCCCAAAACACTGTACAACA

PPARA	5’-GCACTGGAACTGGATGACAG	5’-TTTAGAAGGCCAGGACGATCT
MYH7	5’-ACACCCTGACTAAGGCCAAA	5’-TCCAGGGATCCTTCCAGAT
MYH7B	5’-TCCGCGGATATTGACAGC	5’-TCACCAGGCAACTGGAAGAT

Supplemental Table 4. ChIP primers.		
Mouse Gene	**Forward**	**Reverse**
Myh7 -10.2 k	5’-GGGGAAAGGACACAGCCTA	5’-CTAATCTCCCCTCCTATTATTAGCC
Myh7 -9.4 k	5’-GCCCCTTGCACAAGCCTAAA	5’-CATGGGGATGGTGACCTTGC
Myh7 -2882	5’-GAGACTAGCTCAGCTCCCTAA	5’-AGGAGTGGTAGCCAGCACTT
Myh7 +20077	5’-CCATTGCCAGGGTCTAAGATGGTGCTG	5’-GCAGAGGTGGAAAGTGGAATGAGCTG
Myh7b -7	5’-GGGCTGTGACACGTGGAGAT	5’-CGGAGCACTGCTACCCCTTT
Myh7b -2.0 k	5’-CTCTCCTGGACCGGCTTC	5’-GAAAGGAACTCTGAGGGATGG