Supplemental Data

AMPK and PPARδ **Agonists**

Are Exercise Mimetics

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Table S1. Gene targets unique to combined GW1516 treatment and exercise training. The following genes were identified in microarray analysis as unique targets of combined GW1516 and exercise training. Down-regulated genes are in bold italics. $(N=3,$ each pooled from 3 mice, $p<0.05$).

Table S2. Genes regulated by combination of GW1516 treatment and exercise training in quadriceps. The following is a list of target genes identified by microarray analysis and categorized into functional classes. The down-regulated genes are in bold italics. Data is average of N=3 samples in each group ($p<0.05$). Combination of drug treatment and exercise created a gene signature in muscles that was unique from either treatment alone. Thirty-two percent of these genes encode enzymes of metabolic pathways such as fatty acid biosynthesis/storage (e.g. *Fasn*, *Scd 1 & 2*), uptake [e.g. *Cd36*, fatty acid binding proteins (*Fabp*) and *Lpl*] and oxidation [e.g. adiponectin, hormone sensitive lipase (*Lipe*), *Pdk4*, *Ucp3*]; and carbohydrate metabolism [e.g. fructose bisphosphate 2 (*Fbp2*), phosphoenolpyruvate carboxykinase 1 (*Pck1*), lactate dehydrogenase B], which along with oxygen transporters and mitochondrial proteins form the largest class of genes directly linked to muscle performance (Ikeda et al., 2002; Achten and Jeukendrup, 2004; Hittel et al., 2005; Civitarese et al., 2006; Nadeau et al., 2006; Kiens, 2006; Yamauchi et al., 2006). All but 4 of these genes were induced, suggestive of a general increase in oxidative capacity. Furthermore, additional pathways including angiogenesis (e.g. angiopoietin-like 4 protein/also a known regulator of lipid metabolism), signal transduction (e.g. adrenergic receptor β3, insulin-like growth factor, insulin-like growth factor binding protein 5), transcription (e.g. *Cebpa*, *Nr1d2*, *Nr4a2*) and substrate transport (e.g. transferrin, chloride channel 5) were identified, implicating relevance to muscle remodeling and endurance (Nagase et al., 1996; Singleton and Feldman, 2001; Adams, 2002; Centrella et al., 2004; Lundby et al., 2005; Mahoney et al., 2005a and b; Ramakrishnan et al., 2005).

Table S3. Selective GW1516 and/or exercise induced genes including heat shock proteins, metallothioneins and other stress biomarkers are not changed by the combination possibly reflecting a potential lessening of exercise-based damage (Liu and Steinacker, 2001; Jagoe et al., 2002; Koh, 2002; McArdle et al., 2002; Lecker et al., 2004). Data is average of N=3 samples in each group ($p<0.05$).

Table S4. Targets common to exercise-PPARδ and AMPK-PPARδ gene signatures. Comparison of gene signature generated by either combined PPARδ activation and exercise with that of PPARδ and AMPK co-activation revealed 52 common target genes listed below. Data is average of $N=3$ samples in each group (p<0.05).

Figure S1. PPARδ **activation in muscle. (A-C)** Regulation of oxidative genes by GW1516 in wild type and PPARδ null primary muscle cells. **(D)** Muscle triglycerdise levels. **(E-F)** Epididymal fat to body weight ratio **(E)** and cross-sectional area **(F)** in indicated groups of mice. **(G)** List of selective oxidative genes induced in muscle by combined PPARδ and AMPK activation as well as VP16-PPARδ over-expression determined by microarray analysis. * represents statistical significance between V and indicated groups (p<0.05, One Way ANOVA; post hoc: Dunnett's Multiple Comparison Test).

Figure S2. Synergistic regulation of muscle gene expression by PPARδ **and AMPK. (A)** Venn diagram comparing GW, Tr and AI+GW target genes identified in microarray analysis of quadriceps. Data is an average of $N=3$ samples in each group. The selection criteria used a p<0.05 on Bonferroni's multiple comparison test. **(B)** Classification of AI+GW target genes.

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