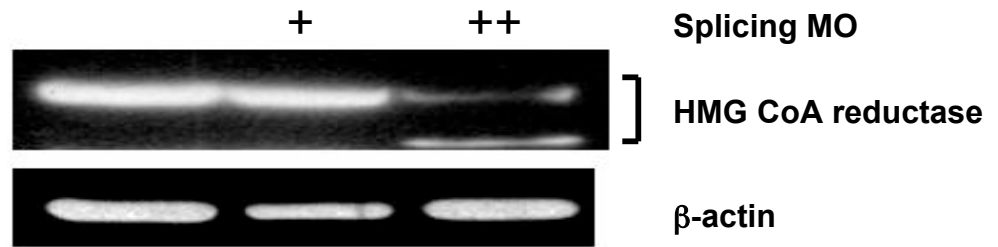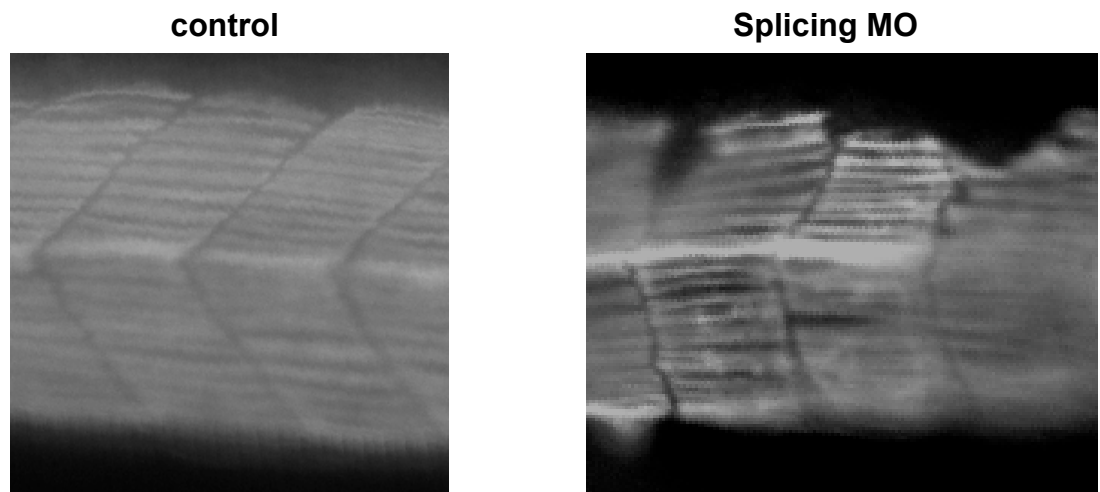Supplemental Figure 1

A.

+ ++   **Splicing MO**

HMG CoA reductase

β-actin

B.

control

Splicing MO

Supplemental Figure 2

A.

24 h   48 h

control   PGC-1α   control   PGC-1α

← myc-PGC-1α

GAPDH

B.

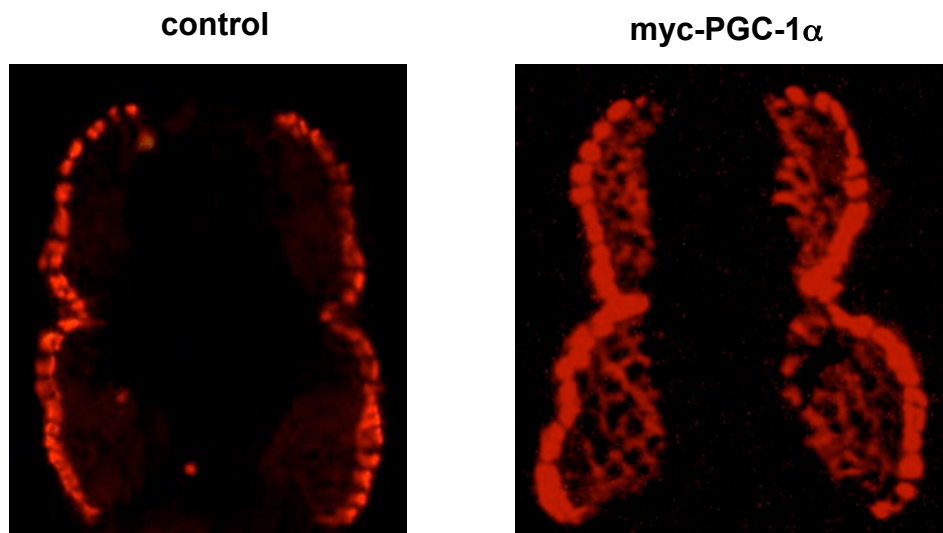control   myc-PGC-1α
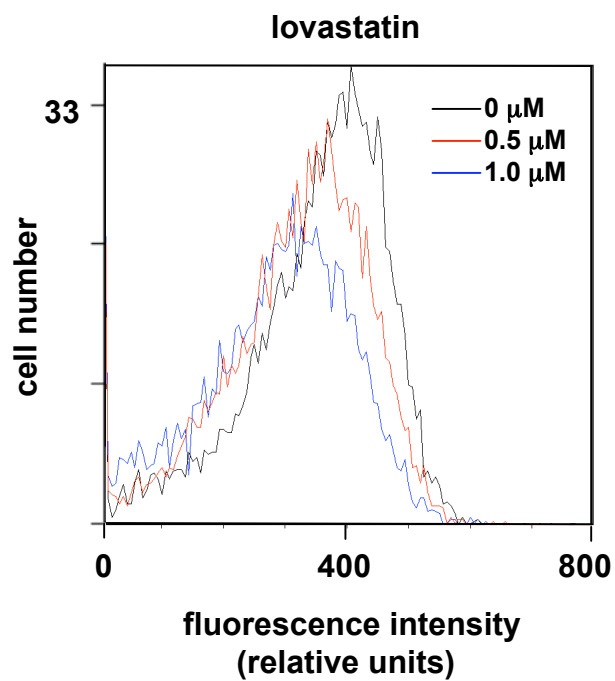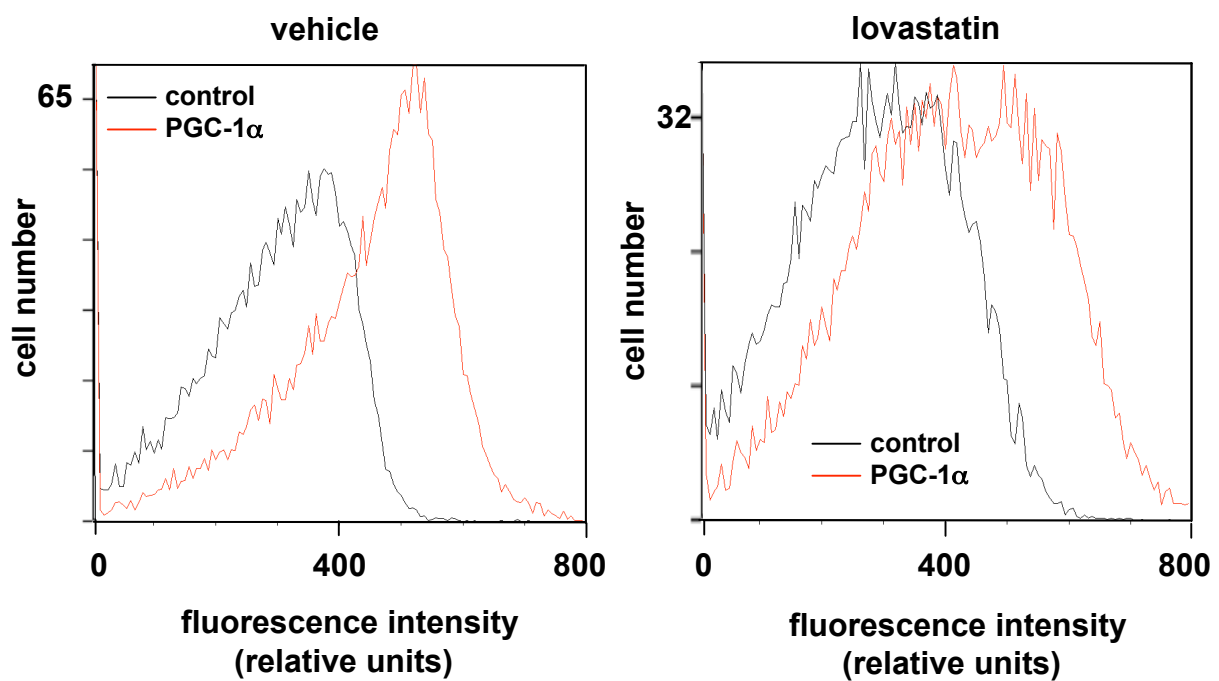
Supplemental Figure 3

Supplemental Figure 4

SUPPLEMENTAL DATA

Supplemental Figure 1. <u>Atrogin-1 mRNA levels are increased in both male and female patients following statin treatment.</u> Total RNA was extracted from human quadriceps muscle biopsies and atrogin-1 mRNA was quantitated by real-time PCR as described in Methods. Results were plotted separately for male and female subjects.

Supplemental Figure 2. <u>Validation of morpholinos against zebrafish HMG CoA reducatse.</u> **A**. Morpholino oligonucleotide (MO) was designed against the common splice site of both splice variants of the zebrafish HMG CoA reductase gene. rtPCR performed using pooled total RNA extracted from 5 zebrafish embryos injected with 0, low (125 μM, +) or high (250 μM, ++) concentrations of the morpholino demonstrating reduction in quantity of full-length message and appearance of smaller splice variant HMG CoA reductase transcript. PCR primers: 5'-ACA AACTGG AGG CCA TGA TGG AGA-3' and 5'-TGG CAC CCA GAA CAC CTA ACA TCT-3' **B**. Myosin heavy chain staining of representative control and HMG CoA reductase knockdown using splicing morpholino oligonucleotides in zebrafish embryos.

Supplemental Figure 3. <u>Injection of PGC-1α cDNA into zebrafish embryos leads to PGC-1α protein overexpression.</u> **A.** Western blot against the myc

epitope in protein lystaes from control injected and myc-PGC-1α-injected

zebrafish embryos. **B.** Cross-sectional F59 staining of representative control and

myc-PGC-1α injected zebrafish embryos.

Supplemental Figure 4. A. Mitochondrial function is diminished by lovastatin

treatment of zebrafish embryos. Raw fluorescence intensity tracings for

experiment presented in Figure 9E. Representative data from 3 independent

experiments is shown. **B.** PGC-1α augments mitochondrial staining and protects

against lovastatin's effects in zebrafish embryos. Raw fluorescence intensity

tracings for experiment presented in Figure 9F.

Supplemental Table 1. Human muscle biopsies from statin-treated and statin-untreated patients.

Group/Bx Number		Age	Sex	Diagnosis	Clinical Data	Statin
Statin-treated	3	51	M	Statin-associated myopathy	Muscle pain and weakness, CK 47	atorvastatin
	4	75	M	Statin-associated myopathy	Muscle pain and weakness, CK 73	atorvastatin
	5	41	M	Statin-associated myopathy	Muscle pain and weakness, CK 62	simvastatin
	6	52	M	Statin-associated myopathy	Muscle pain and weakness, CK 649	simvastatin
	40	60	M	Statin-induced rhabdomyolysis	Weakness, CK 932	lovastatin
	41	82	F	Statin-induced rhabdomyolysis	Weakness, CK 51,080	simvastatin
	43	87	M	Statin-induced rhabdomyolysis	Weakness, CK 8,264	simvastatin
	45	62	F	Statin-induced rhabdomyolysis	Weakness, CK 39,000	simvastatin
Non-statin myopathy	20	46	M	Non-specific myopathy	Muscle pain and weakness, CK 635	None
	22	39	F	Non-specific myopathy	Muscle pain and weakness	None
	24	57	F	Non-specific myopathy	Muscle pain and weakness	None
	27	46	F	Non-specific myopathy	Muscle pain and weakness, CK 2,300	None
	48	31	M	Non-specific myopathy	Recurrent rhabdomyolysis	None
	51	41	M	Minor myopathic changes	Muscle pain and weakness, CK 800	None
Control	31	73	F	osteoarthritis	Knee pain	None
	33	61	F	osteoarthritis	Knee pain	None
	34	71	F	osteoarthritis	Knee pain	None
	35	67	F	osteoarthritis	Knee pain	None
	36	87	F	osteoarthritis	Knee pain	None