Supplementary Figure 1

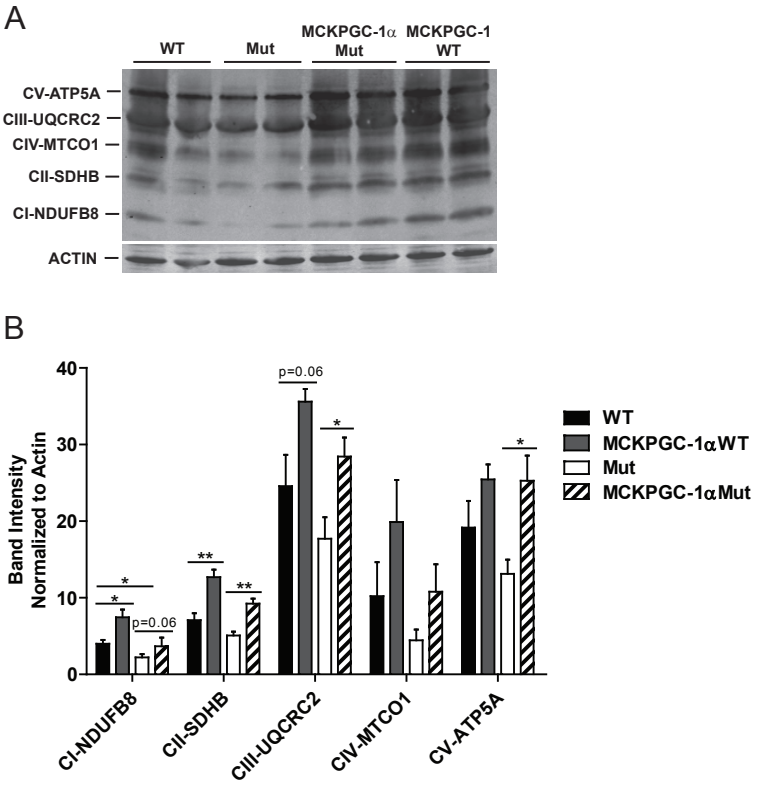

Fig. S1. Increased PGC-1α expression increases mitochondrial protein levels in the gastrocnemius of Mut mice. (A) Western blot showing the levels of mitochondrial proteins in the gastrocnemius of 10 month-old male mice showing loading control actin. ATP5A (subunit of complex V), UQCRC2 (subunit of complex III), MTCO1 (subunit of complex IV), SDHB (subunits of complex II) and NDUFB8 (subunit of complex I) (n = 4/group). (B) Quantification of western blot in (A) showing protein levels normalized to actin. * P< 0.05, **P< 0.01 Student's t-test. Error bars represent S.E.M

Supplementary Figure 2

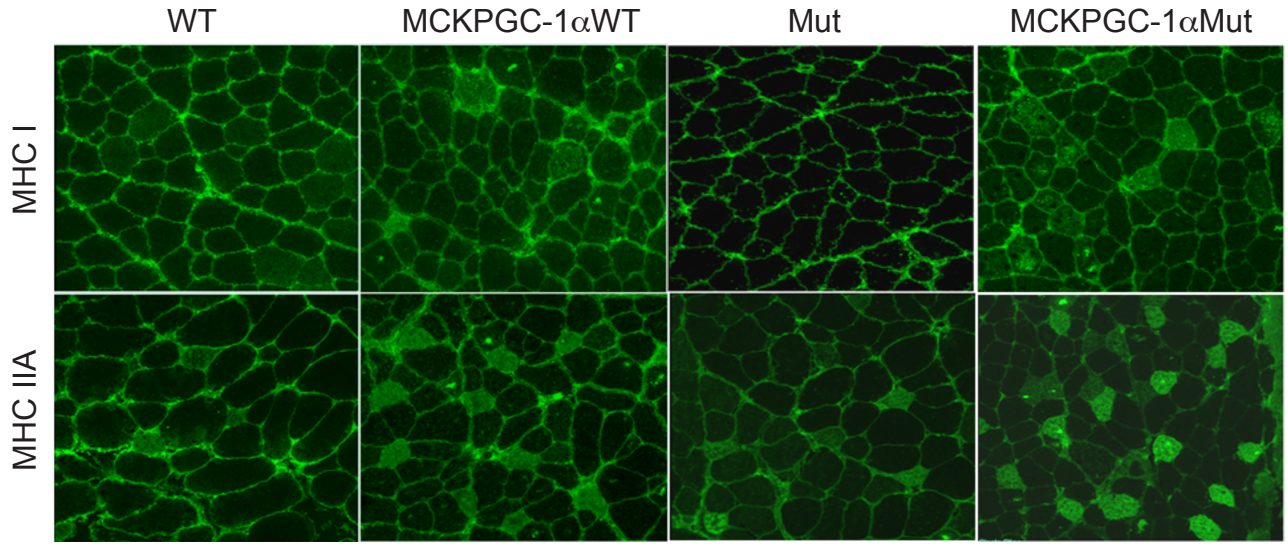

Fig. S2. Increased PGC-1α expression increases oxidative fibers in the quadriceps of Mut mice. (A) Immunohistochemisty results showing MHC I (type I) and MHC IIA (type IIA) (green) positive fibers in frozen transverse sections from the quadriceps of 10 month-old male mice (n = 3/group).

Supplementary Figure 3

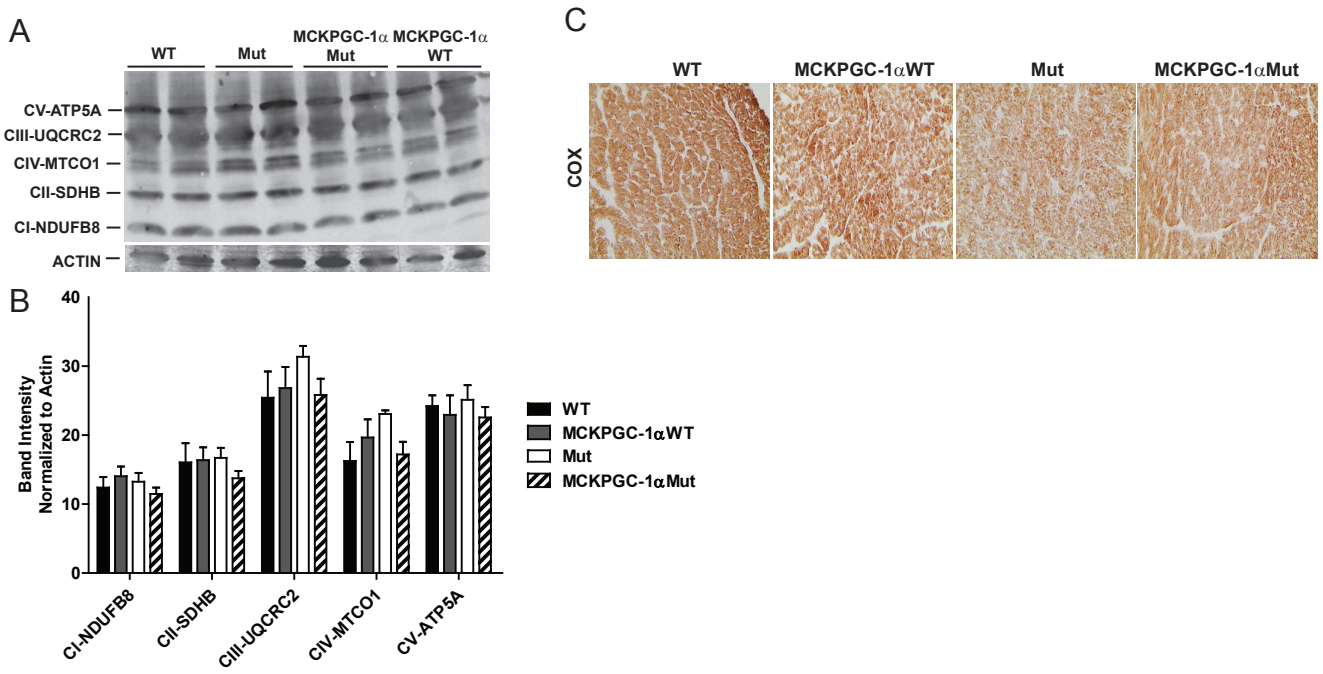

Fig. S3. Increased PGC-1α expression has no effect on mitochondrial protein levels but increases COX activity in the heart of Mut mice. (A) Western blot showing the levels of mitochondrial proteins in the heart of 10 month-old male mice showing loading control actin. ATP5A (subunit of complex V), UQCRC2 (subunit of complex III), MTCO1 (subunit of complex IV), SDHB (subunits of complex II) and NDUFB8 (subunit of complex I) (n = 4/group). (B) Quantification of western blot in (A) showing protein levels normalized to actin. (C) Histology of the heart showing transverse heart sections from 10 month-old mice stained for COX (complex IV) activity (n = 3/group). Error bars represent S.E.M

Supplementary Figure 4

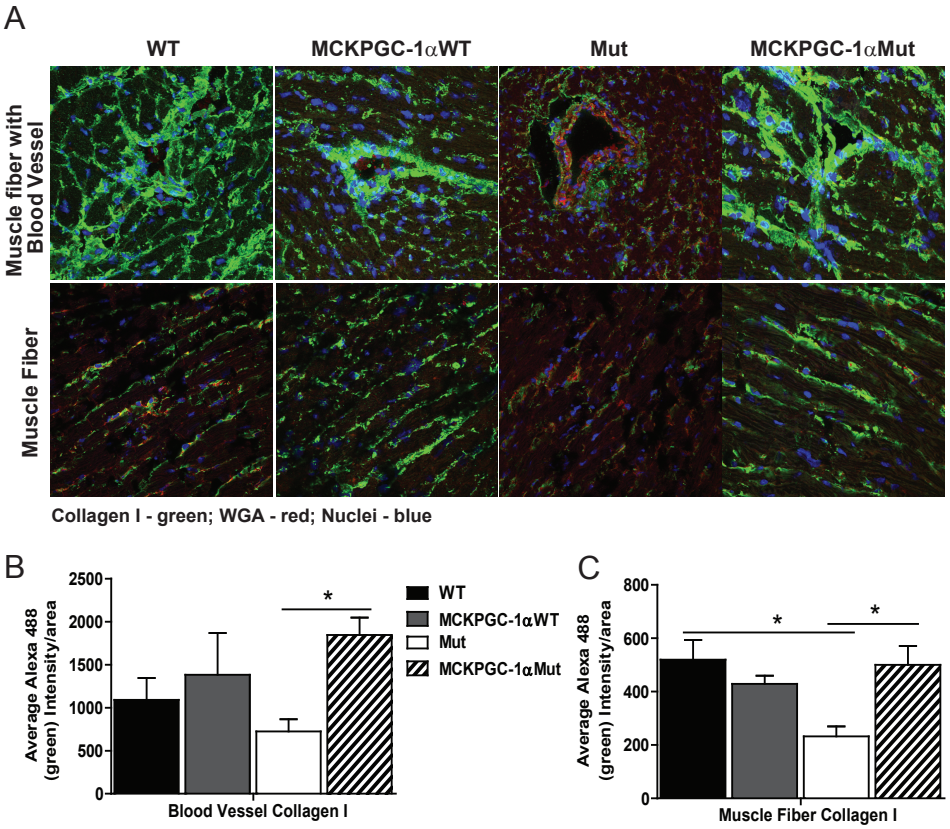

Fig. S4. Increased PGC-1α expression is associated with restored collagen I levels in the heart of Mut mice. (A) Immunohistochemistry results showing collagen I (green), wheat germ agglutinin (WGA) (red) (used to label the plasma membrane) and nuclei (blue) around blood vessels and along muscle fibers in frozen transverse sections from the heart of 10 month-old male mice. (B) Quantification of the intensity of Alexa 488 (green) representing collagen I around blood vessels of the heart shown in (A). (C) Quantification of the intensity of Alexa 488 (green) representing collagen I along muscle fibers of the heart shown in (A). (n = 3/group). * P< 0.05, Student's t-test. Error bars represent S.E.M.

Supplementary Figure 5

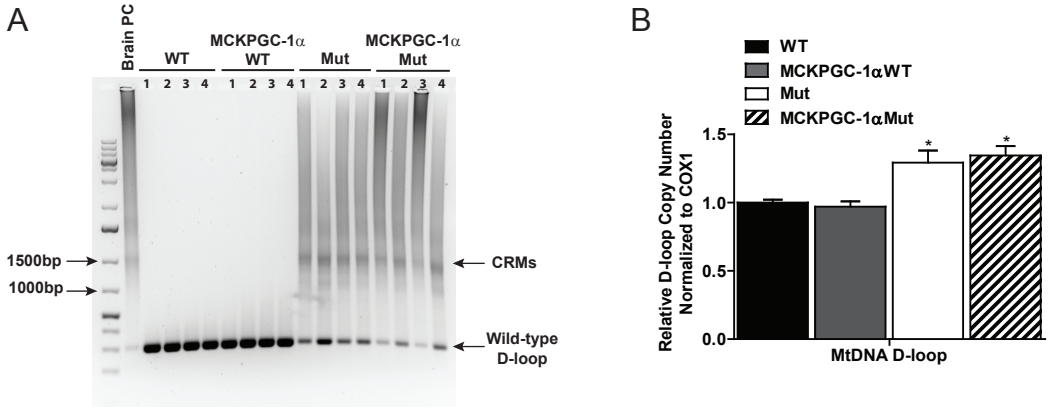

Fig. S5. Increased PGC-1α expression has no effect on CRMs in the heart of Mut mice. (A) Agarose gel showing the amplification of CRMs in total DNA from the heart of 10 month-old male Mut and MCKPGC-1αMut mice. Positive control (PC) Mut mouse brain sample is used as a marker for CRMs. The "wild-type" D-loop is shown in all 10 month-old male mice analyzed. (n = 4/group numbered 1-4). (B) QPCR result showing mtDNA D-loop expression in the heart of 10 month-old mice relative to WT. Expression is normalized to COX1 (subunit of complex IV) (n = 4/group). * $P < 0.05$ Student's t-test. Error bars represent S.E.M.

Supplementary Figure 6

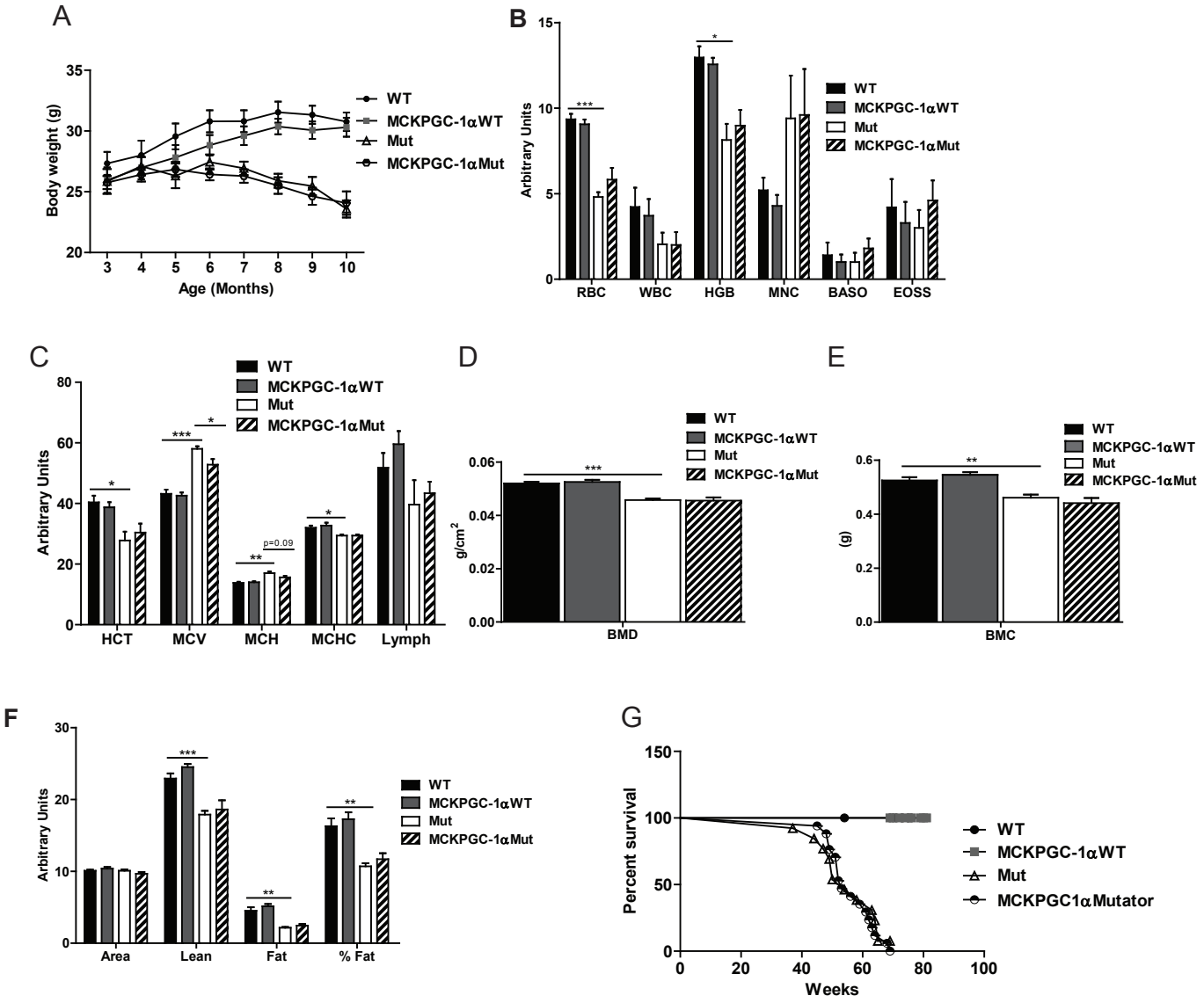

Fig. S6. Increased PGC-1α expression has mild systemic effects on Mut mice. (A) Changes in the body weight of male mice from 3 to 10 months of age (n = 11/group). (B) Data from complete blood cell count in 10 month-old male mice showing RBC (red blood cells, x106µl), WBC (white blood cells, x106µl), HGB (hemoglobin, g/dL), MNC (monocytes, %), BASO (Basophils, %) and EOSS (Eosinophils, %) (n = 5-7/group). (C) Results of complete blood cell count in 10 month-old male mice showing HCT (hematocrit, %), MCV (mean corpuscular volume, fL), MCH (mean corpuscular hemoglobin, pg), MCHC (mean corpuscular hemoglobin concentration, %) and Lymph (lymphocytes, %) (n = 5-7/group). (D) BMD (bone mineral density) and (E) BMC (bone mineral content) measurement in 10 month-old male mice (n = 5-7/group). (F) Measurement of total body area (cm2), lean mass (g), total body fat (g) and percent fat (%) (n = 5-7/group). (G) Percent survival of MCKPGC-1αMut (n = 17) compared to Mut (n = 13), MCKPGC-1αWT (n = 17) and WT mice (n = 17). * P< 0.05, **P< 0.01, ***, P< 0.001 Student's t-test. Error bars represent S.E.M