Appendix:

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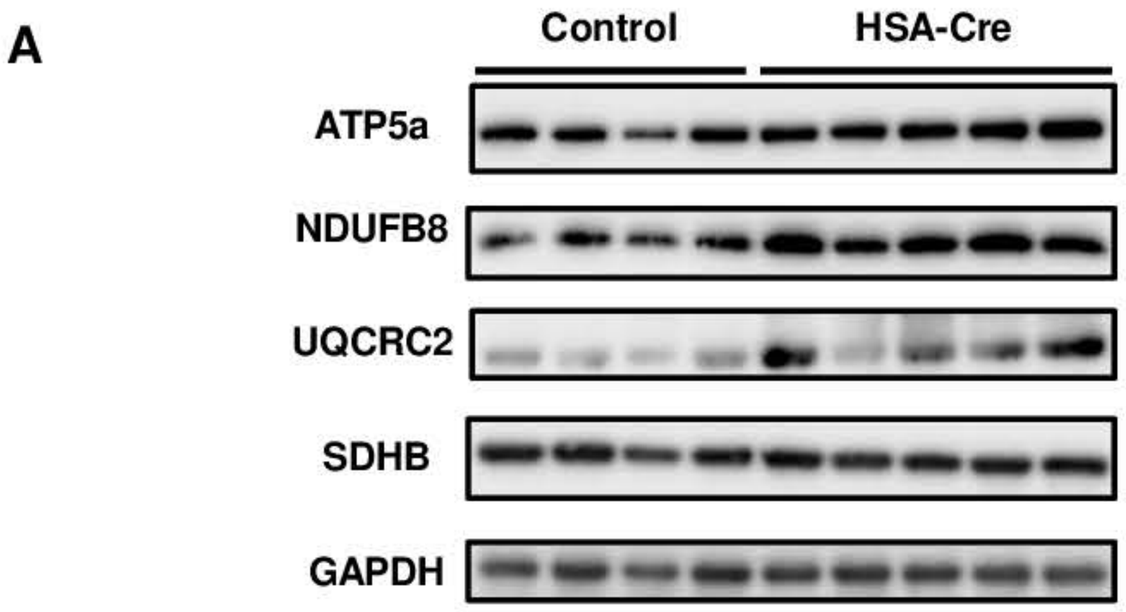
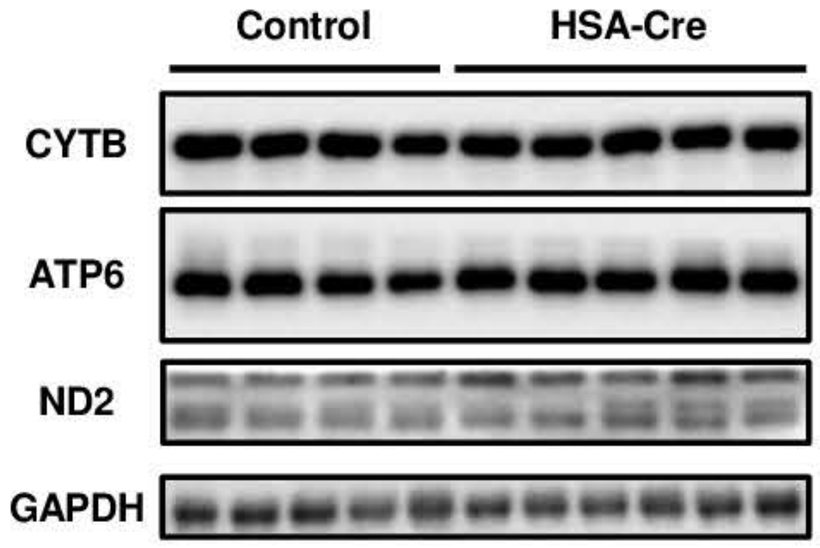
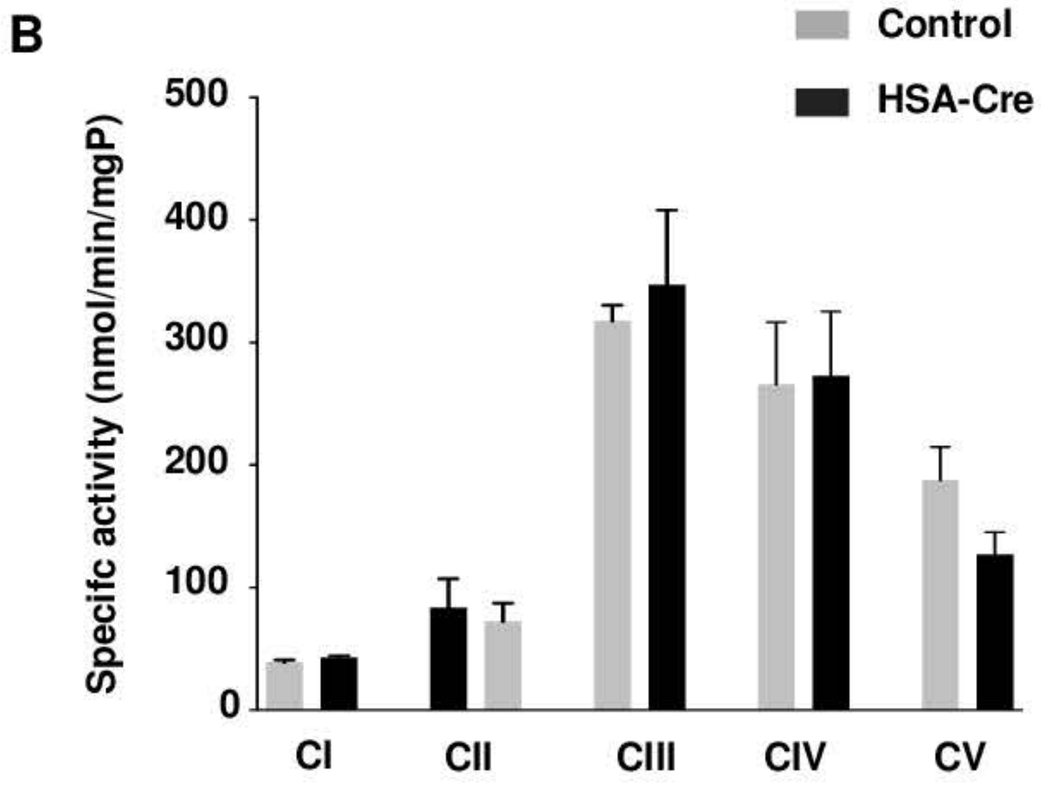
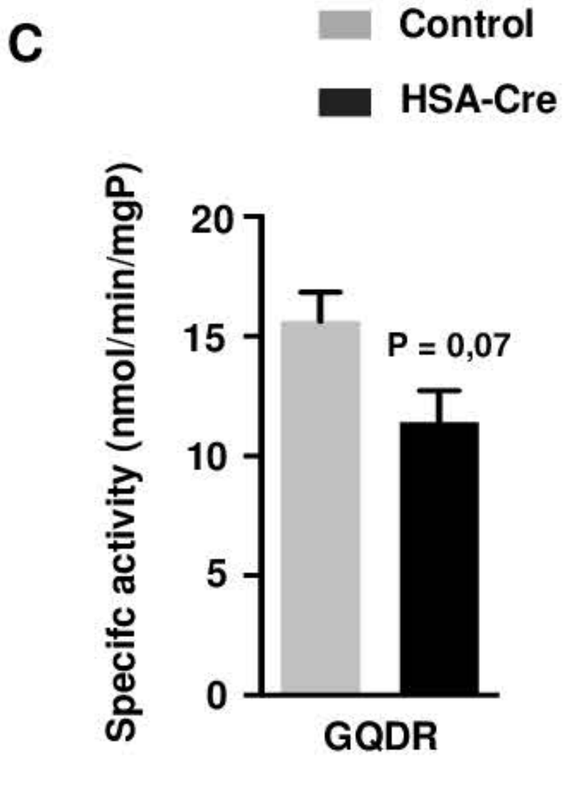
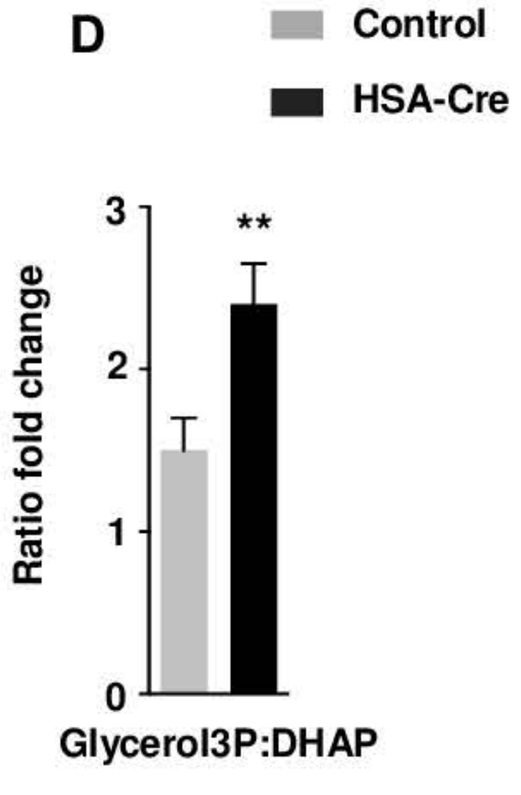
Appendix Figure S1

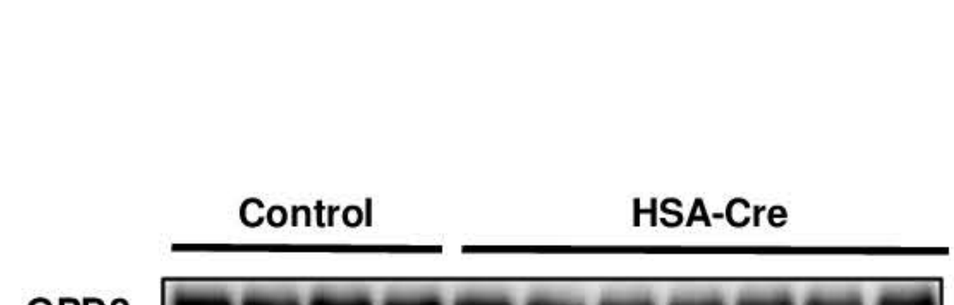


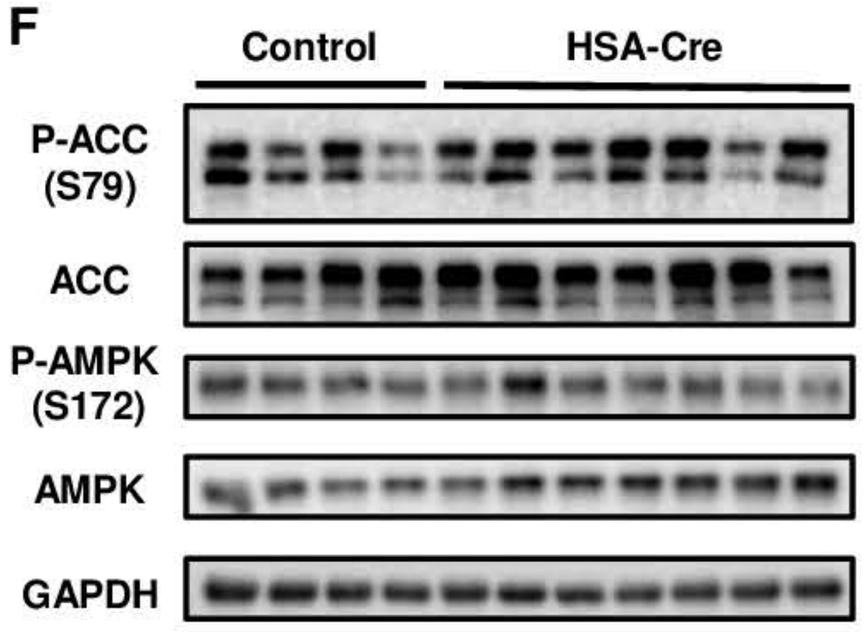


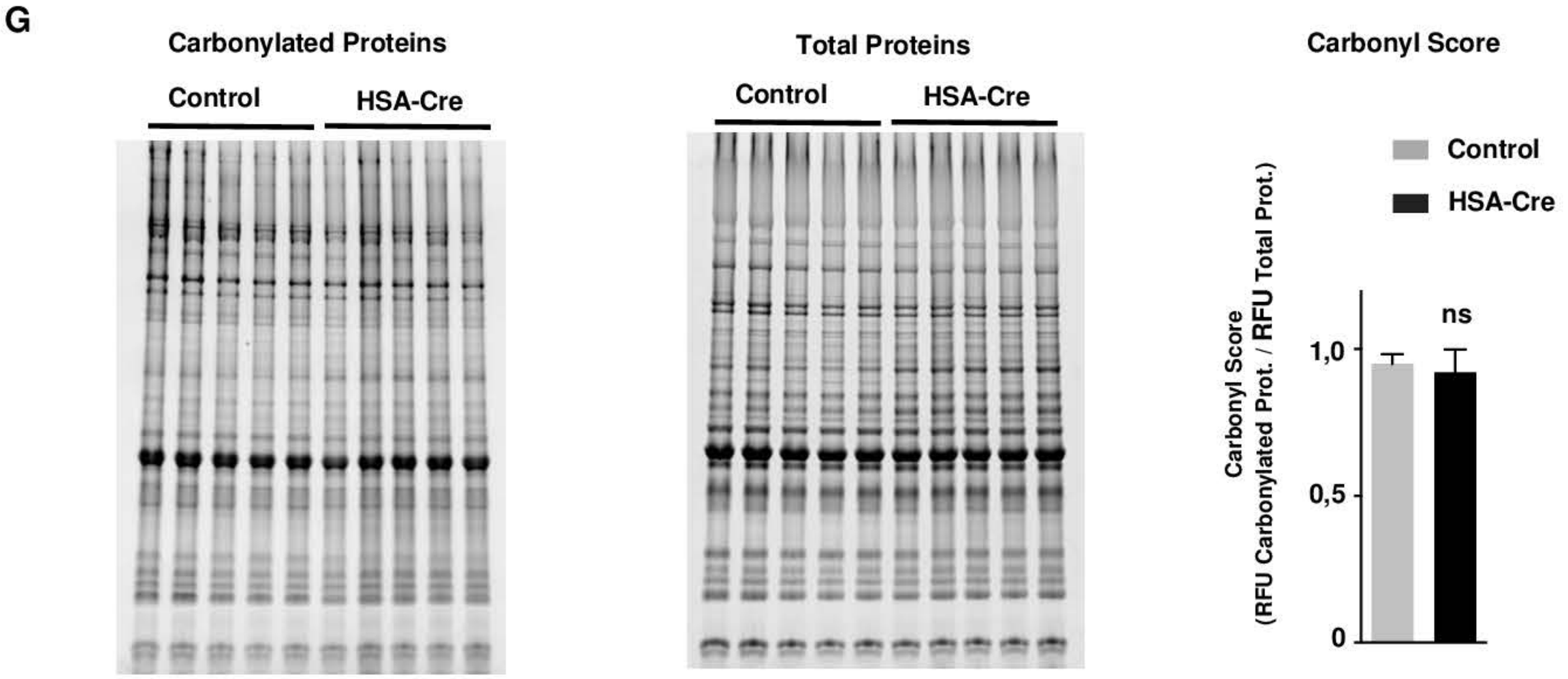












Appendix Fig. S1

(**A**) Representative immunoblots from protein extracts of GC muscles of 4-month-old *HSA-Cre* and control mice, with the indicated antibodies against ATP synthase subunit alpha (ATP5A), NADH:ubiquinone oxidoreductase subunit B8 (NDUFB8), ubiquinol-cytochrome c reductase core protein 2 (UQCRC2), sucinate dehydrogenase complex iron sulfur subunit B (SDHB), Cytochrome B (CYTB), ATP synthase F0 subunit 6 (ATP6), NADH dehydrogenase subunit 2 (ND2).

(**B**) Respiratory chain activity measurements of complex I to V (CI to CV) in GC muscles of 3 month-old *HSA-Cre* and control mice. Data are mean ± SEM.

(**C**) Activity measurement of GQDR in GC muscles of 3 month-old *HSA-Cre* and control mice. Data are mean ± SEM (n =3).

(**D**) Fold change of Glycerol-3P/DHAP in GC muscles of 4 month-old *HSA-Cre* and control mice, assessed by LC-MS. (n=7, 4) $^{**}P<0.01$).

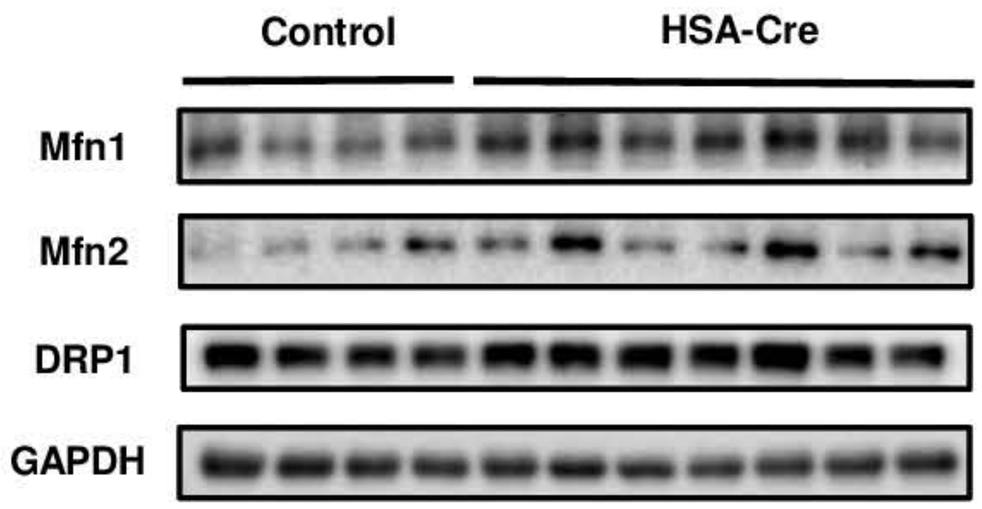
(**E**) Immunoblot analysis of GPD2 in GC muscles of 4-month-old *HSA-Cre* and control mice (n=7, 4).

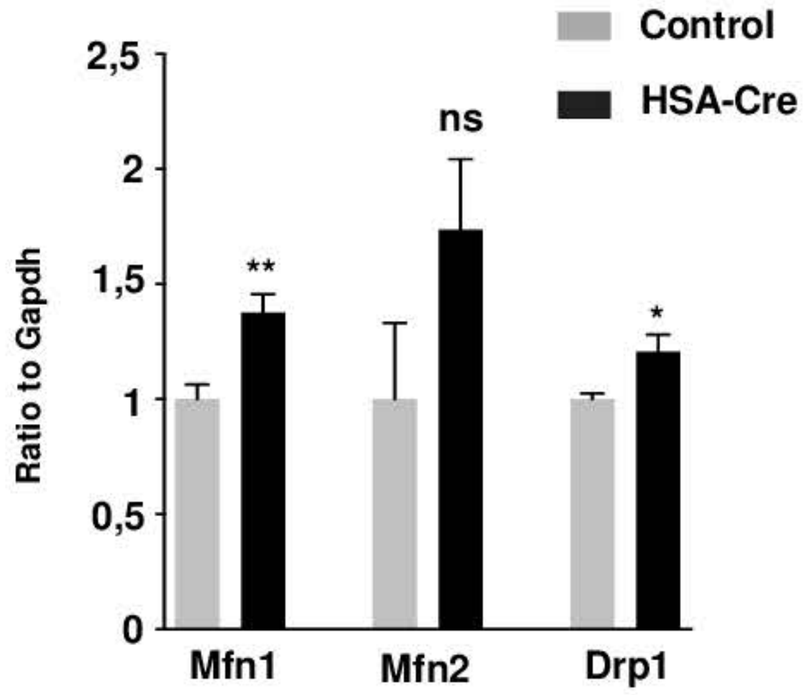
(**F**) Representative immunoblots from protein extract of GC muscles of 4-month-old *HSA-Cre* and control mice, with the indicated antibodies. This experiment was simultaneously run with experiments in EV1A, S2A, S2B and the same loading control was used.

(**G**) Carbonylated and total protein profiles from GC muscles from 6-month-old *HSA-Cre* and control mice. Carbonyl Score calculated by densitometric analysis of carbonylated protein western-blots. (n =5)

Appendix Figure S2

A





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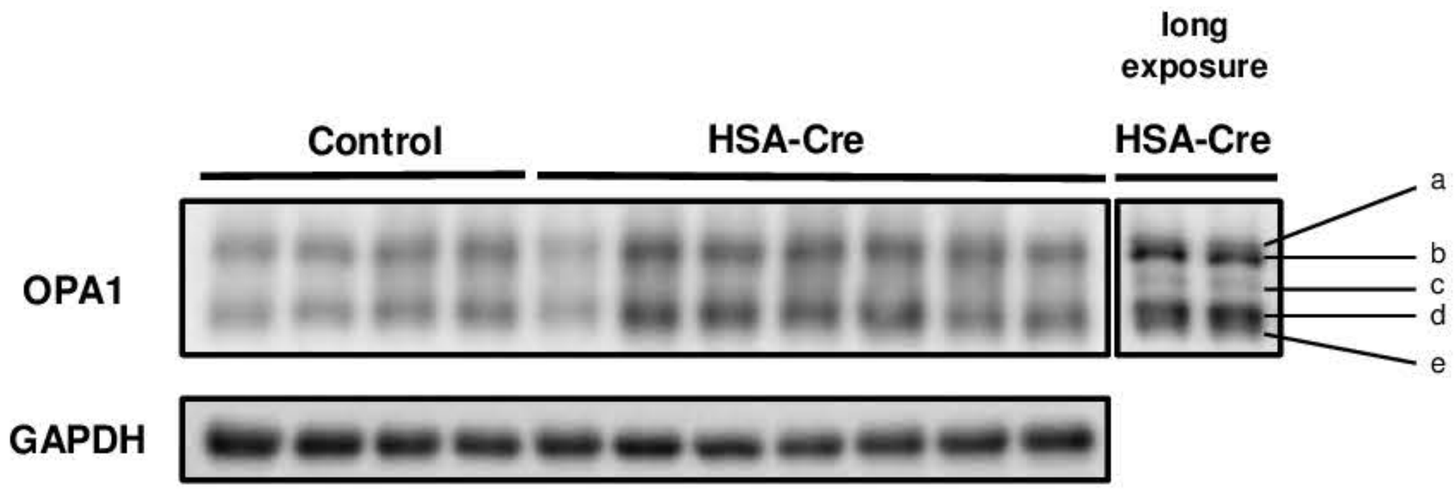

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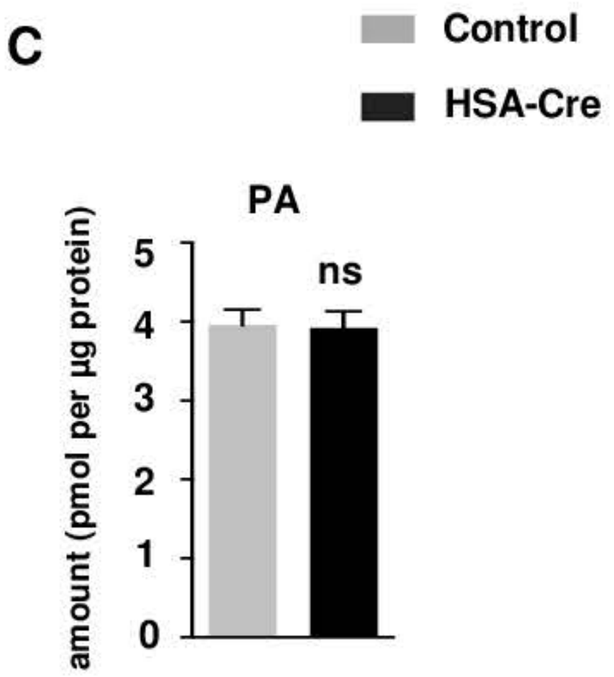

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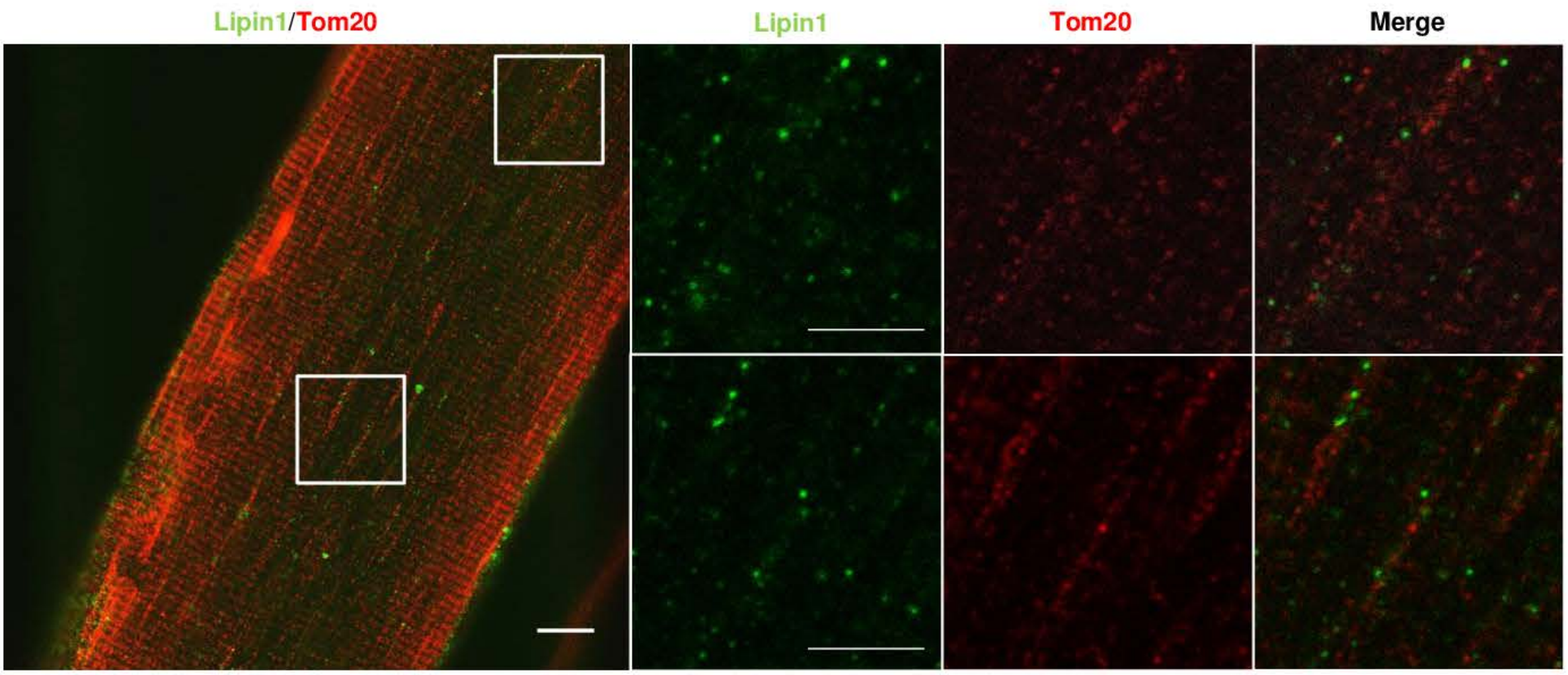


Appendix Fig. S2

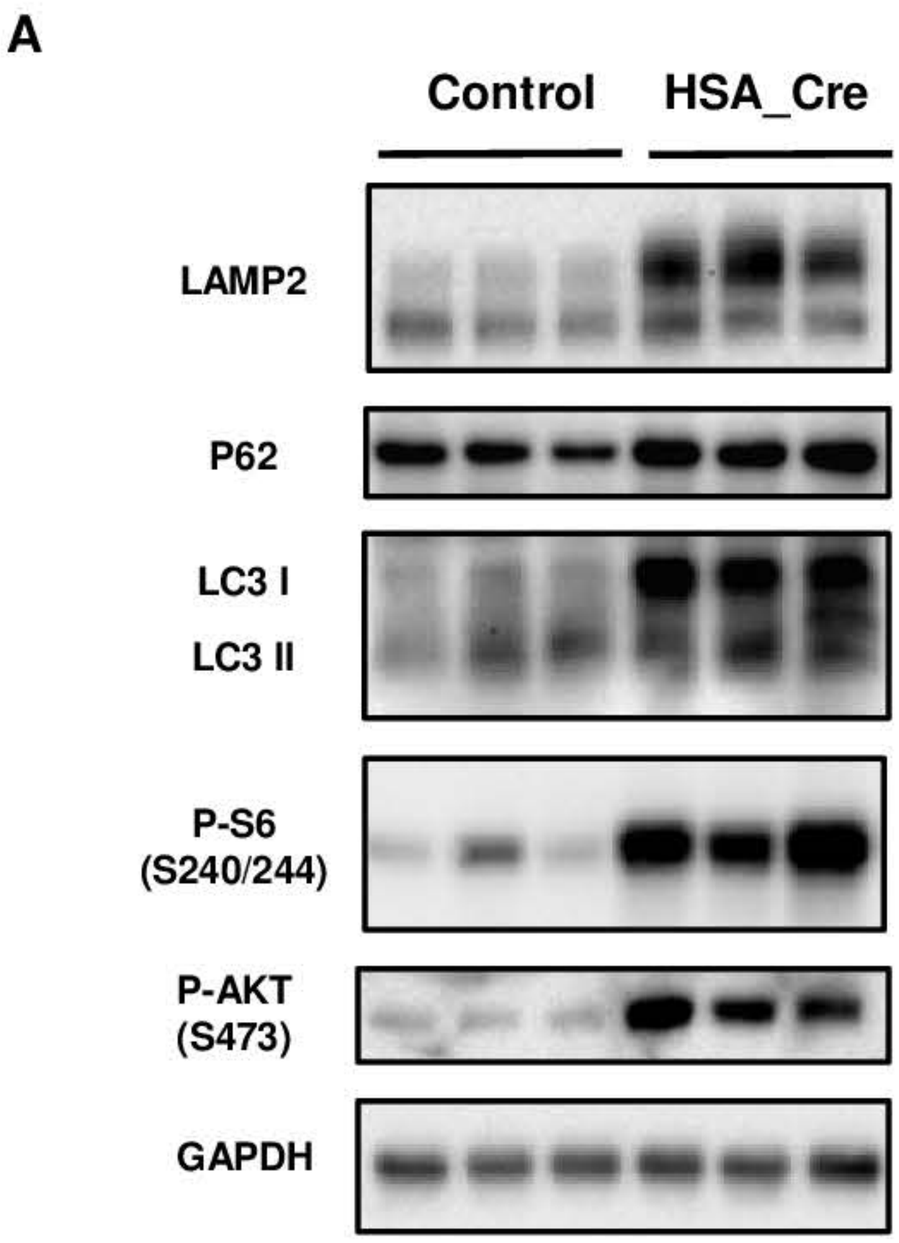
(**A**) Representative immunoblots from protein extract of GC muscles of 4-month-old *HSA-Cre* and control mice, with the indicated antibodies. Quantification by densitometric analyses of Mfn1, Mfn2, and Drp1 protein levels is presented as a graph. Data are normalized to Gapdh and expressed as a fold change relative to the control mice. Data are mean ± SEM (n=7-4; **P*<0.05, ***P*<0.01). This experiment was simultaneously run with experiments in EV1A, S1F, S2B and the same loading control was used.

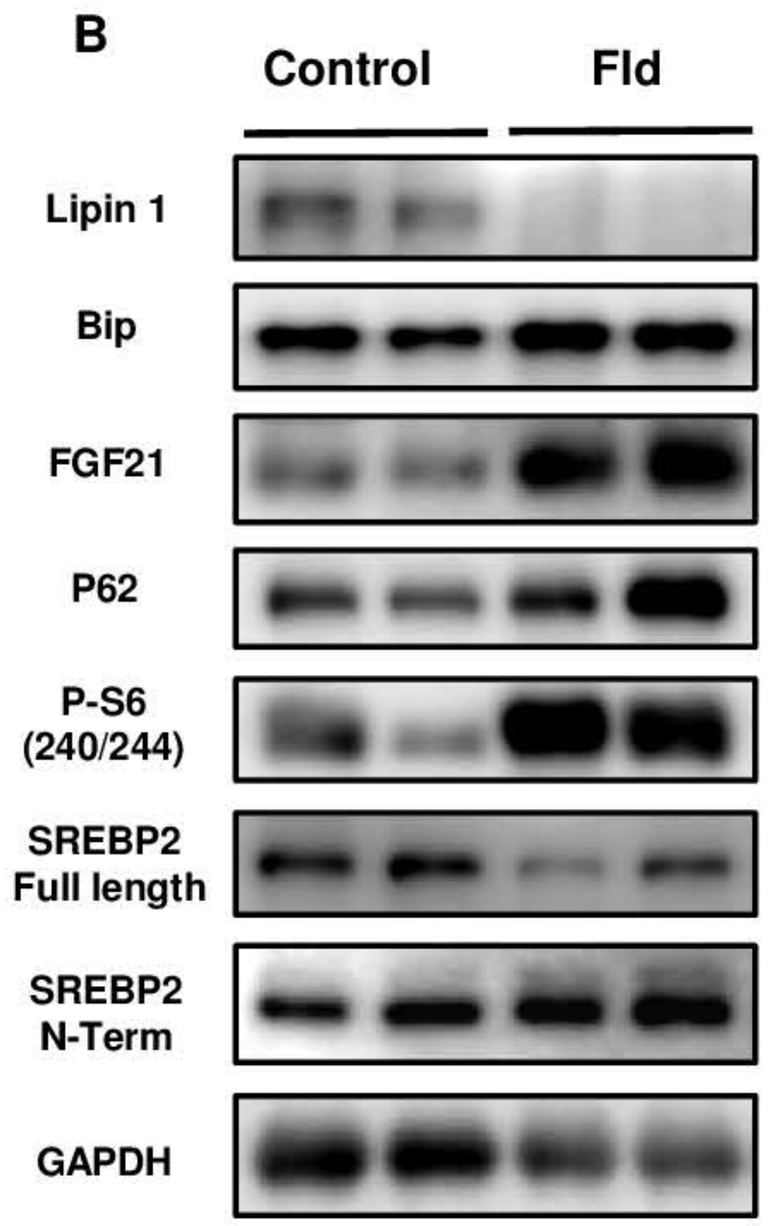
(**B**) Immunoblot analysis of Opa1 in GC muscle of 4-month-old *HSA-Cre* and control mice. This experiment was simultaneously run with experiments in EV1A, S1F, S2A and the same loading control was used.

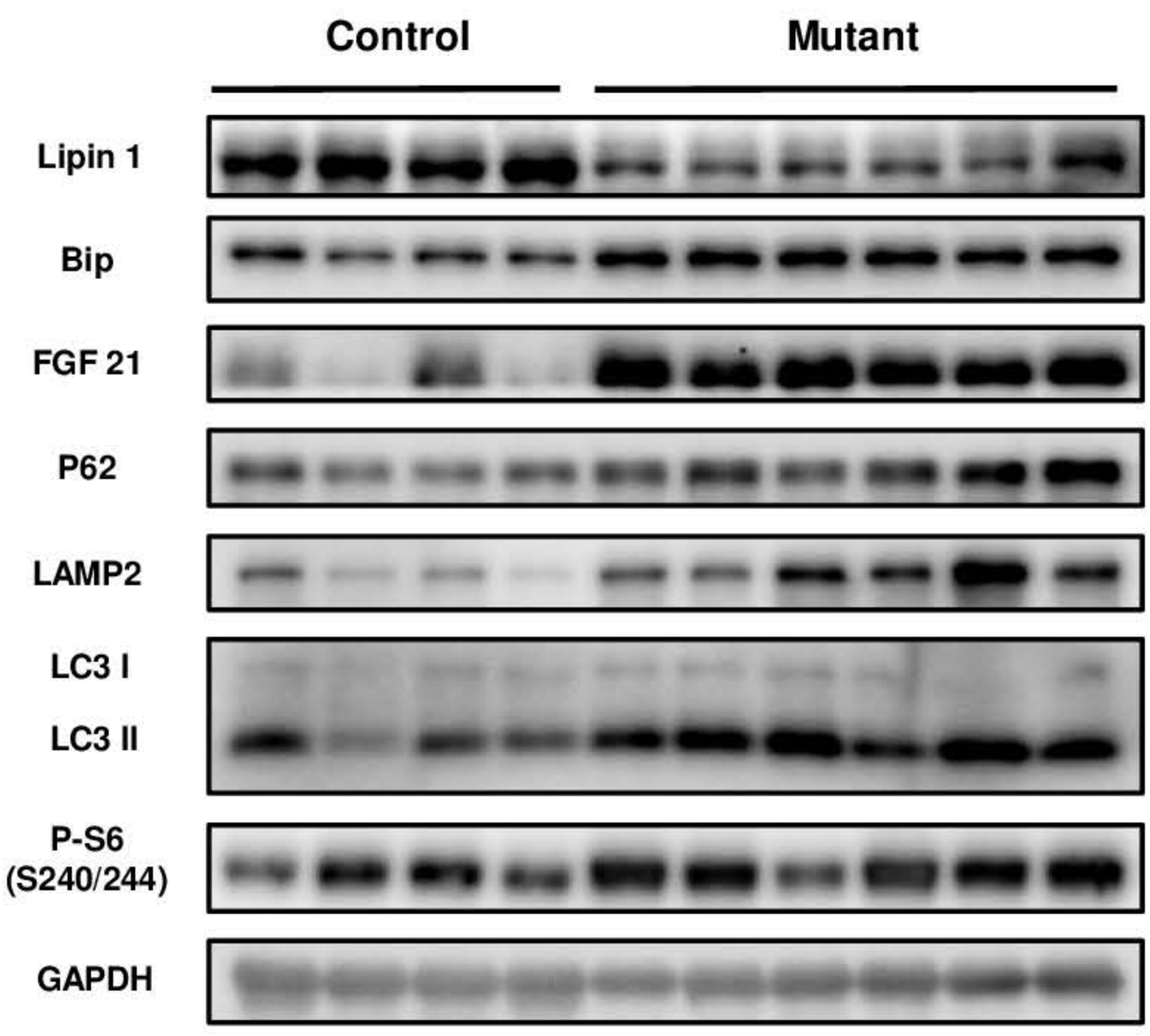
(**C**) PA levels in pure mitochondria fraction from GC from Lipin1 Mutant and control rats. Data are mean ± SEM (n=3).

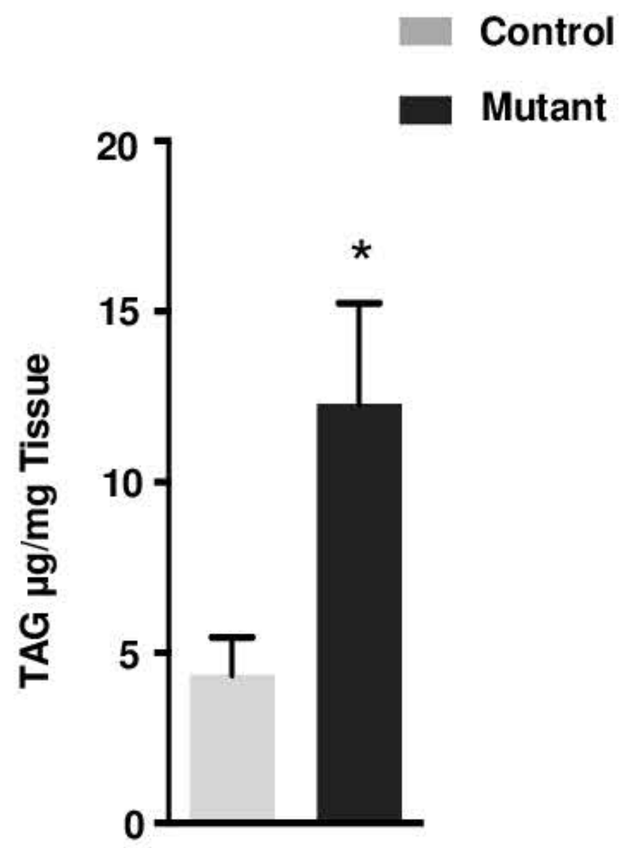
(**D**) Isolated EDL muscle fibers were double-stained with an antibody against Lipin1 (green) and with an antibody against Tom20 (red). Each image represented one single confocal plane. Scale bars: 10 µm

Appendix Figure S3









Appendix Fig. S3

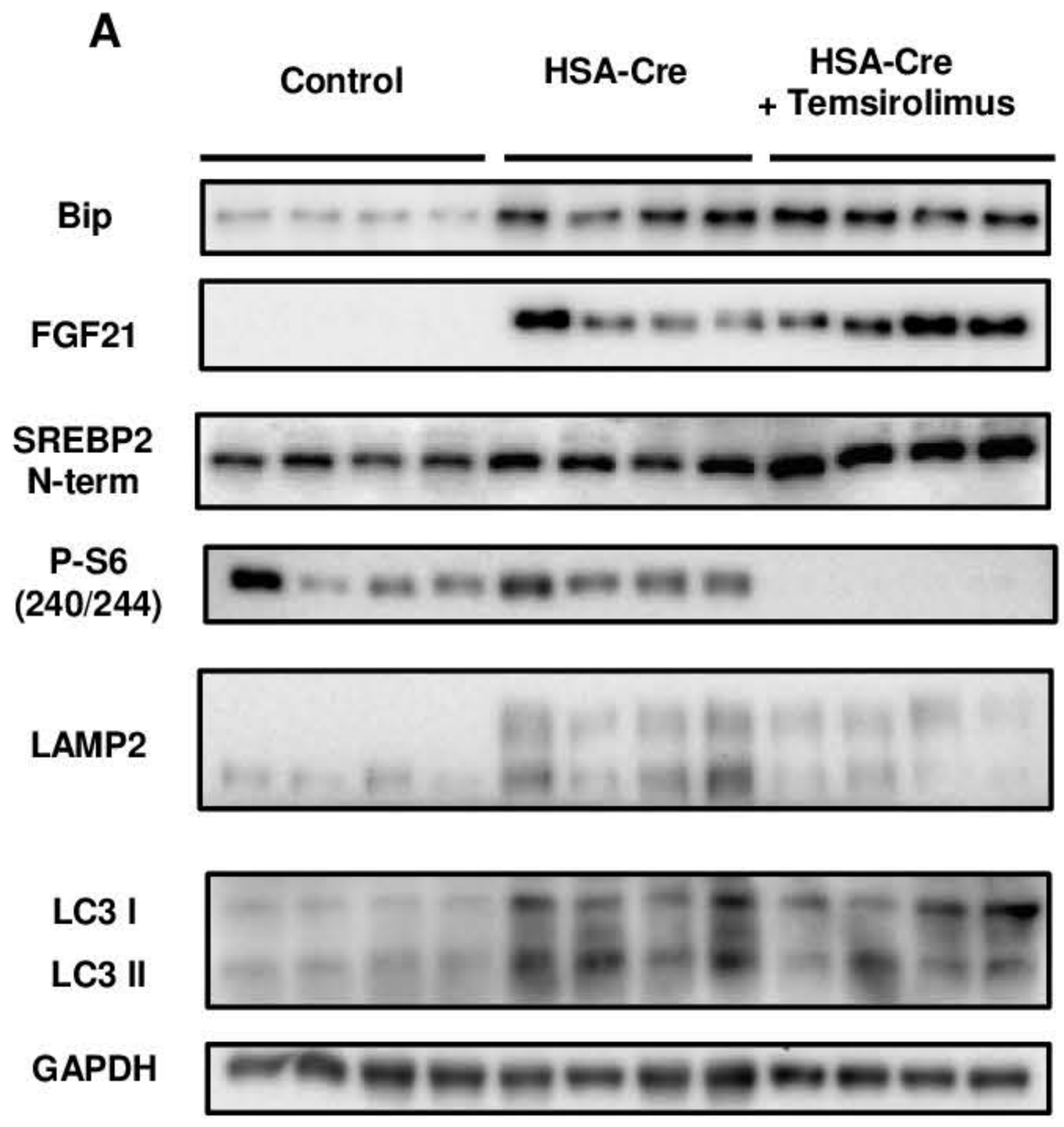
(**A**) Representative immunoblots from protein extract of GC muscles of 4-month-old *HSA-Cre* and control mice, with the indicated antibodies.

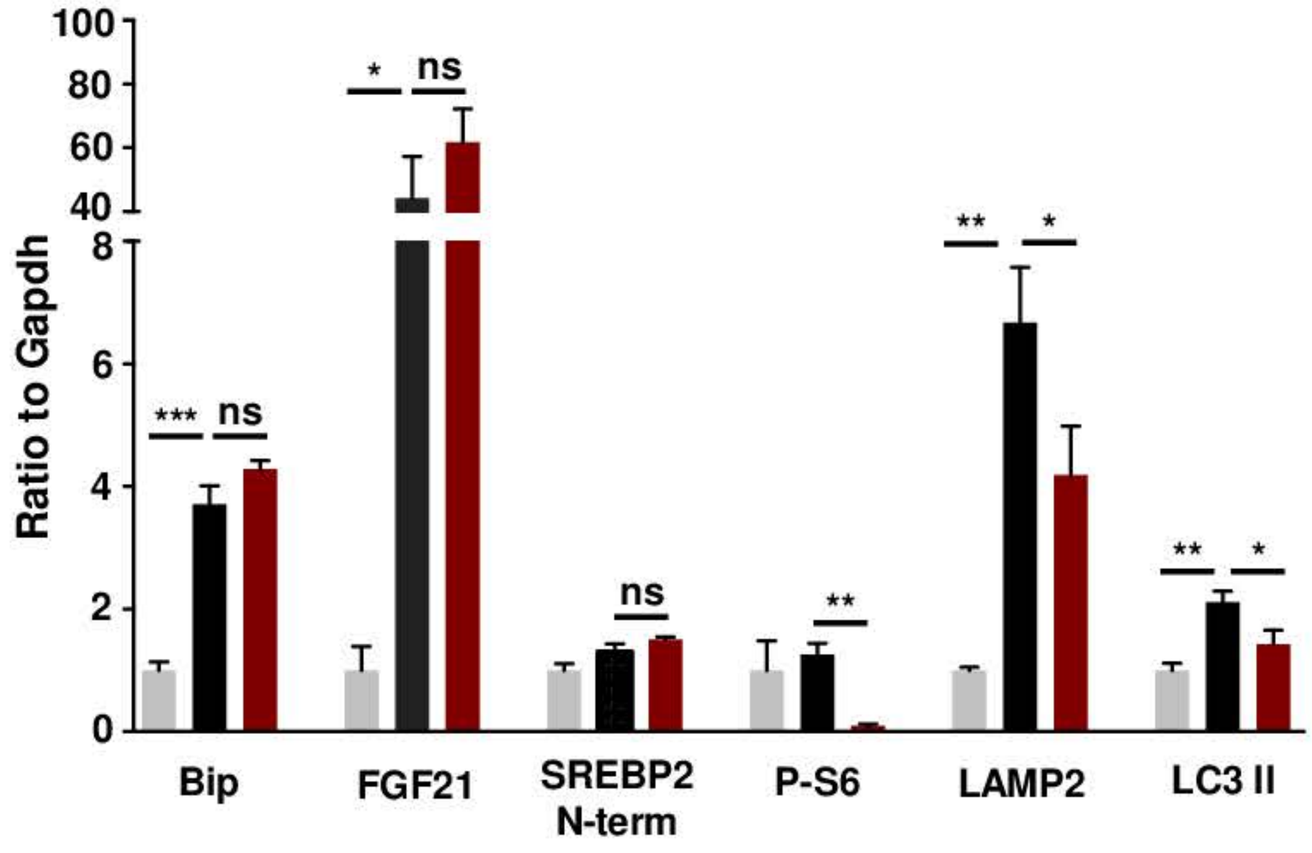
(**B**) Representative immunoblots from protein extract of GC muscles of 3-month-old *Fld* and control mice, with the indicated antibodies.

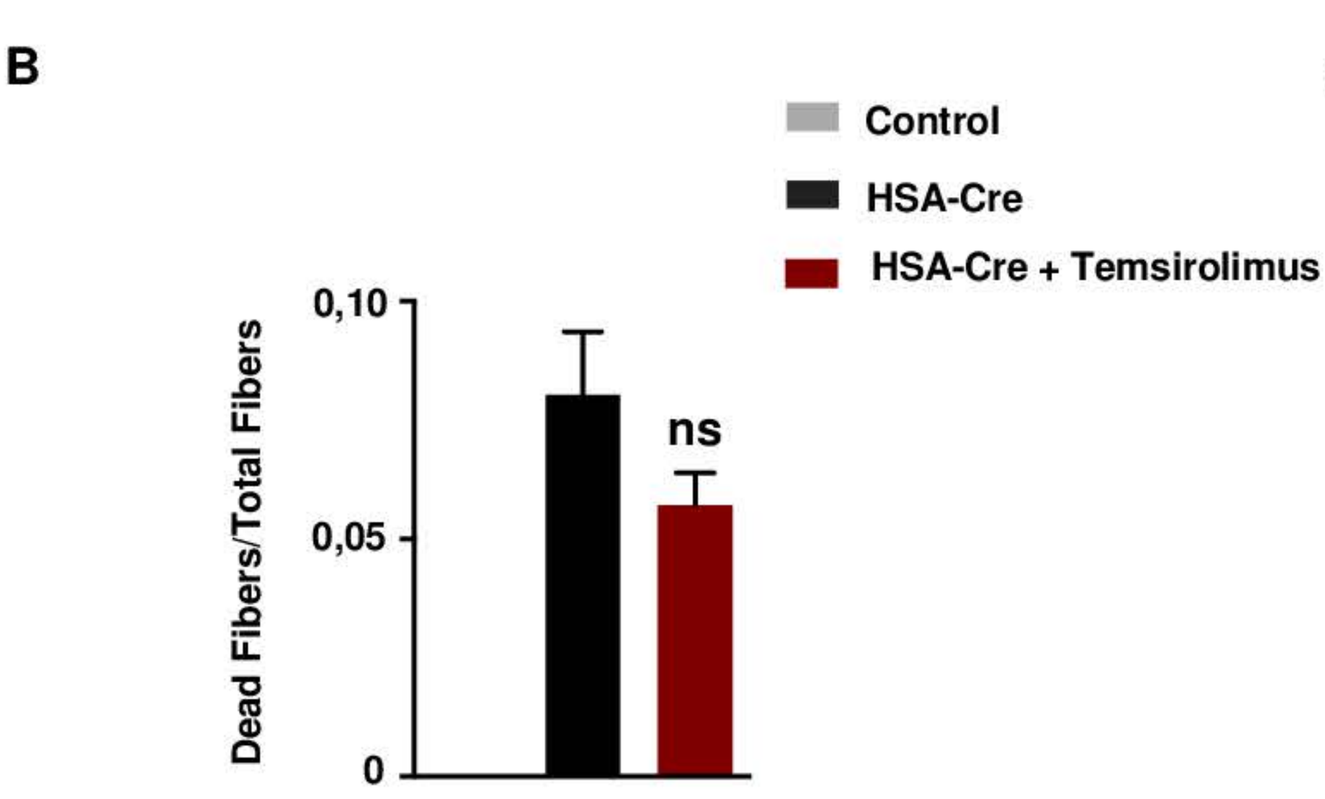
(**C**) Representative immunoblots from protein extract of GC muscles of 3-month-old Lipin1 Mutant and control rats, with the indicated antibodies.

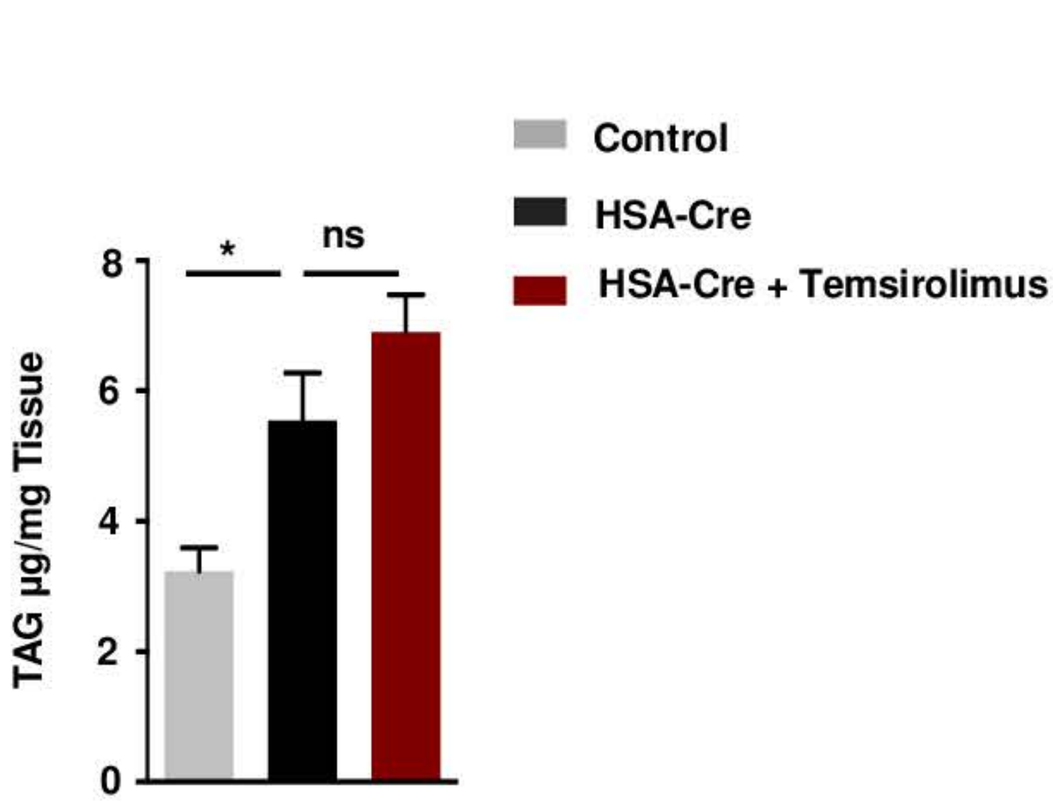
(**D**) TAG level measurement in GC muscles of 3-month-old Lipin1 Mutant and control rats. Data are mean ± SEM (n=5-6; **P*<0.05).

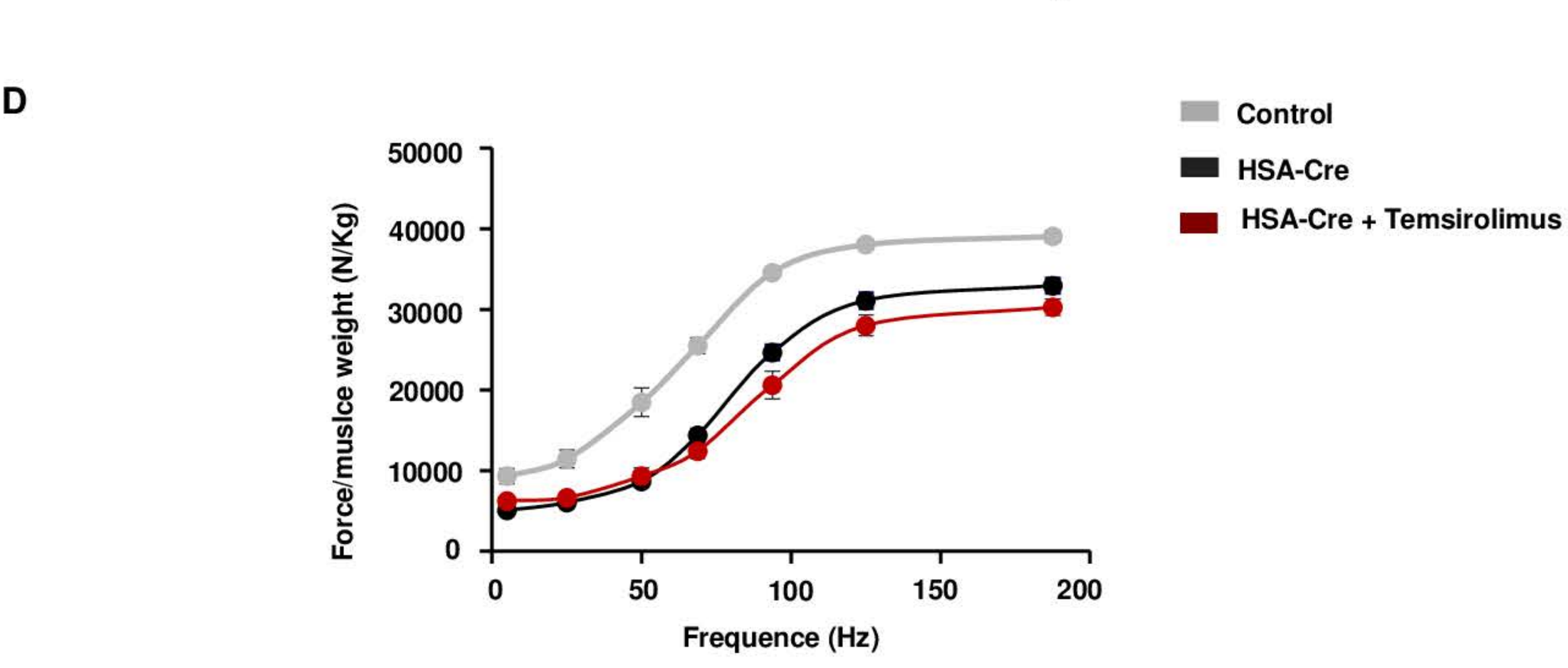
Appendix Figure S4











Appendix Fig. S4

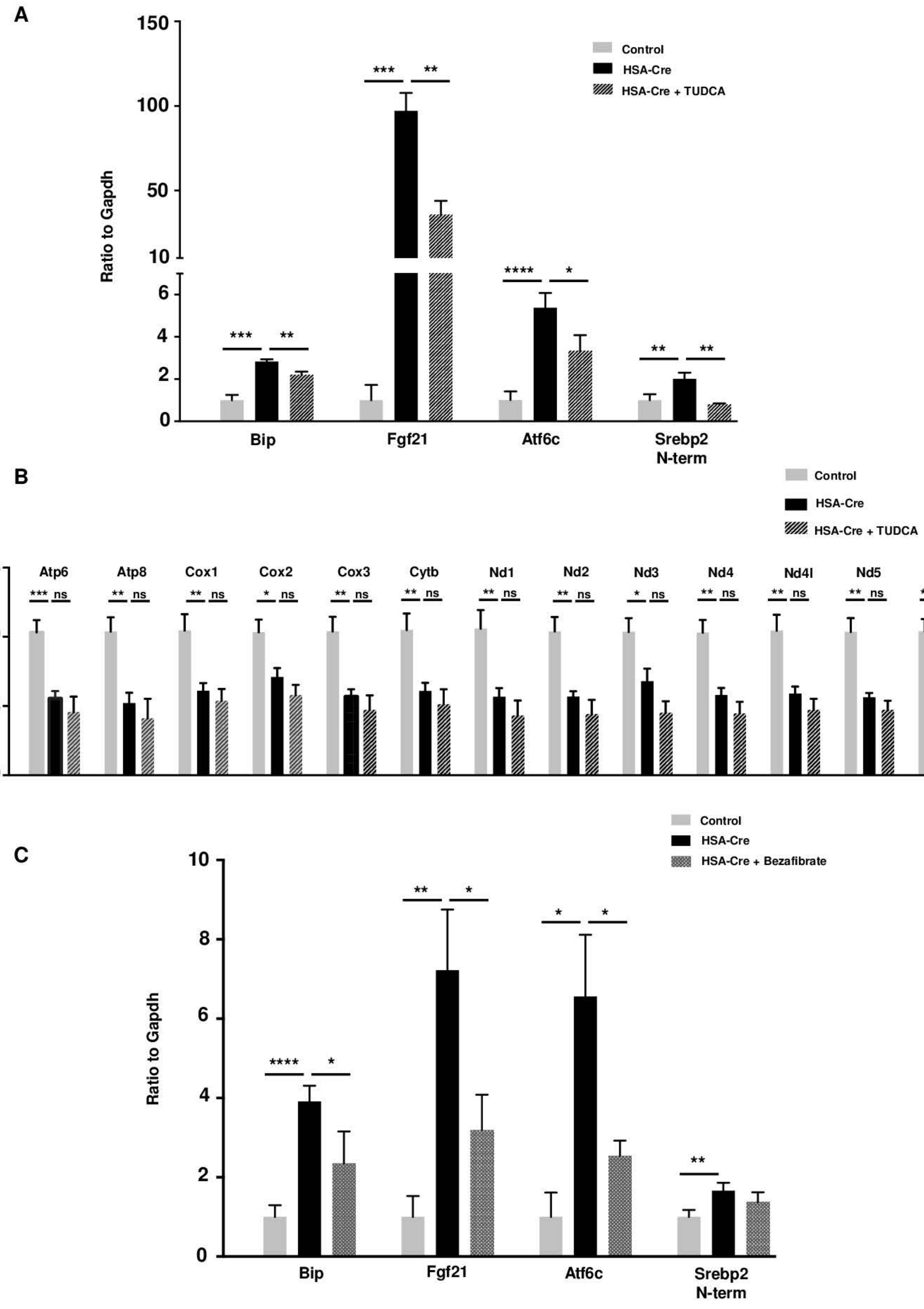
(**A**) Representative immunoblots from protein extract of GC muscles of 4-month-old control, *HSA-Cre* untreated and *HSA-Cre* Temsirolimus-treated mice, with the indicated antibodies. Quantification by densitometric analyses of Bip, FGF21, SREBP2 N-term, P-S6, LAMP2, and LC3 II protein levels is presented as a graph. Data are normalized to Gapdh and expressed as a fold change relative to the control mice. Data are mean ± SEM (**P*<0.05, ***P*<0.01, ****P*<0.001).

(**B**) Quantification of the number of necrotic fibers over the total number of fibers in TA of 4-month-old control, *HSA-Cre* untreated and *HSA-Cre* Temsirolimus-treated mice. Data are mean ± SEM.

(**C**) TAG levels measurement in GC muscles of 4-month-old control, *HSA-Cre* untreated and *HSA-Cre* Temsirolimus-treated mice. Data are mean ± SEM (n=4; **P*<0.05).

(**D**) In vivo force measurements performed on GC muscles of 3-month-old control, *HSA-Cre* untreated and *HSA-Cre* Temsirolimus-treated mice. Data are mean ± SEM (n= 3).

Appendix Figure S5



Appendix Fig. S5

(**A**) Quantification by densitometric analyses of Bip, Fgf21, Atf6 cleaved form, Srebp2 N-term form protein levels (Fig. 8A) is presented as a graph. Data are normalized to Gapdh and expressed as a fold change relative to the control mice. Data are mean ± SEM (n=4-7; **P*<0.05, ***P*<0.01, ****P*<0.001, *****P*<0.0001).

(**B**) Mitochondria-encoded genes expression levels analysis by quantitative RT-PCR in GC muscles from 6-month-old *HSA-Cre* mice treated with TUDCA, untreated and control mice. Data are mean ± SEM (n = 4; **P*<0.05, ***P*<0.01, ****P*<0.001).

(**C**) Quantification by densitometric analyses of Bip, Fgf21, Atf6 cleaved form, Srebp2 N-term form protein levels (Fig. 9A) is presented as a graph. Data are normalized to Gapdh and expressed as a fold change relative to the control mice. Data are mean ± SEM (n=4-7; **P*<0.05, ***P*<0.01, *****P*<0.0001).