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Supplementary Materials for

Rapamycin Reverses Elevated mTORC1 Signaling in Lamin A/C–Deficient Mice, Rescues Cardiac and Skeletal Muscle Function, and Extends Survival

Fresnida J. Ramos, Steven C. Chen, Michael G. Garelick, Dao-Fu Dai, Chen-Yu Liao, Katherine H. Schreiber, Vivian L. MacKay, Elroy H. An, Randy Strong, Warren C. Ladiges, Peter S. Rabinovitch, Matt Kaeberlein,* Brian K. Kennedy*

*To whom correspondence should be addressed. E-mail: bkennedy@buckinstitute.org (B.K.K.); kaeber@uw.edu (M.K.)

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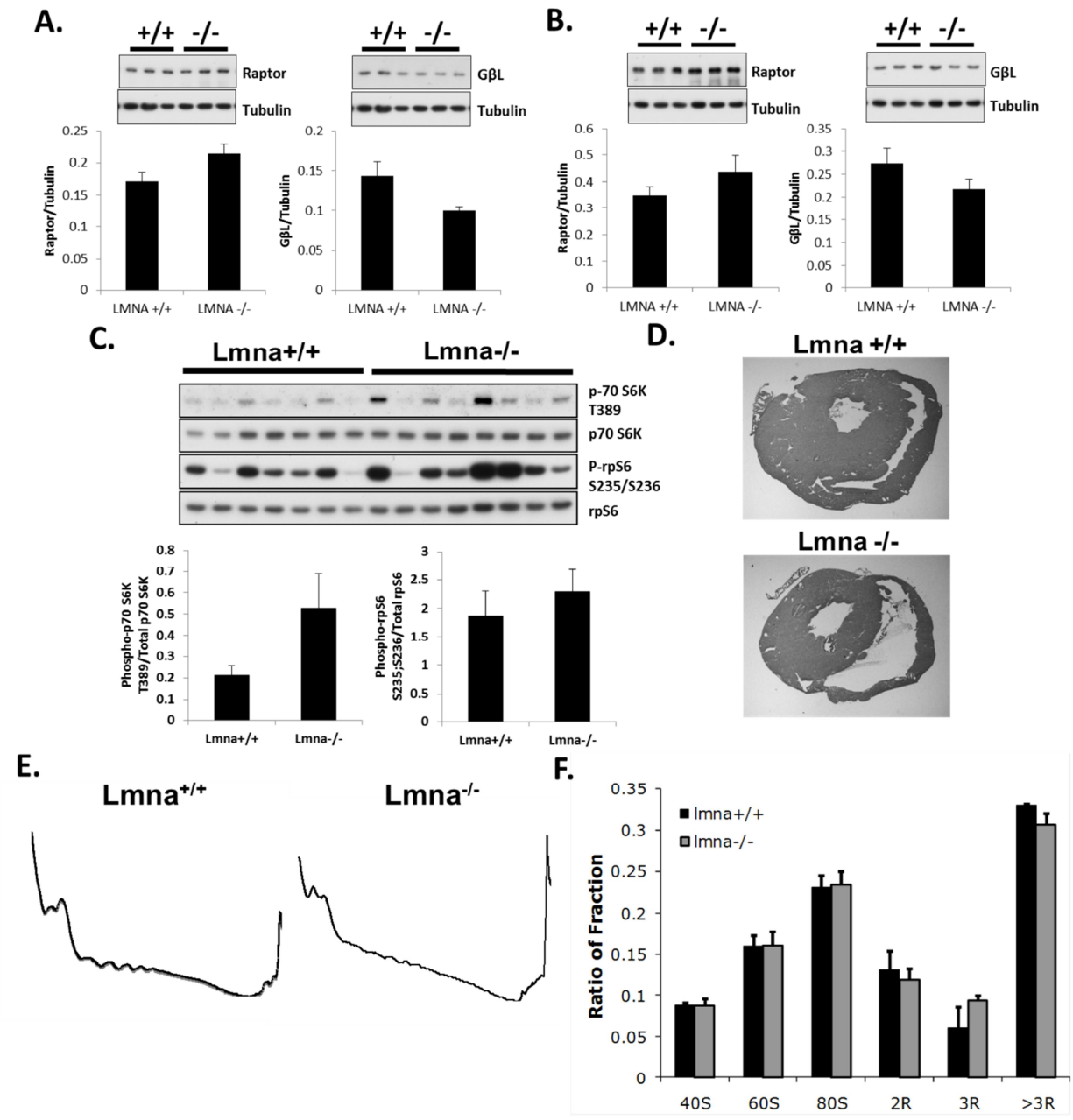

Fig. S1. Further characteristics of *Lmna*$^{+/+}$ and *Lmna*$^{-/-}$ mice. A) Raptor and GβL protein levels in heart, which are not significantly different in *Lmna*$^{-/-}$ mice (n = 4) compared to *Lmna*$^{+/+}$ mice (n = 5). B) Raptor and GβL protein levels in muscle, which are not significantly different in *Lmna*$^{-/-}$ mice (n = 6) compared to *Lmna*$^{+/+}$ mice (n = 7). C) Representative western blots and quantification of liver tissue lysates from *Lmna*$^{+/+}$ (n = 7) and *Lmna*$^{-/-}$ (n = 8) mice. Phosphorylated S6 kinase$^{(T389)}$ and rpS6$^{(S235/S236)}$ are not significantly different in *Lmna*$^{-/-}$ mice compared to *Lmna*$^{+/+}$ mice. D) Heart sections of *Lmna*$^{+/+}$ and *Lmna*$^{-/-}$ mice stained with

hematoxylin and eosin showing left and right ventricular dilatation in *Lmna*$^{-/-}$ mice. E) Representative polysome profiles of heart tissue from *Lmna*$^{+/+}$ (*n* = 3) and *Lmna*$^{-/-}$ (*n* = 3) mice. F) Polysome analysis of heart tissue from *Lmna*$^{+/+}$ and *Lmna*$^{-/-}$ mice showing that protein translation is not increased in *Lmna*$^{-/-}$ mice. Solid black bars, *Lmna*$^{+/+}$ mice; solid gray bars, *Lmna*$^{-/-}$ mice.

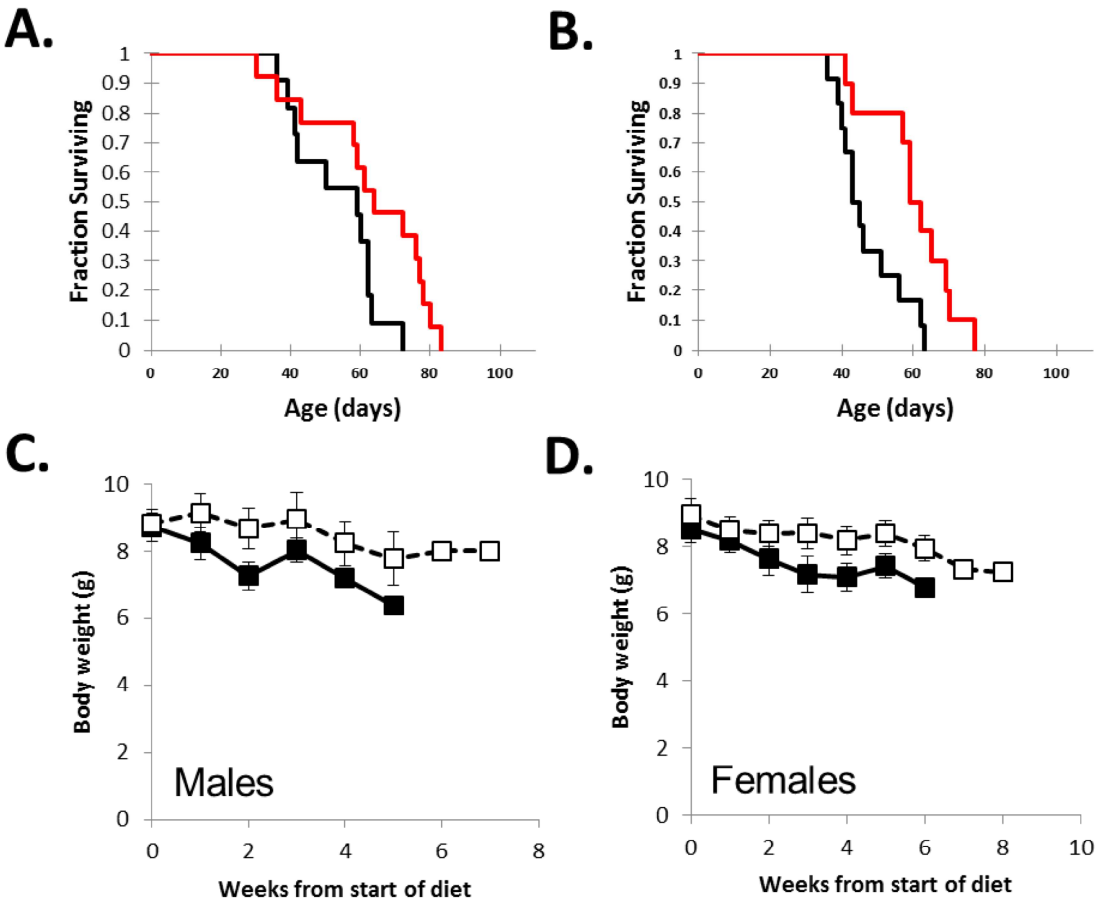

Fig. S2. Effect of rapamycin on survival of *Lmna*$^{+/+}$ and *Lmna*$^{-/-}$ male and female mice. A) Kaplan-Meier plot of male *Lmna*$^{-/-}$ mice fed control (n = 12) (black) or rapamycin (red) diet (n = 10). Survival was significantly increased in male *Lmna*$^{-/-}$ mice fed dietary rapamycin (P = 0.0068). B) Kaplan-Meier plot of female *Lmna*$^{-/-}$ mice fed control (n = 11) (black) or rapamycin (red) diet (n = 13). Survival was significantly increased in female *Lmna*$^{-/-}$ mice fed dietary rapamycin (P = 0.036). C) Body weight of male *Lmna*$^{-/-}$ mice fed rapamycin diet (dashed black line, open squares) was significantly different than control (solid black line, black squares) (P = 0.048). D) Body weight curve of female *Lmna*$^{-/-}$ mice fed rapamycin diet (dashed black line, open squares) was significantly different than control (solid black line, black squares) (P = 0.0060). Error bars are ± SEM.

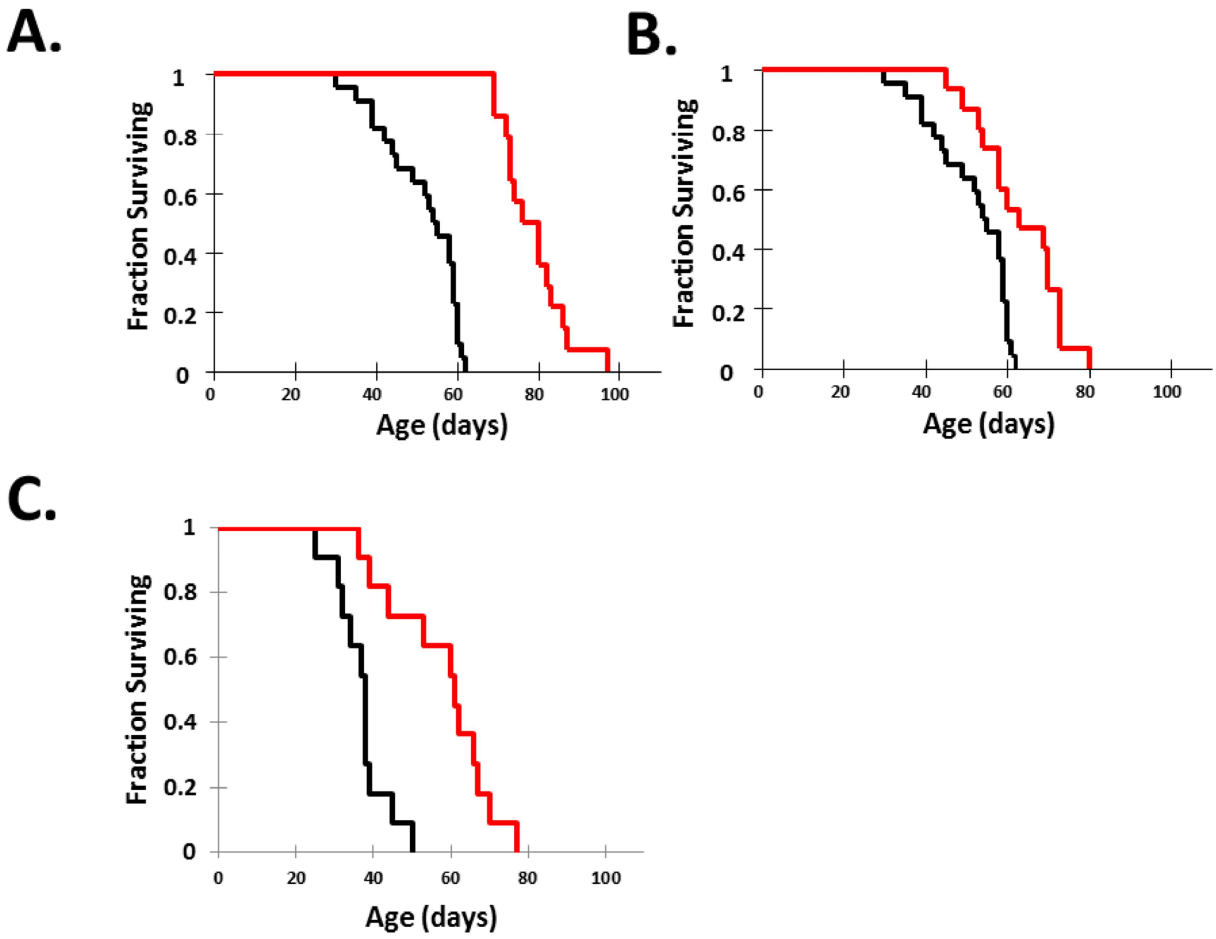

Fig. S3. Effect of rapamycin at different dosing regimens on survival of *Lmna*$^{+/+}$ and *Lmna*$^{-/-}$ mice. A) Kaplan-Meier plot of *Lmna*$^{-/-}$ mice (mixed 129Sv-C57BL/6J genetic background) injected with vehicle (n = 11) or 8 mg/kg rapamycin (n = 9) once a week. Survival was significantly increased in male *Lmna*$^{-/-}$ mice injected with rapamycin ($P < 0.0001$). B) Kaplan-Meier plot of *Lmna*$^{-/-}$ mice (mixed 129Sv-C57BL/6J genetic background) injected with vehicle (n = 11) or 8mg/kg rapamycin (n = 12) every other day for one week (3 injections total). Survival was significantly increased in *Lmna*$^{-/-}$ mice injected with rapamycin (P = 0.025). C) Kaplan-Meier plot of *Lmna*$^{-/-}$ mice (C57BL/6J genetic background) injected with vehicle (n = 11) or 8mg/kg rapamycin every other day (n = 11). Survival was significantly increased in *Lmna*$^{-/-}$ mice injected with rapamycin (P = 0.0002). For all Kaplan-Meier plots, control=black and rapamycin=red.

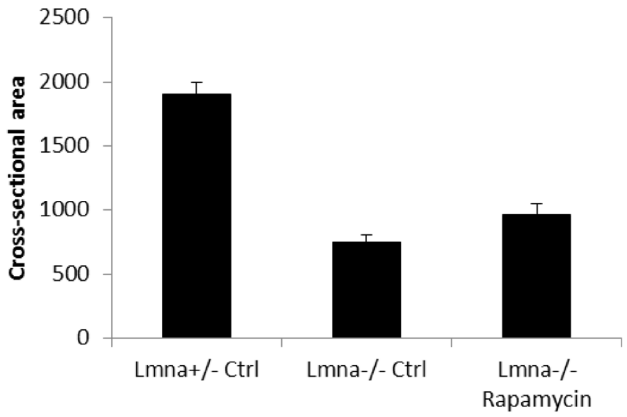

Fig. S4. Effect of rapamycin on myofiber cross-sectional area in *Lmna*$^{-/-}$ mice. The cross sectional area was not significantly different between the *Lmna*$^{-/-}$ and the rapamycin-treated *Lmna*$^{-/-}$ groups of mice ($P = 0.071$).

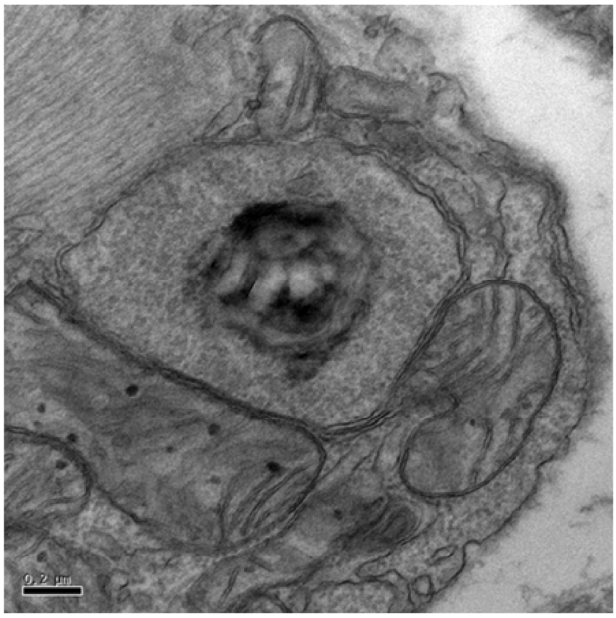

Fig. S5. Autophagosome formation in *Lmna*$^{-/-}$ mice. A representative electron micrographs from *Lmna*$^{-/-}$ heart sections displaying autophagosome formation.