Supplementary material

Deficiency of Telomere-associated Repressor Activator Protein 1 Precipitates Cardiac Aging in Mice *via* p53/PPARα Signalling

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Supplemental Table

Table S1 Basic information of recruited patients.

	Young group (n = 7)	Middle age/aged group (n = 5)
Age (year)	31.3 ± 1.7	58.8 ± 3.9*
BW (kg)	55.4 ± 12.7	64.0 ± 8.2
BP (systolic, mmHg)	118 ± 12	140 ± 22
BP (diastolic, mmHg)	72 ± 9	80 ± 11
LVEF%	56.8 ± 7.9	40.5 ± 8.6

Data are shown as means ± S.E.M; *P < 0.05 middle age/aged group *vs*. young group. Abbreviations: BW = body weight; BP = blood pressure; LVEF = left ventricular ejection fraction.

Supplemental Figures

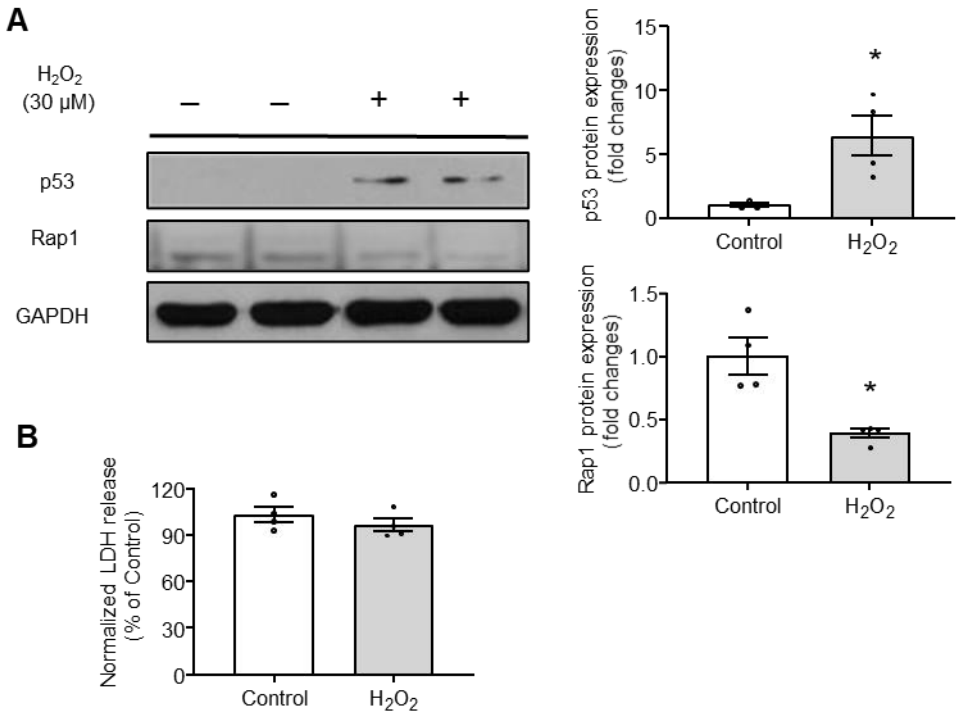

Figure S1. Protein expression of Rap1 was reduced in H_2O_2-treated H9C2 cells. (A) Representative Western blots of p53, Rap1 expression and (B) lactate dehydrogenase (LDH) release in H9C2 cells stimulated with or without H_2O_2 [24 h following 2 h H_2O_2 (30 μM) treatment], n = 4; Protein presence of p53 and Rap1 was normalized to GAPDH. Data are shown as means ± S.E.M; $^{*}P < 0.05$ H_2O_2 *vs.* Control.

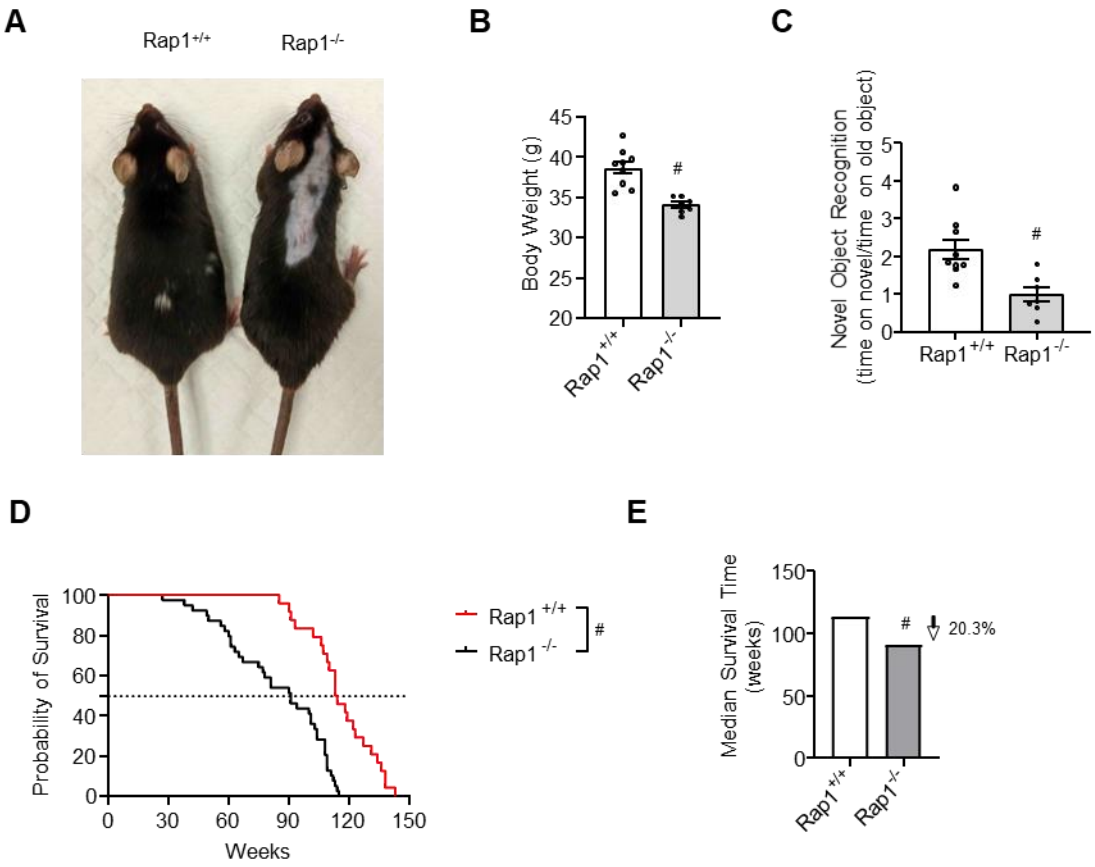

Figure S2. Rap1 deficiency leads to more pronounced age-associated phenotypes. (A) Representative photograph of male $Rap1^{+/+}$ (left) and $Rap1^{-/-}$ (right) mice at 20-months of age. (B) Body weight of $Rap1^{+/+}$ (n = 9) and $Rap1^{-/-}$ (n = 7) mice at 20-months of age. (C) Novel object recognition test (time spends on novel/time spends on old object) in the aged $Rap1^{+/+}$ (n = 9) and $Rap1^{-/-}$ (n = 7) mice (20-months of age). (D) Kaplan–Meyer survival curves and (E) median survival from Kaplan–Meyer plots of male $Rap1^{+/+}$ (n = 24) and $Rap1^{-/-}$ (n = 40) mice. Data are shown as means ± S.E.M.; $^{\#}P < 0.05$ $Rap1^{-/-}$ *vs.* $Rap1^{+/+}$.

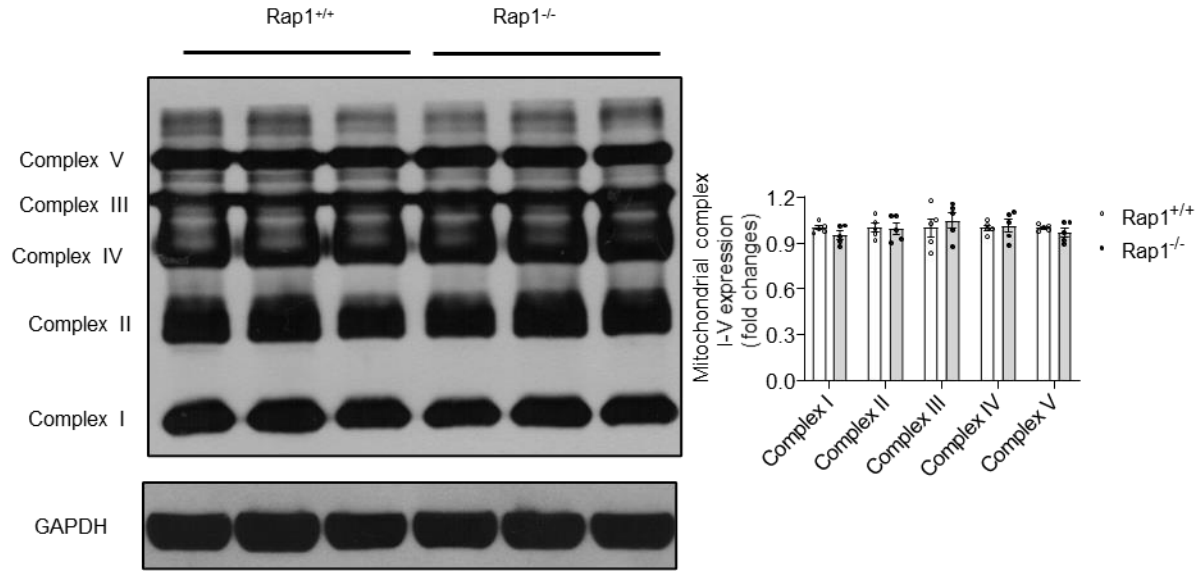

Figure S3. Rap1 does not alter the protein presence of mitochondrial complex I-V. Representative Western blots of mitochondrial complex I-V in the hearts of $Rap1^{+/+}$ and $Rap1^{-/-}$ mice at 12-month of age. Protein presence of mitochondrial complex I-V was normalized to GAPDH. Data are shown as means ± S.E.M. n = 5.

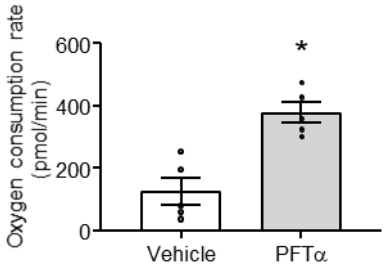

Figure S4. Pharmacological inhibition of p53 enhances mitochondrial respiration in wildtype primary cardiomyocytes. Oxygen consumption rates (OCR) using fatty acids as a substrate were measured under basal conditions in the primary cardiomyocytes from the hearts of $Rap1^{+/+}$ mice at 12-month of age, with or without treatment of PFTα (a selective p53 inhibitor, 10 μM, 12 h). Data are shown as means ± S.E.M. $^{*}P < 0.05$ PFTα *vs.* Vehicle. n = 5.