

Supplemental Figure Legend

Supplemental Fig. 1. *Gata5*Cre activity is restricted in the epicardium at E15.5, 2-month-old heart.

(A, B) β -galactosidase staining (blue) of E15.5 (A) and 2-month-old (B) *Gata5Cre;Rosa26* mice heart. Red: nuclear staining. Scale bar: 200 μ m.

Supplemental Fig. 2. Thickness of trabeculae and myocardial wall is normal in epicardium-restricted *Cnb1* mutant mice.

(A-B) Hematoxylin and Eosin staining showing E16.5 control and *Gata5Cre;Cnb1^{ff}* heart ventricles. Scale bar: 100 μ m.

(C-D) Morphometric analysis of trabecular thickness (C) and the ratio of trabecular area to compact wall length (D). Error bars represent one standard deviation. Three hearts were measured for each group and *p* values were calculated using two-tailed Student's *t* tests.

(E-F, H-I) Hematoxylin and Eosin staining showing P1 (E-F, Scale bar: 500 μ m.) and 2-month-old (H-I, Scale bar: 1mm.) control and *Gata5Cre;Cnb1^{ff}* heart ventricles.

(G, J) Quantification of right and left ventricular wall thickness. Three hearts were measured for each group and *p* values were calculated using two-tailed Student's *t* tests.

Supplemental Fig. 3. No apoptotic cells were detected in epicardium-restricted *Cnb1* mutant hearts by TUNEL staining.

(A-B) TUNEL staining in two-month-old hearts of littermate control and *Gata5Cre;Cnb1^{ff}* mice. Green: TUNEL staining. Blue: DAPI nuclear staining. Scale bar: 100 μ m.

(C) Positive control of TUNEL staining in mice heart section after myocardial infarction for 24h. Green: TUNEL staining. Blue: DAPI nuclear staining. Scale bar: 100 μ m.

Supplemental Fig. 4. The population of fibroblast developed normal in epicardium-restricted *Cnb1* mutant mice.

(A-D) Co-immunostaining of α -SMA and Periostin in two-month-old hearts of littermate control and *Gata5Cre;Cnb1^{ff}* mice. C and D are magnified zone indicated in A and B. Red: α -SMA staining, Green: Periostin staining. Blue: DAPI nuclear staining. Scale bar: 100 μ m.

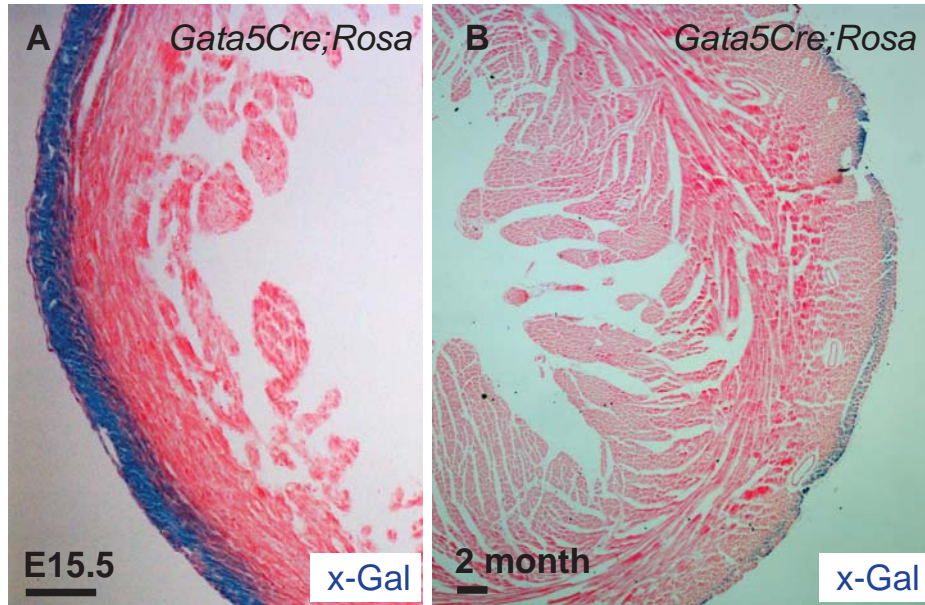
Supplemental Fig. 5. The patterning of both right and left coronary arteries is normal in epicardium-restricted *Cnb1* mutant heart.

(A-D) Vascular casting of the coronary arteries emerging from the two-month-old heart in control (A, C) and *Gata5Cre;Cnb1^{ff}* (B, D) mice. Scale bar: 1mm.

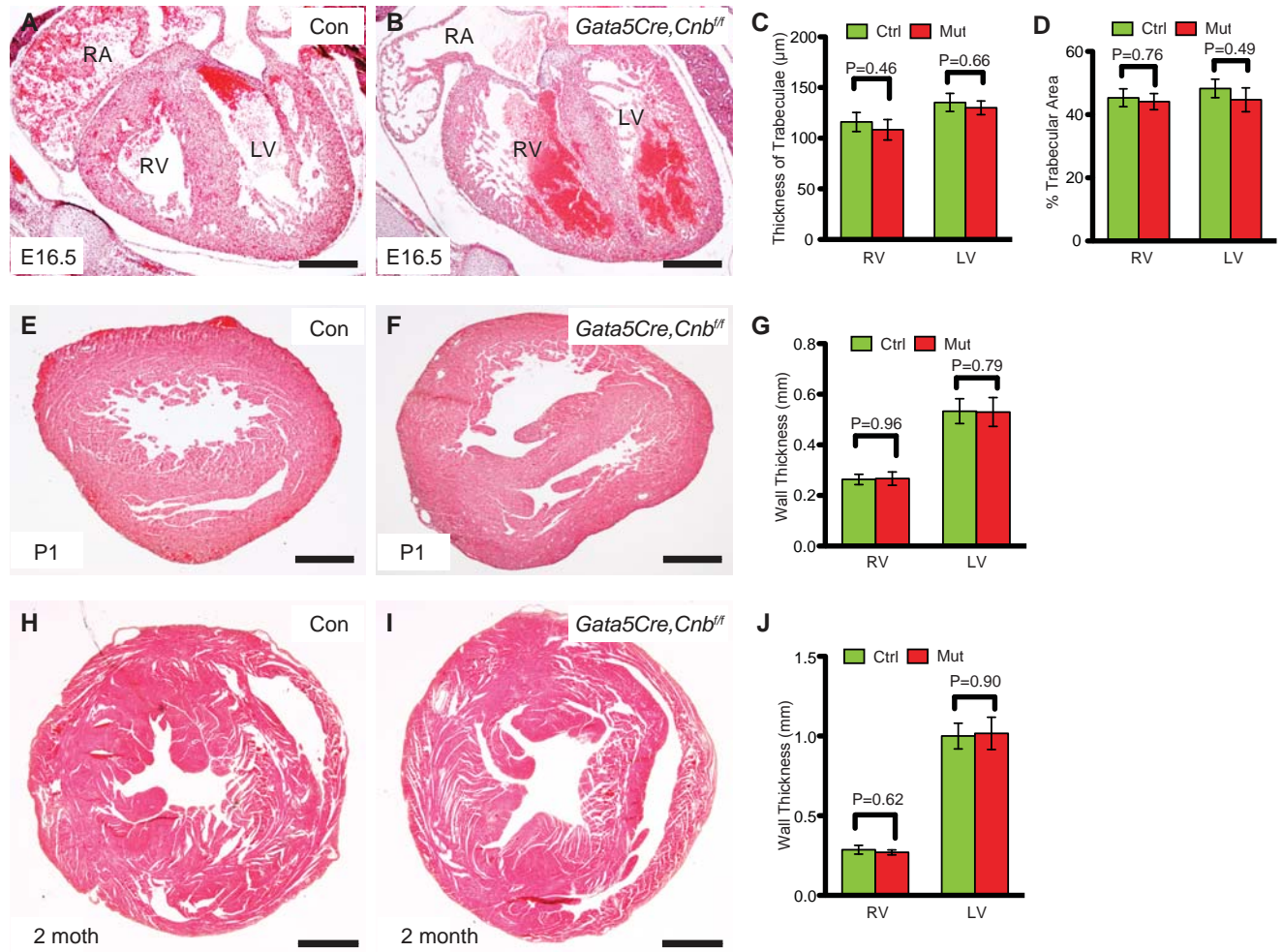
Supplemental Fig. 6. Only coronary arteries have maturation defects of SMCs in epicardium-restricted *Cnb1* mutant heart.

(A, B) Immunostaining of Myh11 in two-month-old hearts of littermate control and *Gata5Cre;Cnb1^{ff}* mice. Red arrow indicates veins and lymphatics on surface; black arrow indicates coronary arteries located deeper in the myocardium. Brown: Myh11 staining. Blue: haematoxylin nuclear staining. Scale bar: 200 μ m.

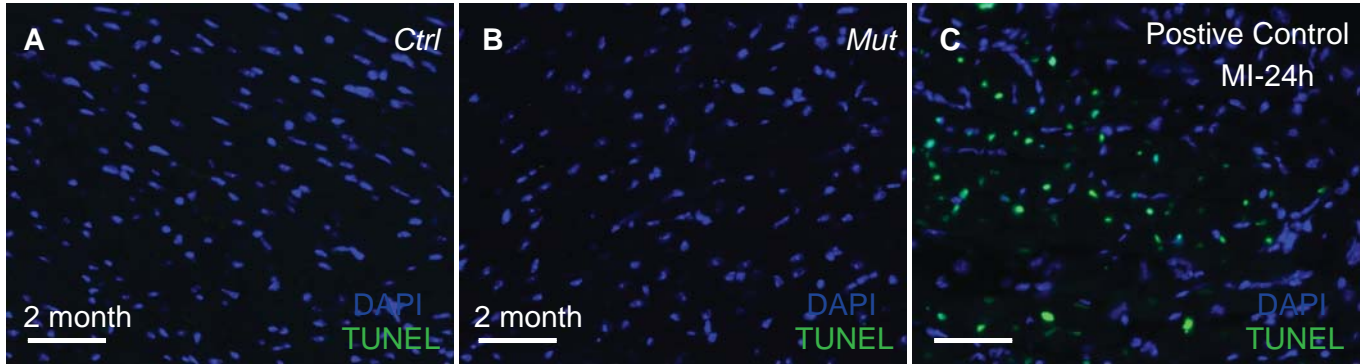
Gata5Cre activity is restricted in the epicardium at E15.5, 2-month-old heart



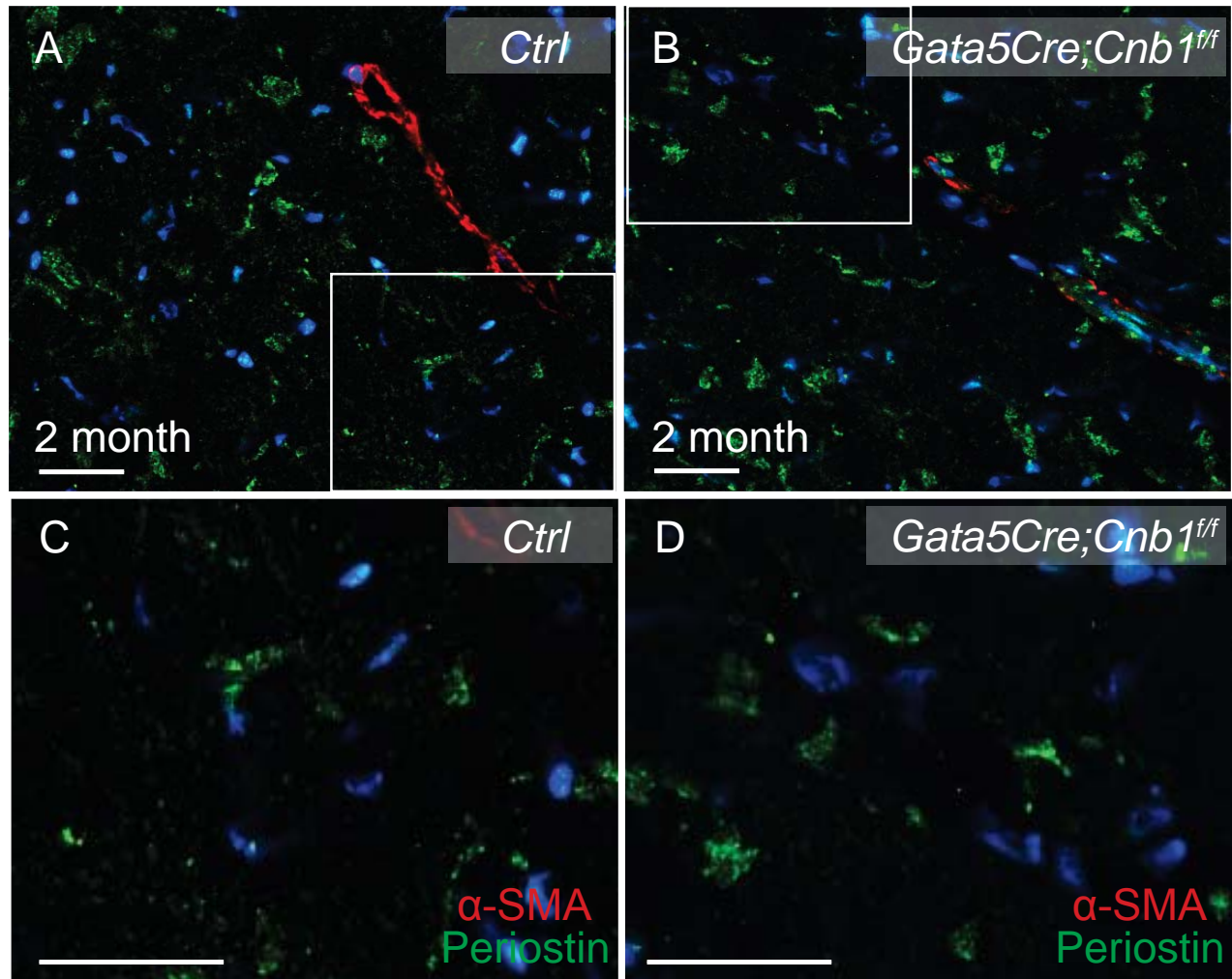
Thickness of trabeculae and myocardial wall is normal in epicardium-restricted *Cnb1* mutant mice



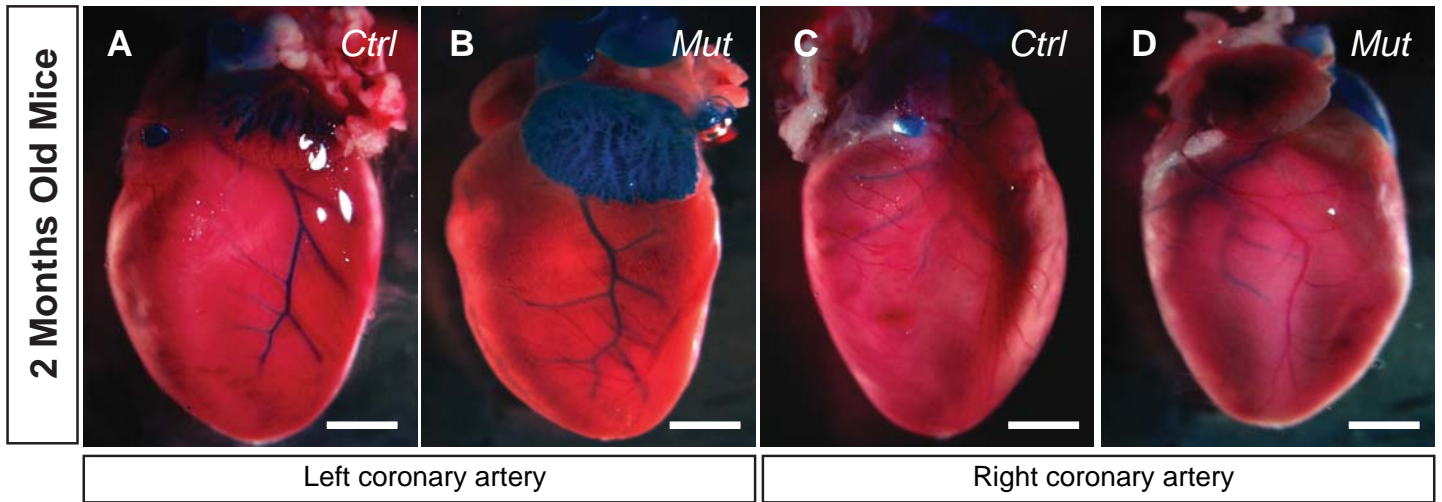
**No apoptotic cells were detected in epicardium-restricted
Cnb1 mutant hearts by TUNEL staining**



The population of fibroblast developed normal in epicardium-restricted *Cnb1* mutant mice



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Only coronary arteries have maturation defects of SMCs in epicardium-restricted *Cnb1* mutant heart

