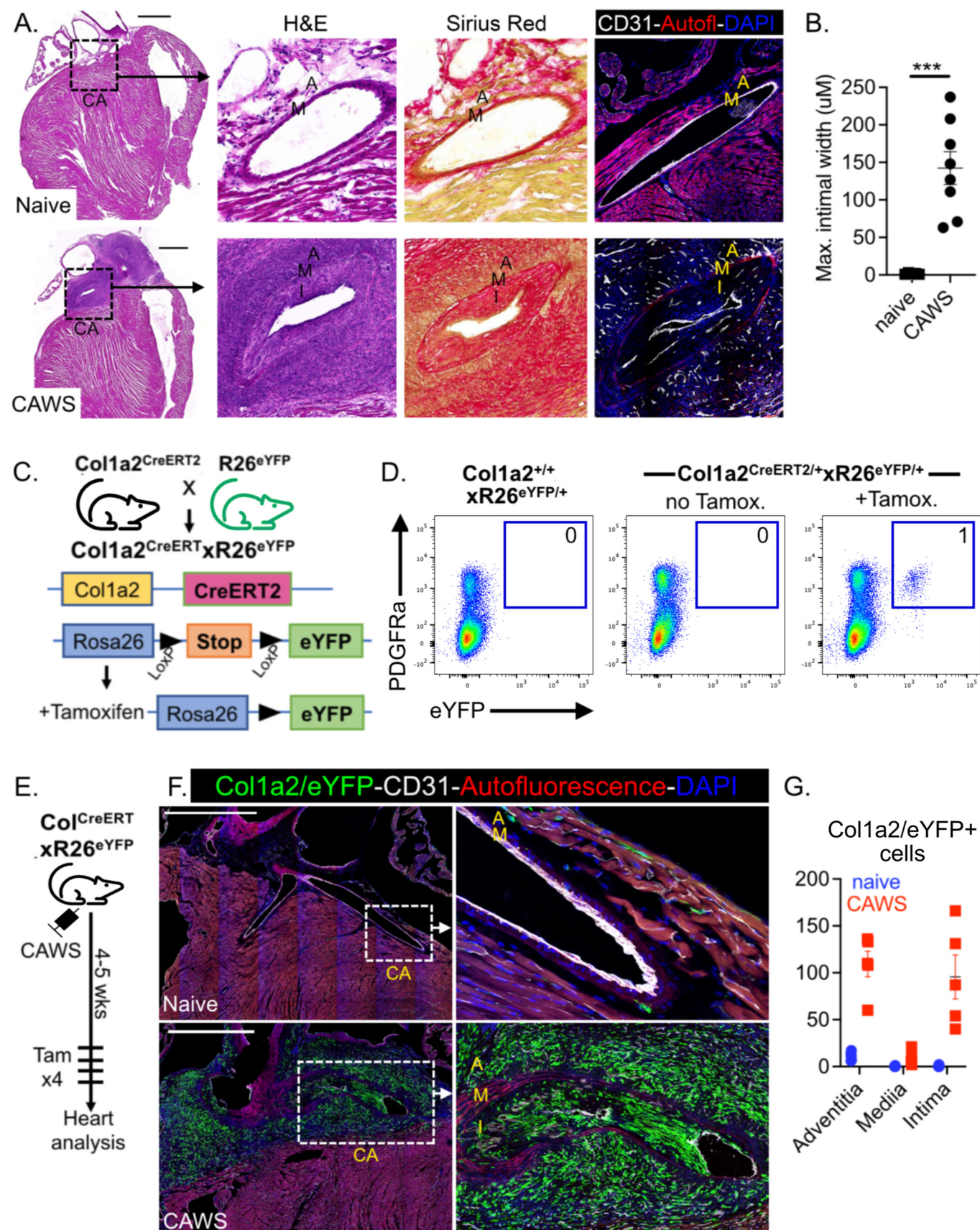


Expanded View Figures

Figure EV1. CAWS-induced vasculitis triggers the formation of collagen-expressing luminal myofibroblasts.

(A) Cardiac sections from naive or CAWS-injected mice (4–5 weeks post injection) analysed by histology or immunofluorescent microscopy. For the latter, sections were stained for CD31 to label endothelial cells and autofluorescence was used to identify elastin fibres of the media. (B) Graphs show the maximum width of the coronary artery intima for individual mice (with mean $\pm$ SEM) pooled from 3 independent experiments. (C) Genetic schema for Col1a2^{CreERT2}.R26^{eYFP} system. (D) Flow cytometric analysis of cardiac cells from Col1a2^{CreERT2}.R26^{eYFP} (and control) mice showing endogenous eYFP⁺ expression and PDGFR α staining. Inset value is the mean of 4–6 mice from 3 independent experiments. (E) Experimental schema. (F) Cardiac sections from naive or CAWS-injected Col1a2^{CreERT2}.R26^{eYFP} mice stained for GFP to identify Col1a2⁺/eYFP⁺ cells (green), CD31 to label endothelial cells (white) and autofluorescence to identify elastin fibres of the media (red). (G) Graphs show the number of Col1a2⁺/eYFP⁺ cells within each vessel layer for individual mice (with mean $\pm$ SEM) pooled from 3 independent experiments. The coronary artery (CA), adventitia (A), media (M) and intima (I) are annotated and scale bars are 1000 μ m. *** $P < 0.001$ with two-tailed Student's t tests. Exact P values (to 4 decimal points) for: (B) 0.0004 (***). Source data are available online for this figure.



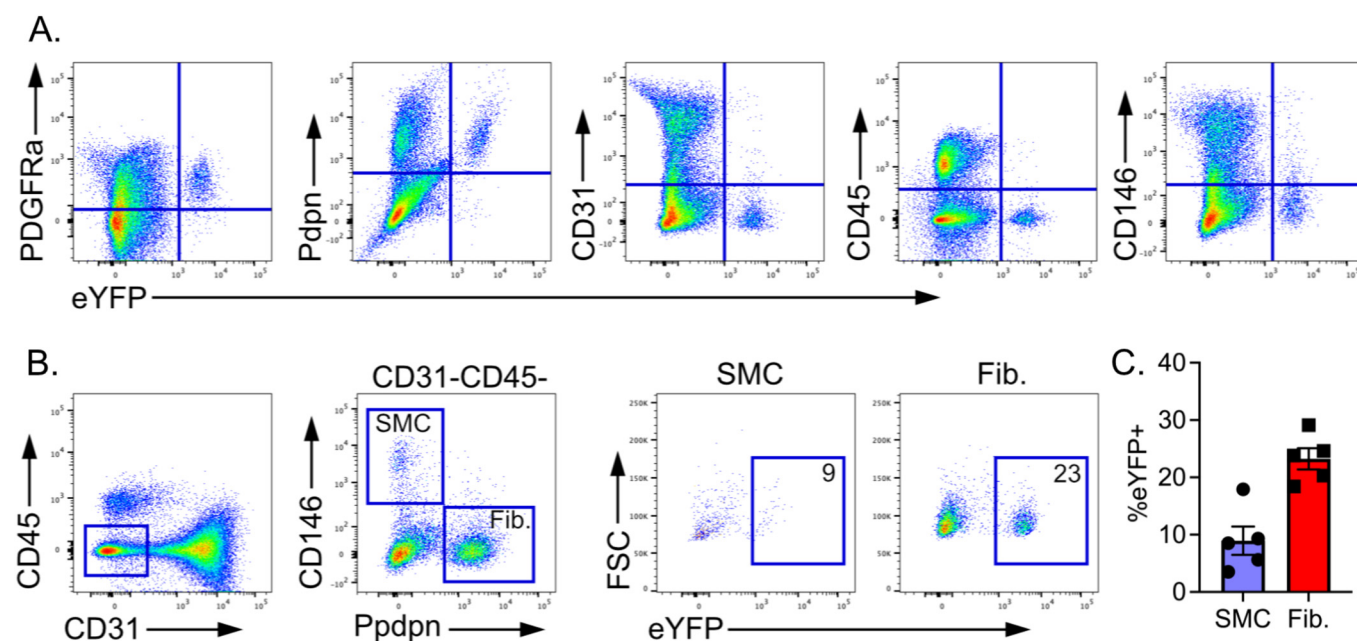
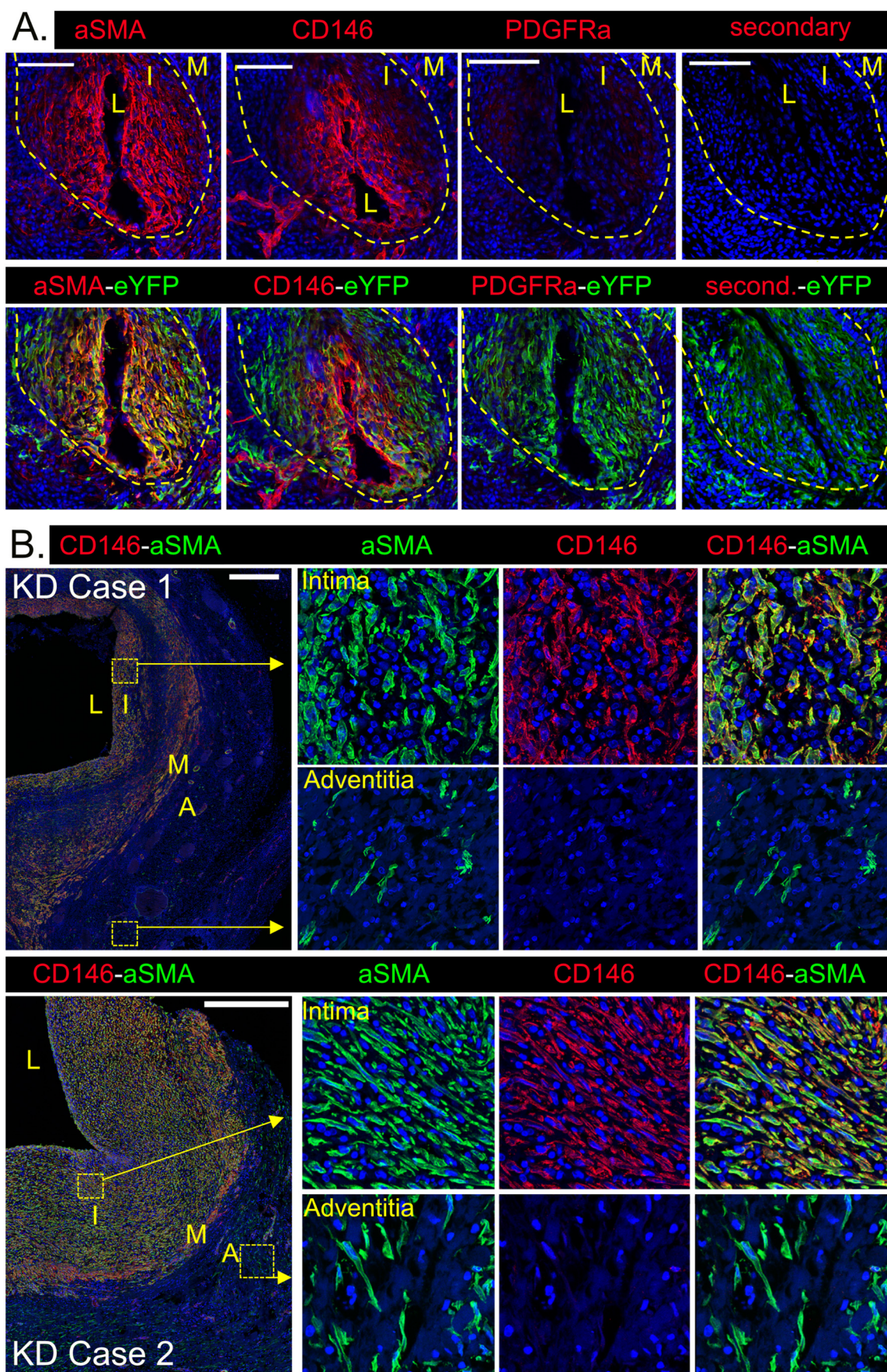


Figure EV2. E10.5 Wt1 recombination predominantly labels resident cardiac fibroblasts.

(A) Flow cytometric analysis of cardiac cells from $Wt1^{CreERT2}.R26^{eYFP}$ mice (administered tamoxifen at E10.5) showing endogenous eYFP+ expression versus lineage-specific markers. (B) Gating strategy and eYFP labelling of SMC (CD45-CD31-CD146+) and fibroblasts (CD45-CD31-Pdpn+). (C) Graphs show the proportion of eYFP labelling in SMCs and fibroblasts for individual mice (with mean $\pm$ SEM) pooled from 2 independent experiments. Source data are available online for this figure.



**Figure EV3. Luminal myofibroblasts express mural cell markers.**

(A) Cardiac sections from CAWS-injected *Myh11^{CreERT2}R26^{eYFP}* mice (4–5 weeks post CAWS) analysed by immunofluorescent microscopy. Sections were stained for GFP to identify *Myh11*⁺/*eYFP*⁺ cells (green) and either α -SMA, CD146 or PDGFR α (red). Scale bars are 100 μ m. (B) Coronary artery sections from two acute KD fatalities stained for α -SMA (green) and CD146 (red) and analysed by confocal microscopy. Scale bars are 1000 μ m. The adventitia (A), media (M), intima (I) and lumen (L) are annotated throughout. Source data are available online for this figure.

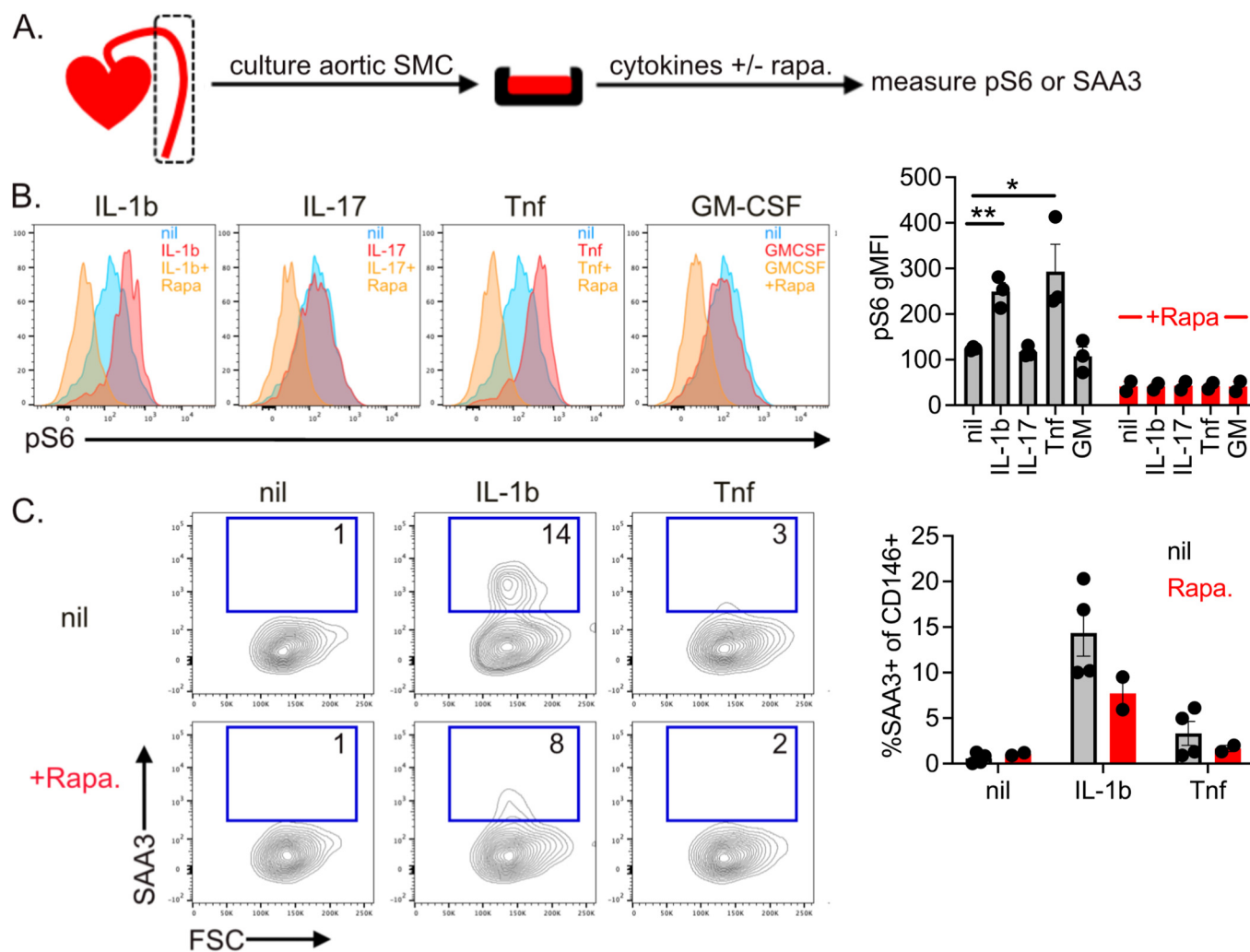


Figure EV4. IL-1 β activates mTOR in SMCs in vitro.

(A) Experimental schematic. (B, C) FACS plots are gated on CD146⁺ cells and show intracellular staining for pS6 (B) or SAA3 (C) in cultured SMCs stimulated with cytokines +/- rapamycin. Graphed points depict individual lines (with mean $\pm$ SEM) pooled from 2 independent experiments. * P < 0.05; ** P < 0.01 with two-tailed Student's t tests. Exact P values (to 4 decimal points) for (B) IL-1 β 0.0032 (**), Tnf 0.0482 (*). Source data are available online for this figure.

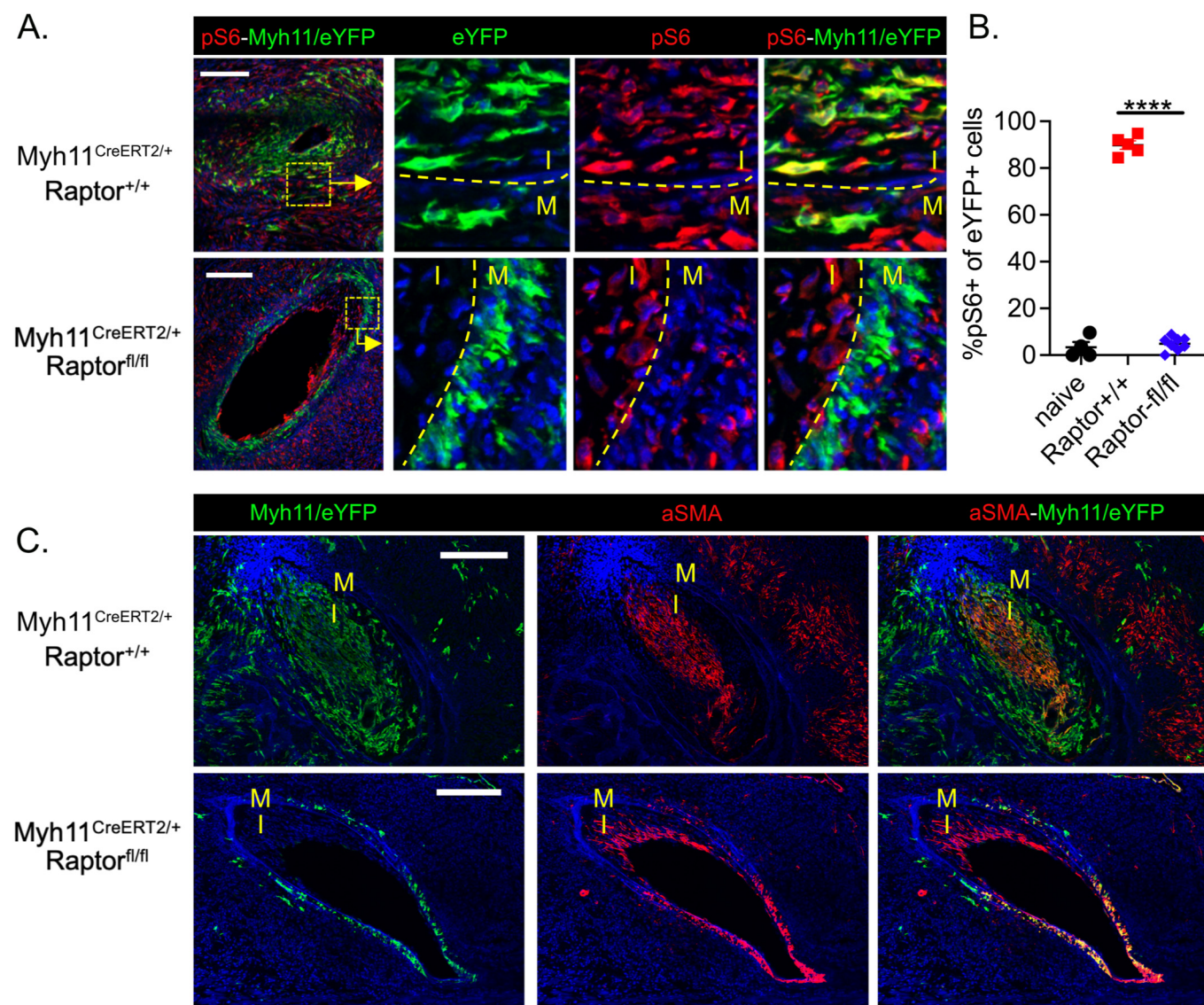


Figure EV5. Analysis of Raptor-deficient SMCs.

(A–C) Representative cardiac sections from CAWS-injected *Myh11^{CreERT2}.Raptor^{+/+}.R26^{eYFP}* or *Myh11^{CreERT2}.Raptor^{fl/fl}.R26^{eYFP}* mice (4–5 weeks post injection). (A, B) Sections are stained for GFP to identify *Myh11* + /eYFP+ cells (green) and pS6 (red) to assess mTOR signalling. Graphs depict the % eYFP+ cells that are pS6+ for individual mice (with mean ± SEM) pooled from 3 independent experiments. (C) Sections show eYFP+ cells and α-SMA expression. The IEL is shown as a dashed line in (A) and the adventitia (A), media (M), intima (I) and lumen (L) are annotated throughout. Scale bars are 100 μm. *****P* < 0.0001 with two-tailed Student's *t* tests. Exact *P* values (to 4 decimal points) for (B) < 0.0001 (****). Source data are available online for this figure.