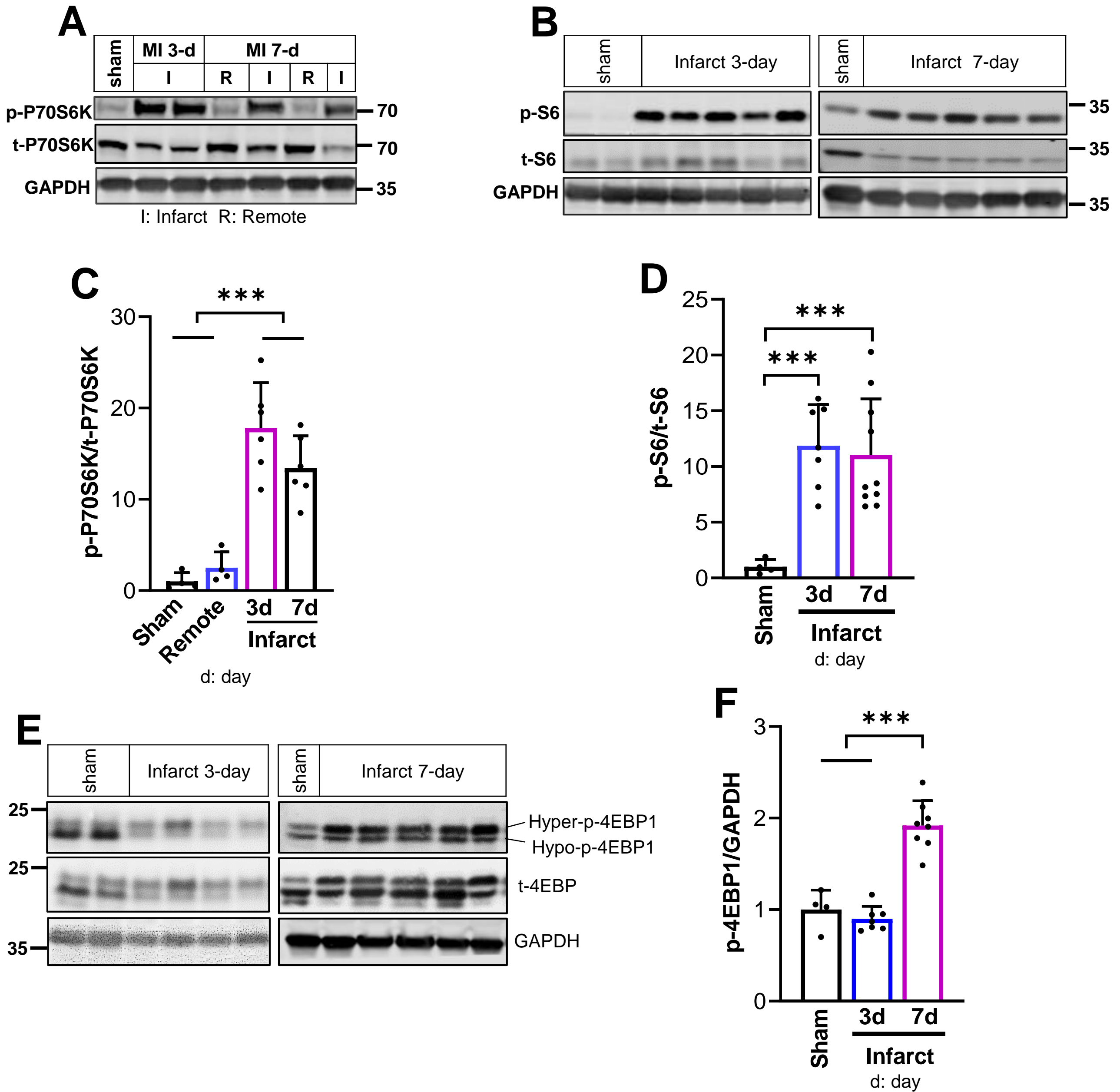
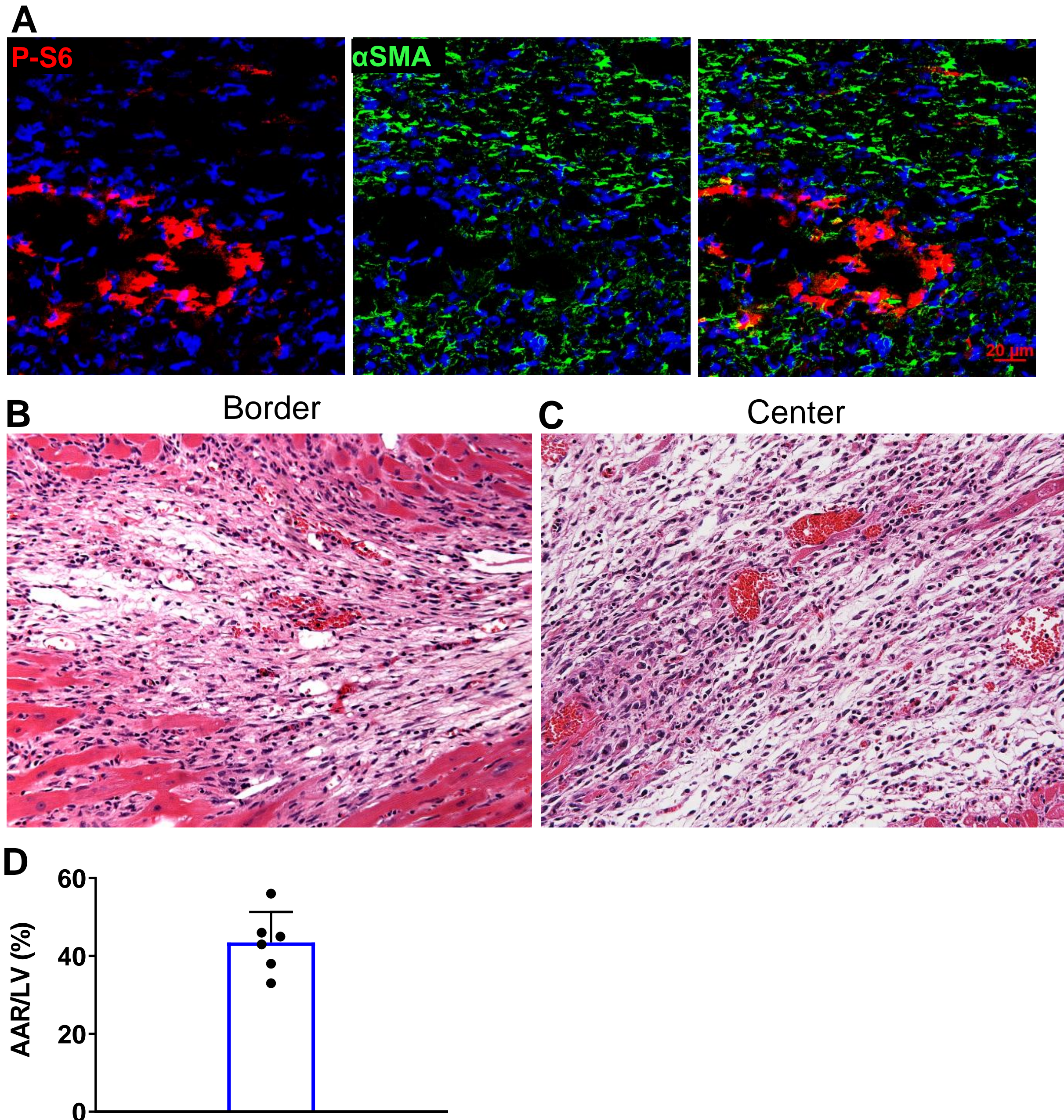
S-Figure 1. Robust activation of mTORC1 in the ischemic myocardium



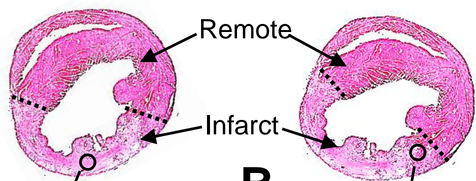
S-Figure 1. C57BL/6J mice were subjected to sham procedure or LAD ligation to generate myocardial infarction. Heart tissue was separated into remote and infarct region under a dissection scope. Immunoblot analyses were performed using samples from cohorts as indicated. Individual lane on all immunoblots represents different experimental animals. **A.** Immunoblot analysis of p-P70S6K, t-P70S6K, and GAPDH from samples obtained 3-day or 7-day after MI. **B.** Immunoblot analysis of p-S6, t-S6, and GAPDH using samples from sham or infarct tissues at the time points as indicated. **C.** Summarized data from different experiments performed as in A. n=4 to 6 hearts. **D.** Summarized data of different experiments performed as in B. n= 4 to 10 hearts. **E.** Protein samples obtained from sham or infarct tissue at different time points were analyzed for p-4EBP1. The hyper- and hypo-phosphorylated 4EBP1 were indicated. **F.** Quantification of the p-4EBP1 (combined both hyper and hypo-p-4EBP1) after normalization to GAPDH. n= 4 to 8 hearts. *** $p<0.001$

S-Figure 2. Lack of mTORC1 activation in myofibroblasts



S-Figure 2. A. Myocardial infarction was generated by LAD ligation. One week after the MI procedure, the heart was perfusion fixed and prepared for cryosection. The tissue sections were labeled with p-S6 and αSMA antibodies. **B and C**. Representative images of HE staining performed on MI hearts. Hearts were harvested 7-day after the MI procedure and fixed with 4%PFA for 48 hours at 4°C. HE staining were performed on cross-sections obtained from paraffin-embedded tissue blocks. Images were acquired from both infarct border and Infarct center. **D**. Estimation of area at risk (AAR). Following occlusion of a coronary artery, The heart was perfused with 2% Evans blue. Unstained area (AAR) to total LV area were quantified using ImageJ. n=6 hearts.

S-Figure 3. Digesting tissue debris activates mTORC1



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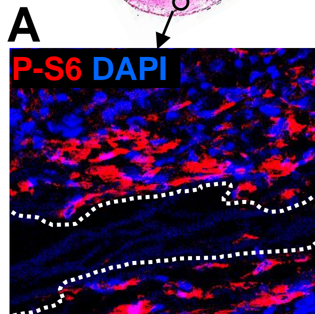

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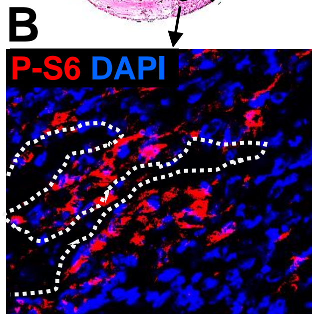

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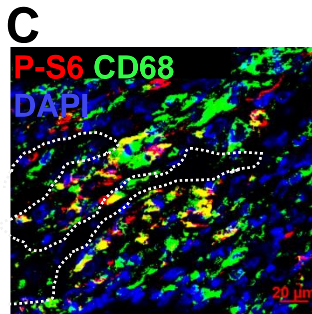

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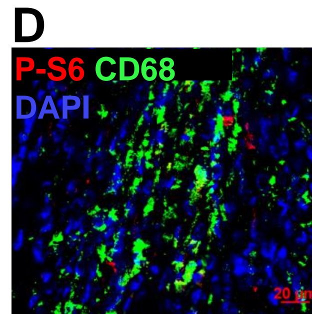

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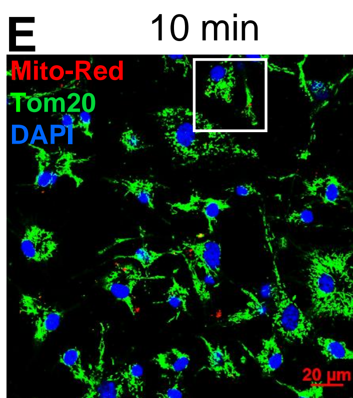

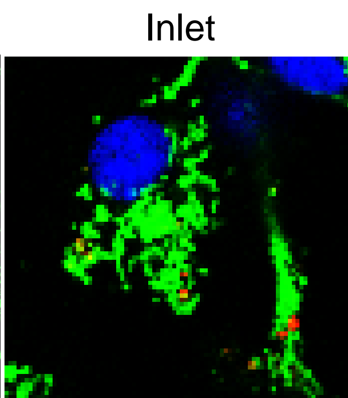

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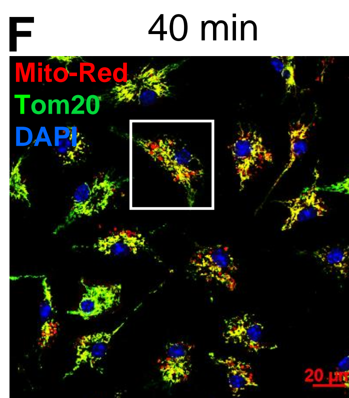

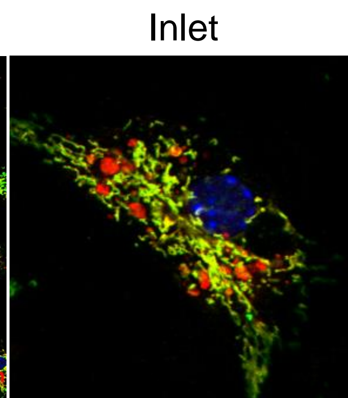

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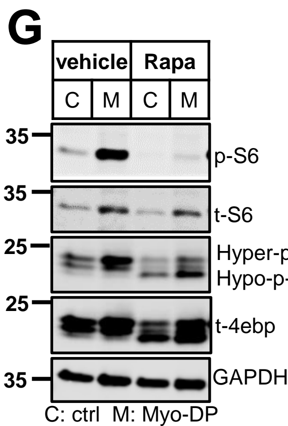

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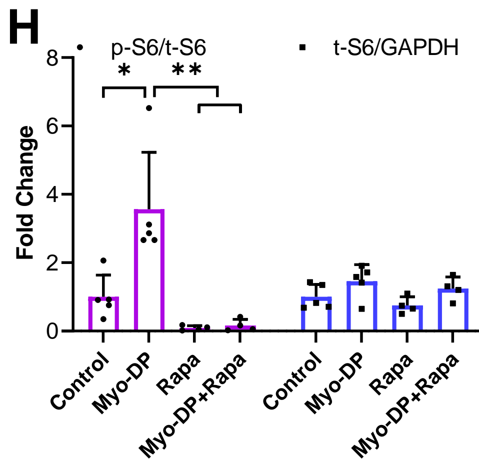

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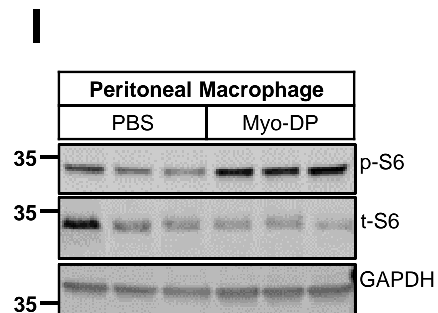

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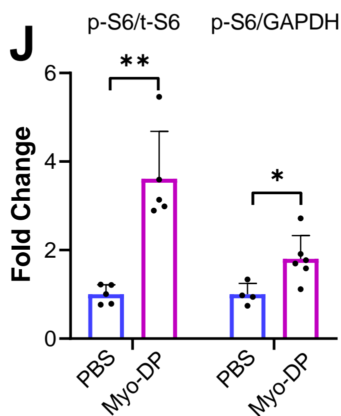

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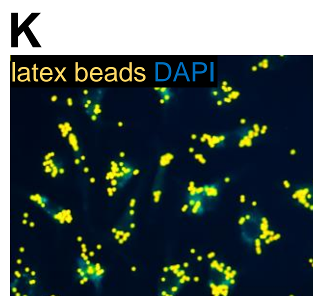

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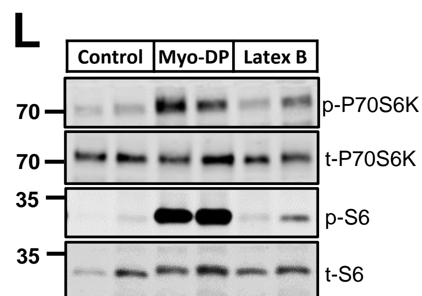
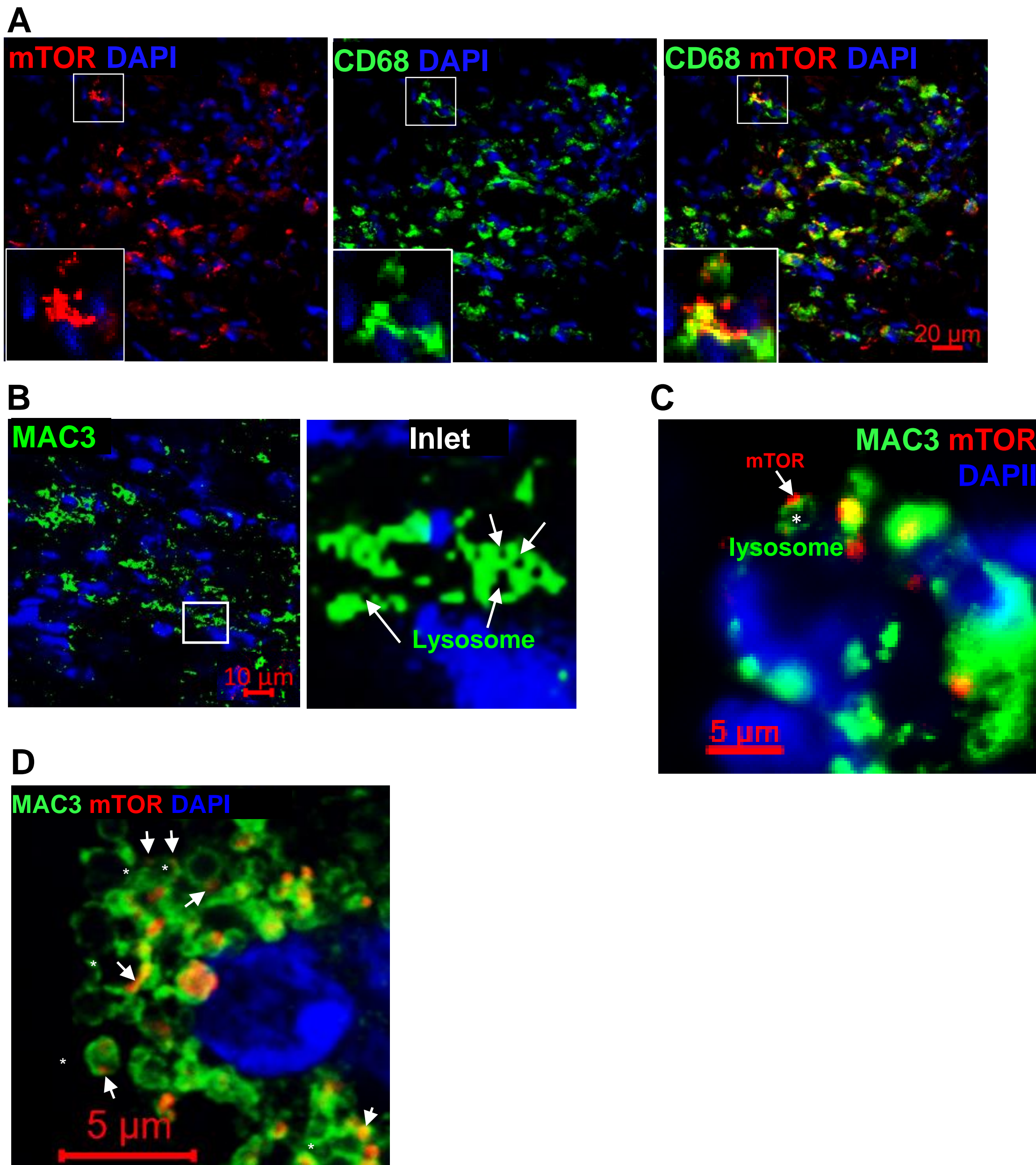


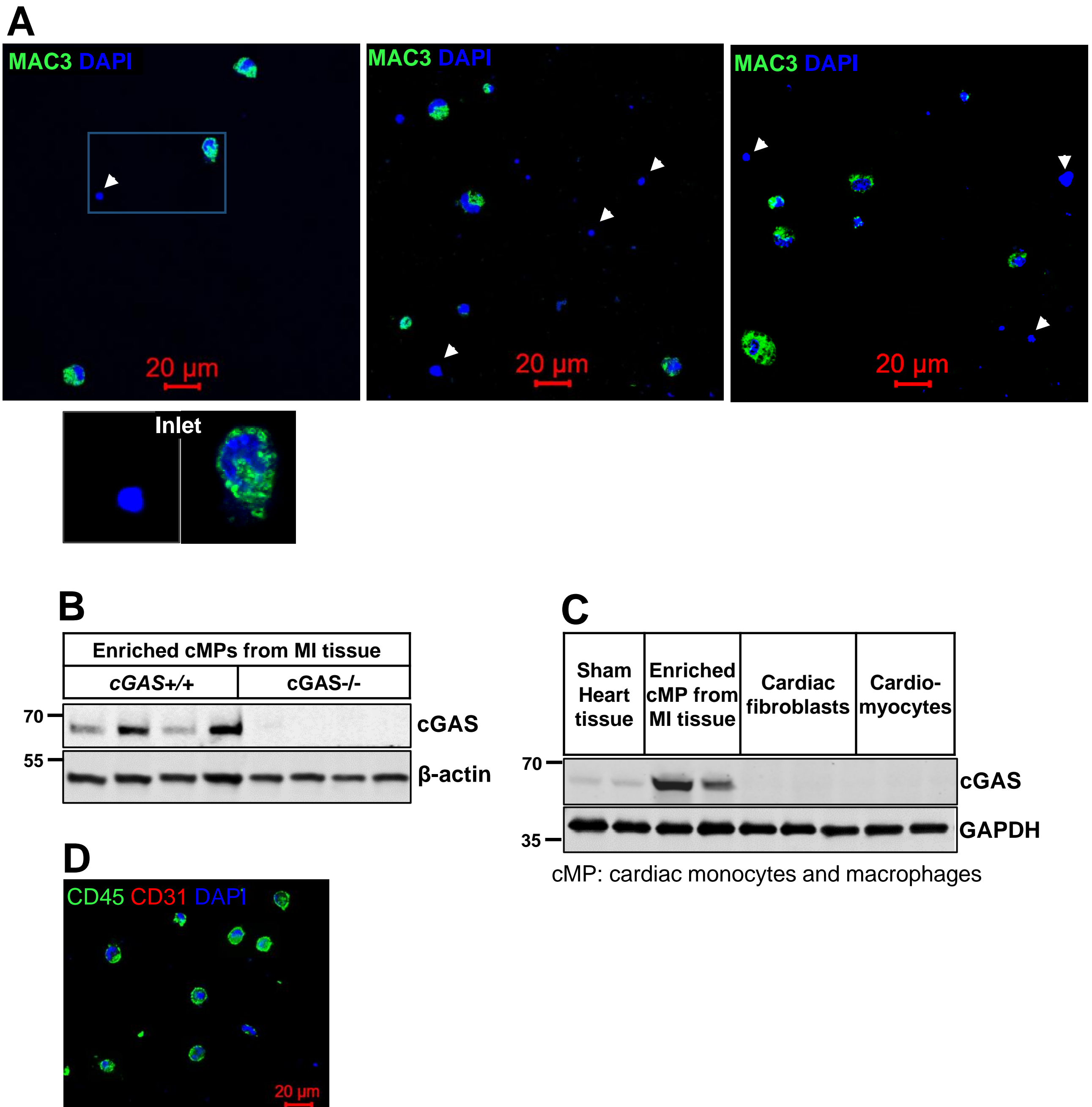
S-Figure 3. **A** and **B**. Cryosections from hearts 7-day after LAD ligation were labeled with p-S6 and CD68 antibodies. The residue necrotic tissue section was demarcated with the dotted line. The spatial location of views obtained for **A** (infarct center) and **B** (infarct border) were indicated on the HE stained cross sections. **C**. Co-labeling of CD68 and p-S6 to confirm cMPs was the main cell type with positive p-S6. **D**. Co-labeling of CD68 and p-S6 in regions where the necrotic tissue had been replaced with provisional matrix. **E** and **F**. Phagocytotic assay with myocardial derived particles (Myo-DP). Myo-DPs were labeled with MitoTracker Red at 100 nM for 30 minutes. The labeled particles were washed and incubated with BMDM for the 10 minutes (**E)** and 40 minutes (**F**). Endogenous mitochondria was labeled with Tom20 (green). Engulfed particles was shown in red. **G**. Macrophages (BMDM) were treated with control or Myo-DP for 6 hours in the absence or presence of 20 nM rapamycin. The levels of p-S6, t-S6, p-4EBP and t-4EBP were detected by immunoblot. **H**. Quantified data for p-S6 level normalized to t-S6 and t-S6 level normalized to GAPDH. n=4 to 5 experiments. **I**. Peritoneal macrophages were treated with PBS or Myo-DP for 15 hours. Protein samples were subjected to immunoblot analysis for p-S6, t-S6, and GAPDH. **J**. Summarized data from different experiments performed as in **I**. n=4 to 6 experiments. **K.** Macrophages (BMDM) were incubated with latex beads for 6 hours. **L**. Protein samples prepared from macrophages treated with either beads or Myo-DP were subjected to SDS-PAGE. n=2 experiments for each group. Membranes were probed with p-P70S6, t-P70S6, p-S6, t-S6, and GAPDH. Individual lane on all immunoblots represented different experiments. * $p<0.05$ ** $p<0.01$.

S-Figure 4. mTOR in cMPs localizes to the lysosomes membrane



S-Figure 4. A. Tissue sections of the heart obtained 1 week after LAD ligation were labeled with mTOR and CD68 antibodies. **B**. Cryosections of the heart were stained with a lysosomal marker MAC3. Inlet demonstrates the circular lysosomal structure. **C.** Tissue sections from MI heart 7-day after LAD ligation was co-labeled with mTOR and MAC3. The arrow indicates the mTOR on the membrane of lysosomes (indicated with *). **D.** cMP isolated from infarct tissue was labeled with MAC3 and mTOR. Arrows indicate the mTOR localized to the membrane of lysosomes (circular structure, some indicated with *). For **A** and **B**, crysosections from 3 hearts were examined. For **D**, cMPs from at least three infarcts were examined.

S-Figure 5. Characterization of cMPs enriched from infarcting myocardium



S-Figure 5. A. Condensed and fragmented nuclei without cytosol from multiple fields were indicated with arrows. **B.** Protein samples prepared from cells enriched with cMPs from infarct tissue of cGAS+/+ or cGAS-/- mice were subjected to immunoblot analysis to detect cGAS. **C.** Protein samples from sham myocardium, cells enriched with cMPs from infarct tissue, mouse cardiomyocytes, and fibroblasts were probed for cGAS. **D.** Cells isolated from infarct tissue were labeled with CD45 and CD31. For **B** and **C**, each lane represents 1 heart. For **D**, the cells were pooled from MI tissue obtained from two hearts.