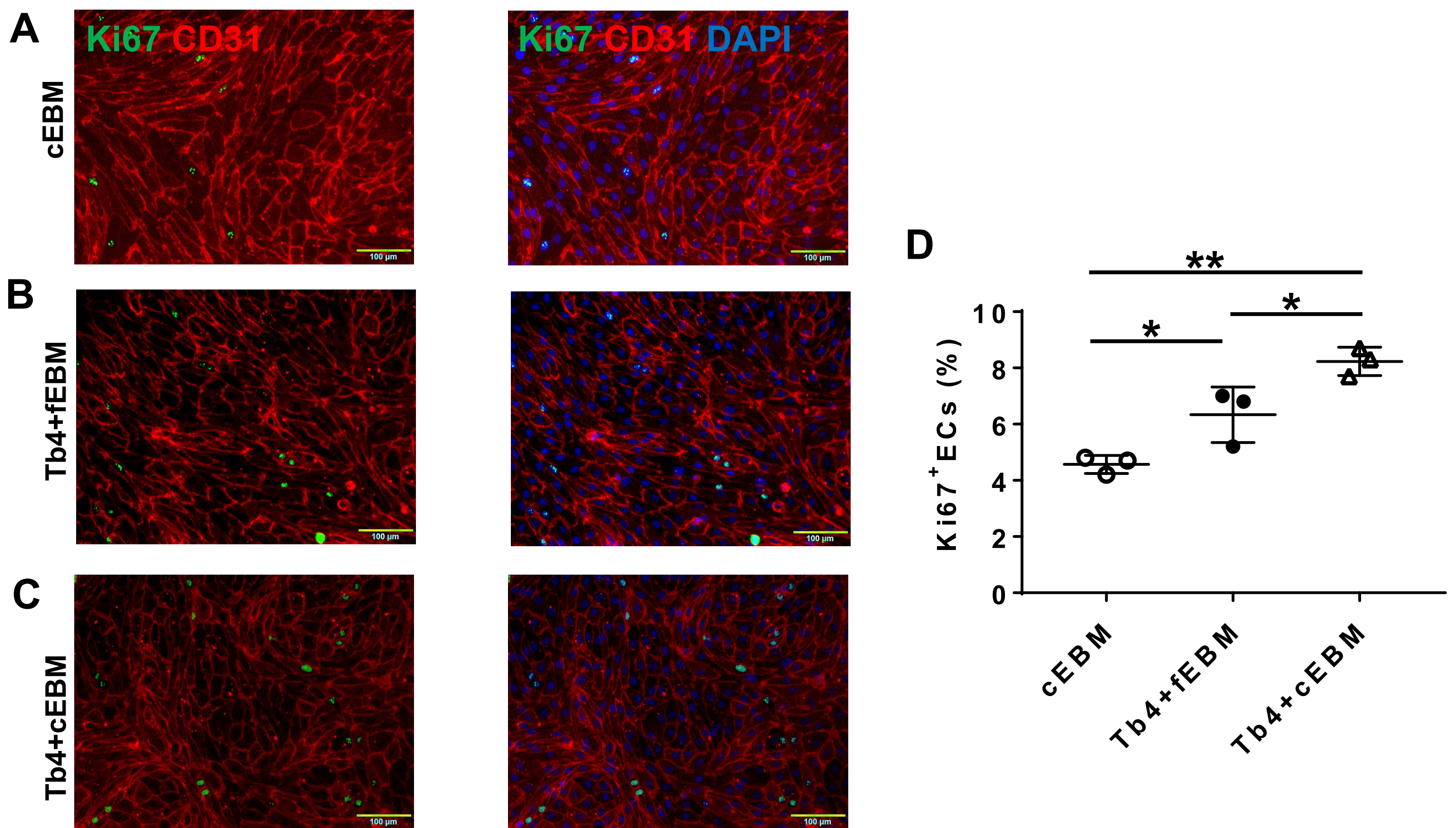
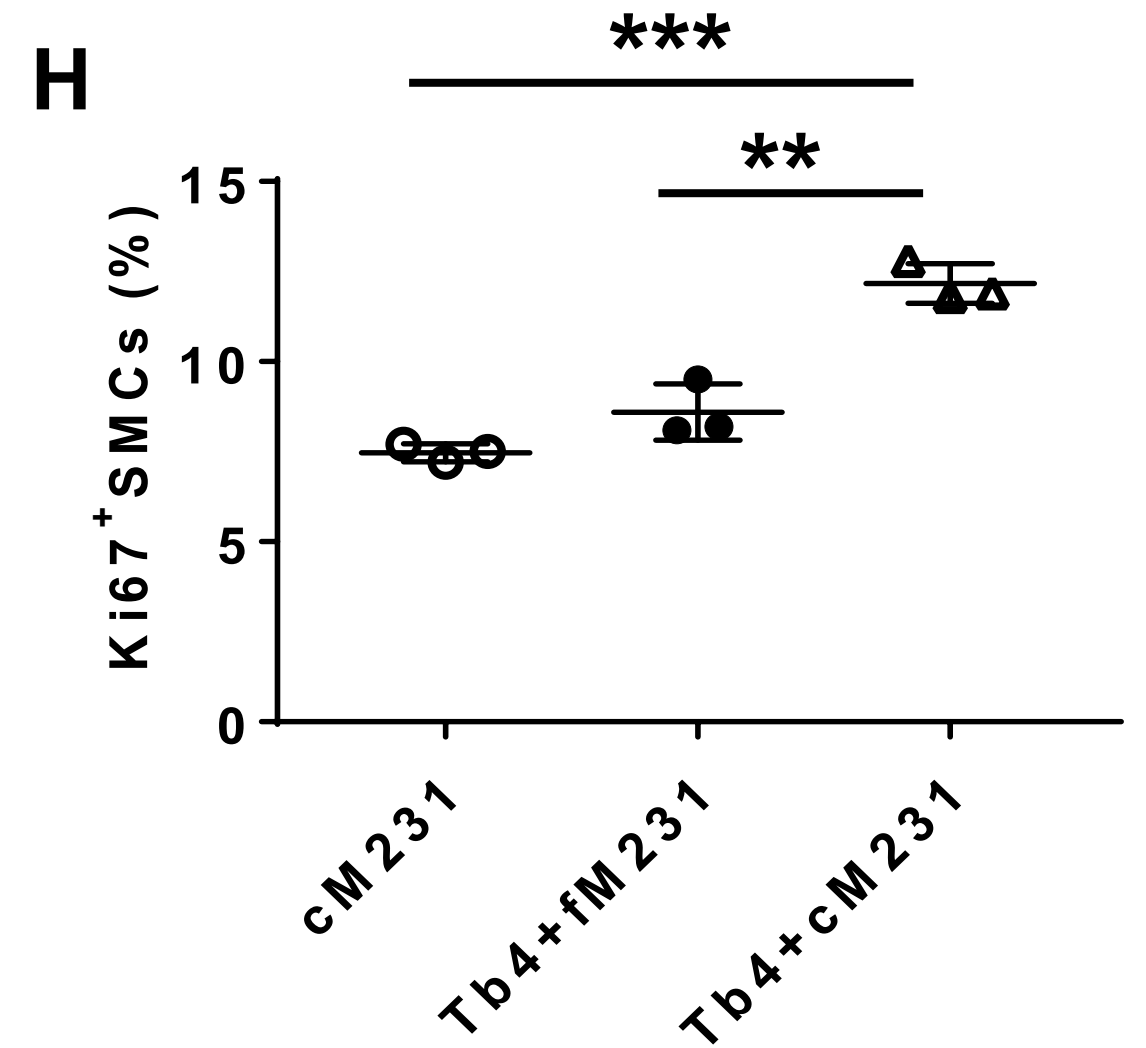
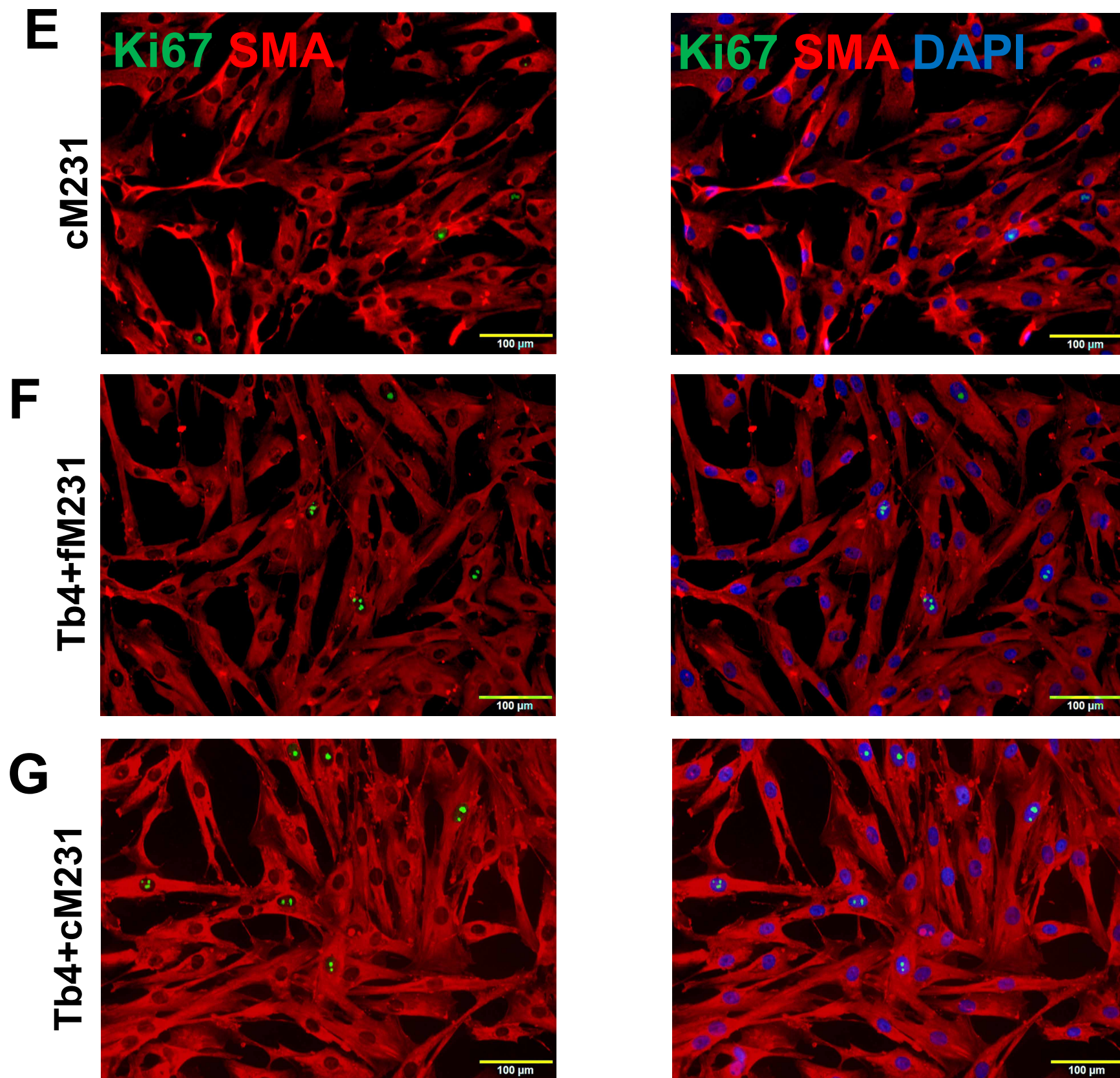


**Figure S1: Purity and viability of hiPSC-CMs.** (A) Representative flow cytometry images of cTnT<sup>+</sup>hiPSC-CMs before and after purification. (B) Quantification of cTnT<sup>+</sup>hiPSC-CM before and after purification. (n = 8) (Independent T-test. \*\*: p < 0.01). (C) Percentage of viable hiPSC-CMs after recovered from liquid nitrogen. (n = 6). Values are presented as the means ± SD.

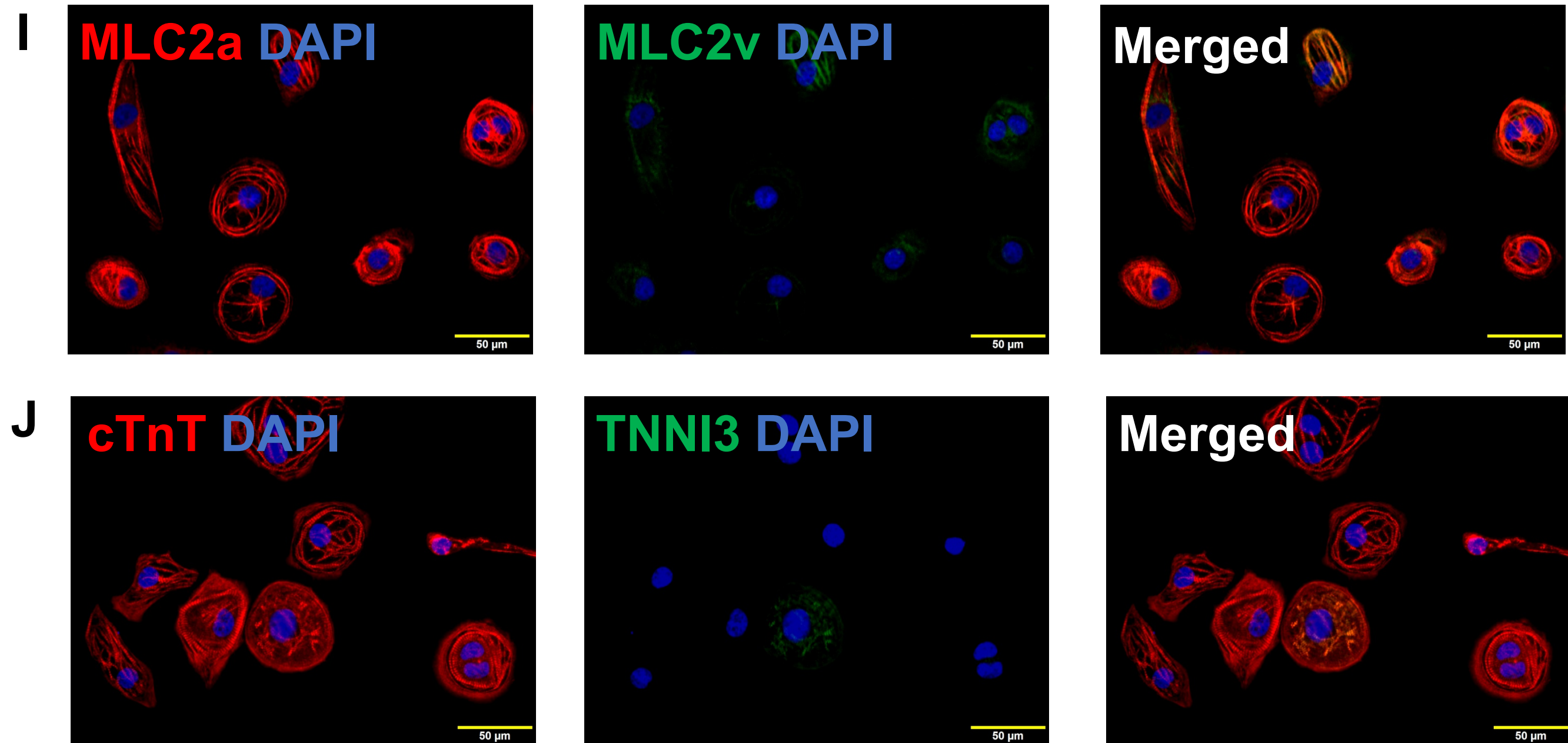


**Figure S2.** Representative images of hiPSC-ECs cultured in either hiPSC-CM conditioned endothelial basal medium (cEBM) (**A**), or fresh endothelial basal medium (fEBM) supplemented with 600 ng / mL Tb4 (**B**), or cEBM supplemented with 600 ng / mL Tb4 (**C**) for 48 h, and then cells were co-stained for expression of Ki67 and CD31 proteins. (**D**) Quantification of hiPSC-ECs expressing Ki67. (Bar = 100  $\mu$ m). (n = 3. Independent T-test. \*: p < 0.05, \*\*: p < 0.01). Values are presented as the means  $\pm$  SD.

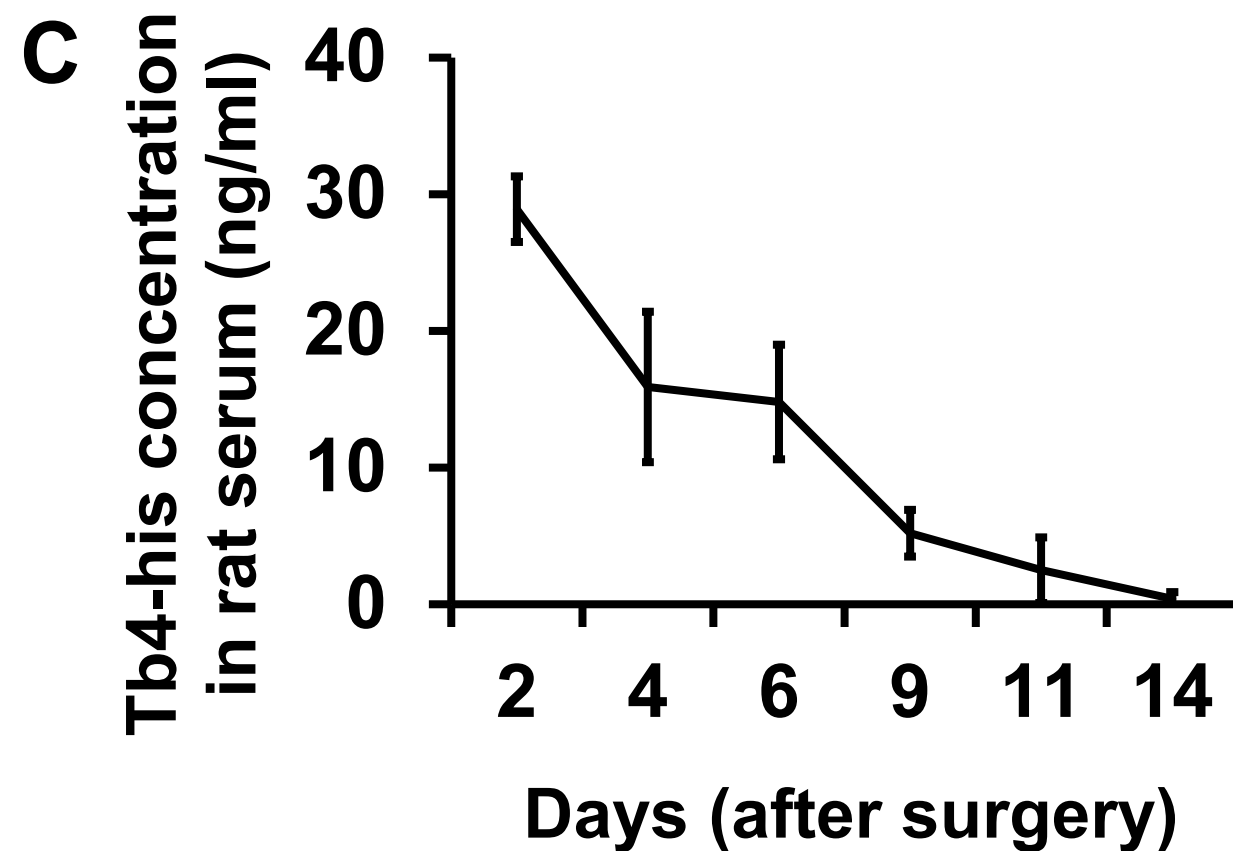
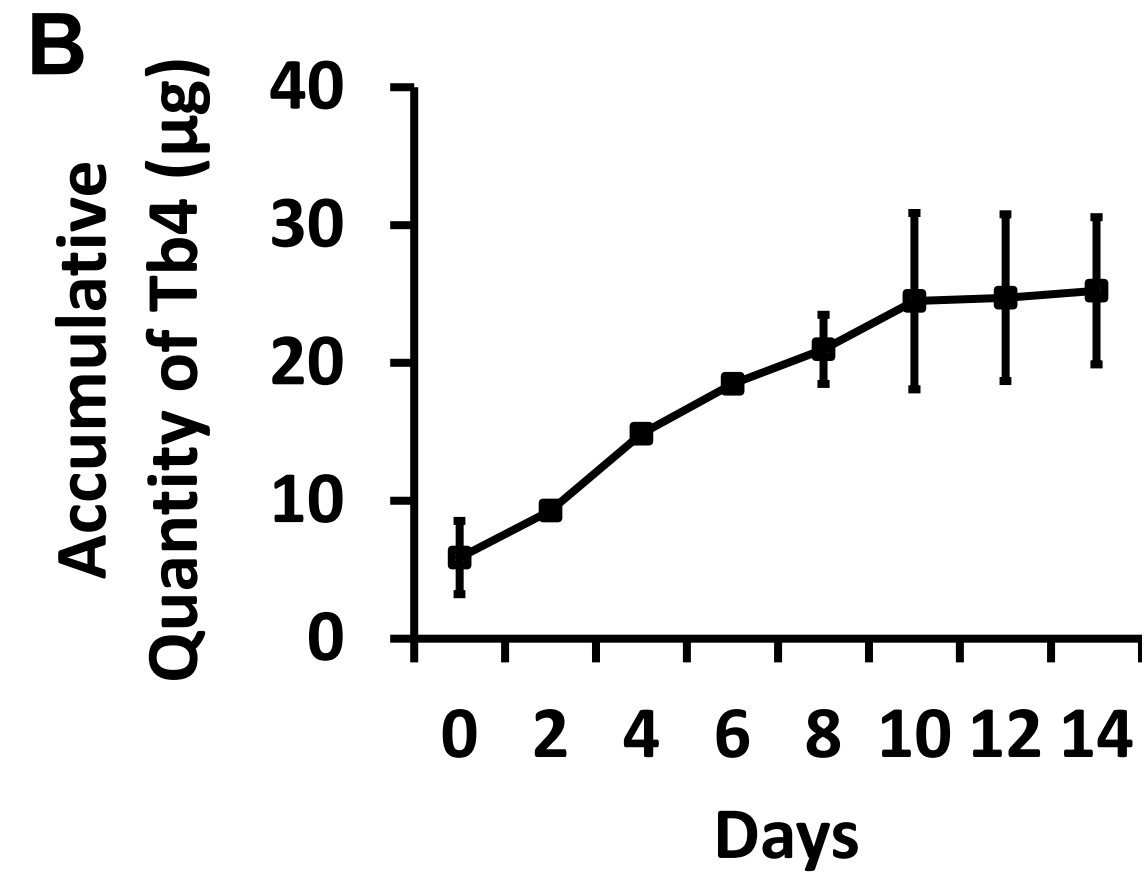




**Figure S2.** Representative images of smooth muscle cells (SMCs) cultured in either hiPSC-CM conditioned M231 medium (cM231) (E), or fresh M231 medium (fM231) supplemented with 600 ng / mL Tb4 (F), or cM231 supplemented with 600 ng / mL (G) for 24 h, and then cells were co-stained for expression of Ki67 and smooth muscle actin (SMA) proteins. (H) Quantification of SMCs expressing Ki67. (Bar = 100 μm). (n = 3. Independent T-test. \*\*: p < 0.01, \*\*\*: P < 0.001). Values are presented as the means ± SD.

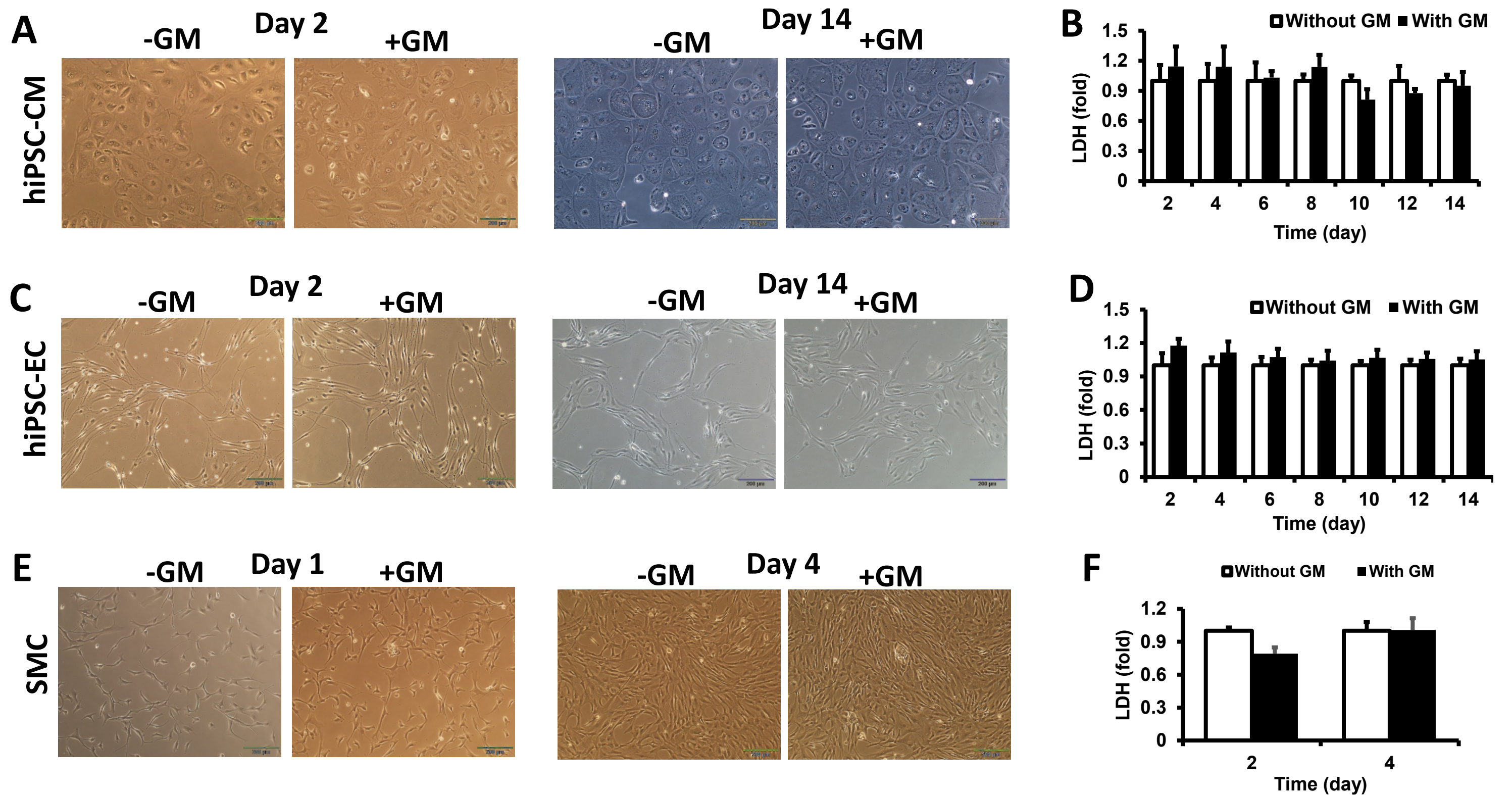


**Figure S2.** Dual immunostaining of hiPSC-CMs for protein expression of atrial isoform myosin light chain 2 (MLC2a) and ventricular isoform myosin light chain 2 (MLC2v) (I). Protein expressions of cardiac troponin T (cTnT) and troponin I isoform 3 (TNNI3) in hiPSC-CMs (J). (Bar = 50 μm).



**Figure S3. Gelatin microspheres for controlled release of Tb4.** (A) Typical images of fresh manufactured gelatin microspheres. (Bar = 100  $\mu\text{m}$ ). (B) Accumulative release profile of Tb4 that was loaded into microspheres up to 14 days *in vitro*. (n=2). (C) Tb4-his concentration in rat serum as a function of time *in vivo*. (n=4). Values are presented as the means  $\pm$  SD.



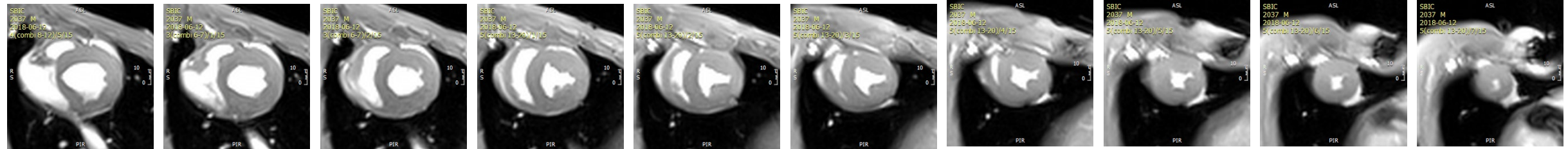


**Figure S4. Tests to determine the toxic effect of gelatin microspheres on cardiac cells. (A)** Morphological profile of hiPSC-CM treated with or without gelatin microspheres (+GM or -GM). **(B)** Lactate dehydrogenase (LDH) concentration in hiPSC-CM supernatant as a function of time. **(C)** Morphological profile of hiPSC-ECs treated with or without gelatin microspheres. **(D)** LDH concentration in hiPSC-EC supernatant as a function of time. **(E)** Morphological profile of human coronary artery SMCs treated with or without gelatin microspheres. **(F)** LDH concentration in hiPSC-EC supernatant as a function of time. (Bar = 200 $\mu$ m. Values are presented as the means  $\pm$  SD).

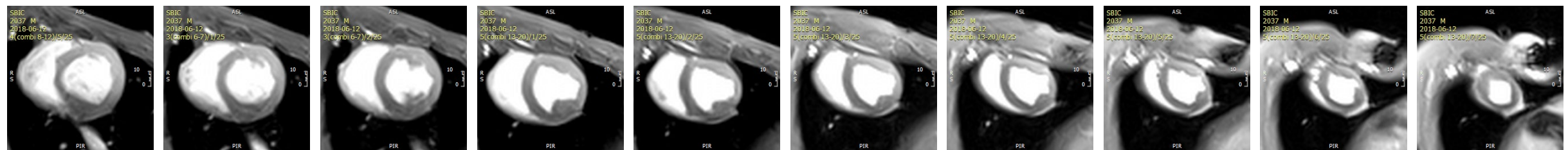


**A**

**The end  
of systole**



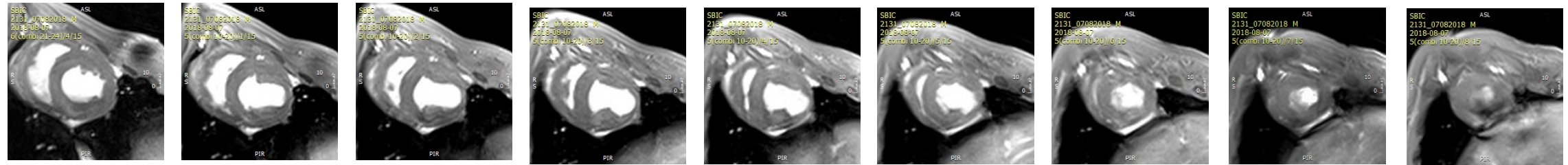
**The end  
of diastole**



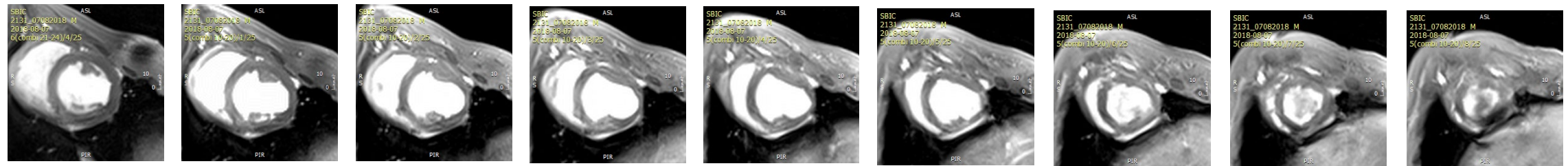
**Figure S5. MRI images of pig hearts for measuring left ventricular ejection fraction (LVEF). (A) Representative images of short-axis left ventricular chamber at the end of systole and the end of diastole in a pig heart of the Sham Group.**

## B1

The end of systole

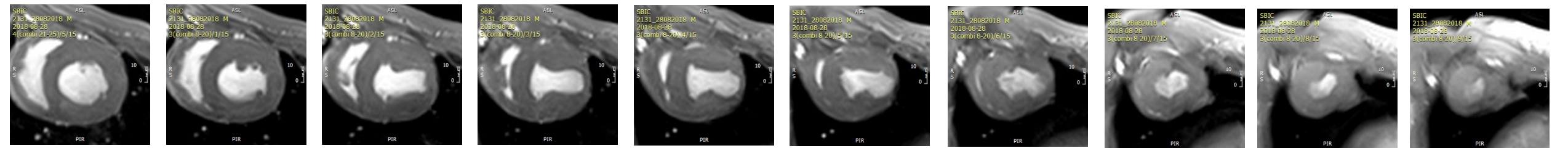


The end of diastole

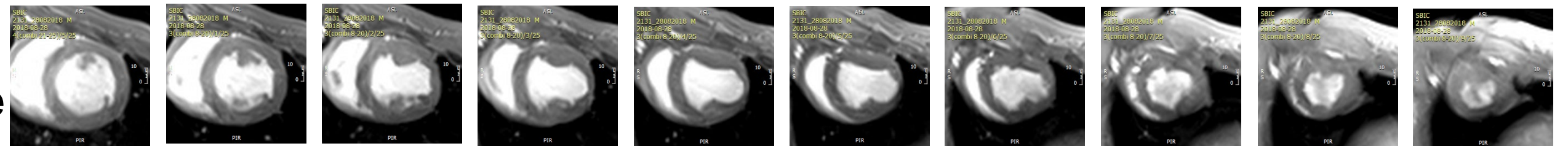


## B2

The end of systole



The end of diastole

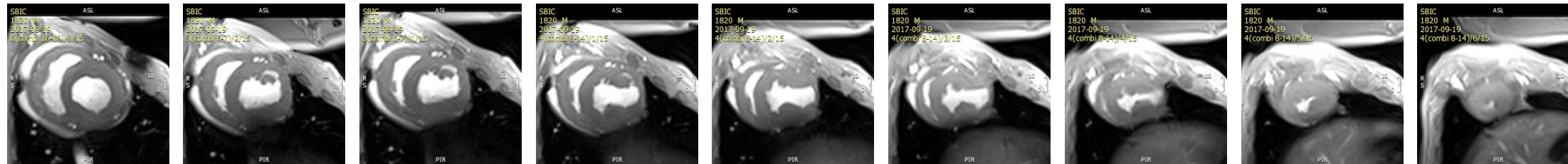


**Figures S5.** Representative images of short-axis left ventricular chamber at the end of systole and the end of diastole in the pig hearts of the MI Group at weeks-1 (**B1**) and -4 (**B2**) after MI and treatment.

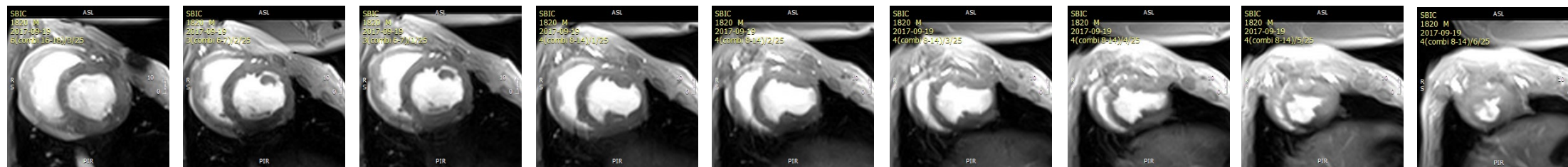


# C1

The end of systole

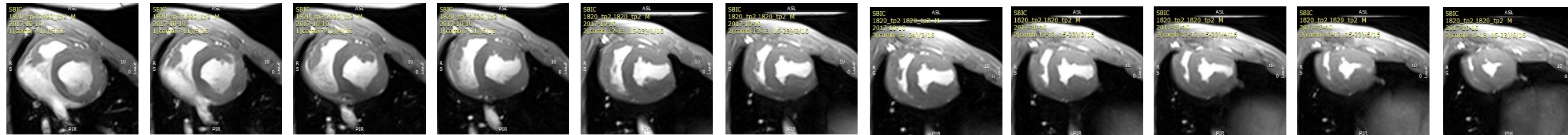


The end of diastole



# C2

The end of systole



The end of diastole

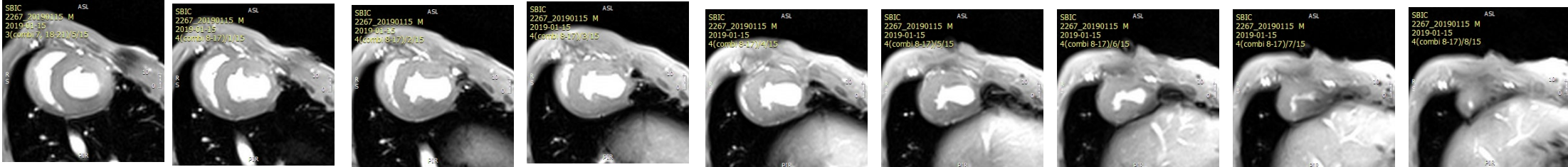


**Figures 5C1&C2.** Representative images of short-axis left ventricular chamber at the end of systole and the end of diastole in pig hearts of the Tb4 Group at weeks-1 (**C1**) and -4 (**C2**) after MI and treatment.

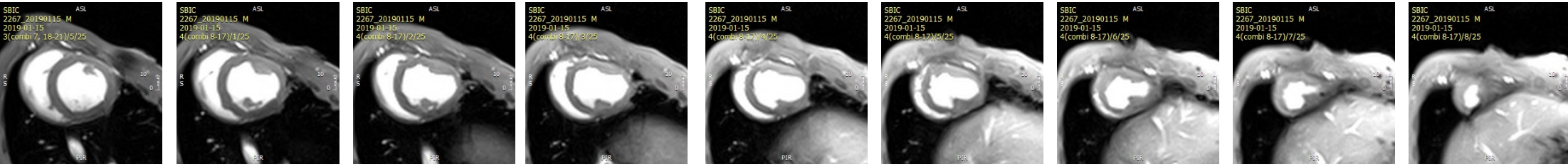


# D1

The end of systole

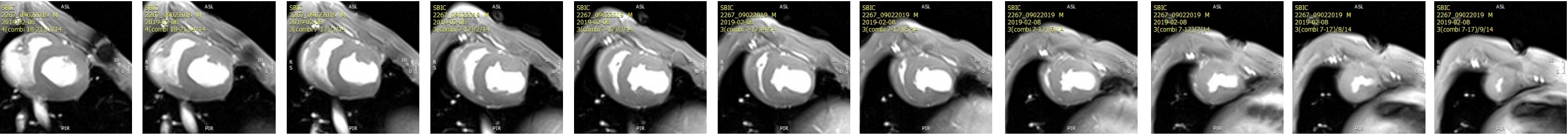


The end of diastole

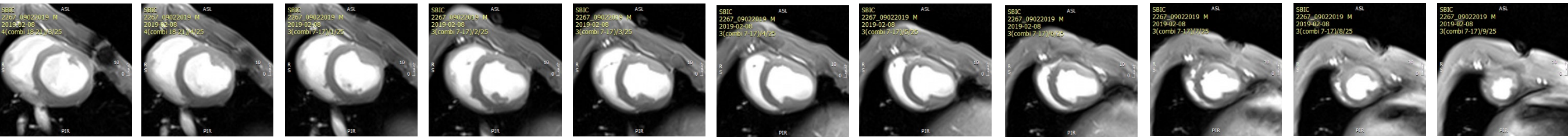


# D2

The end of systole



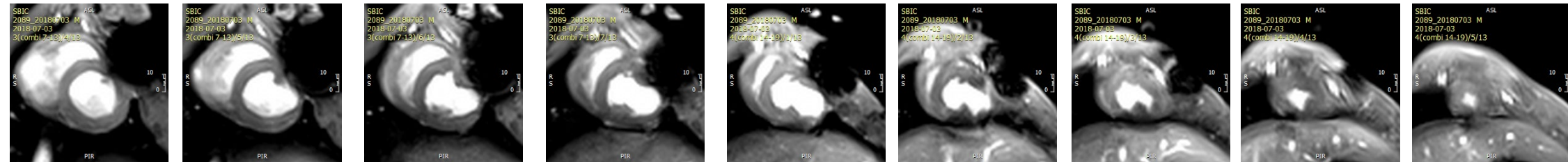
The end of diastole



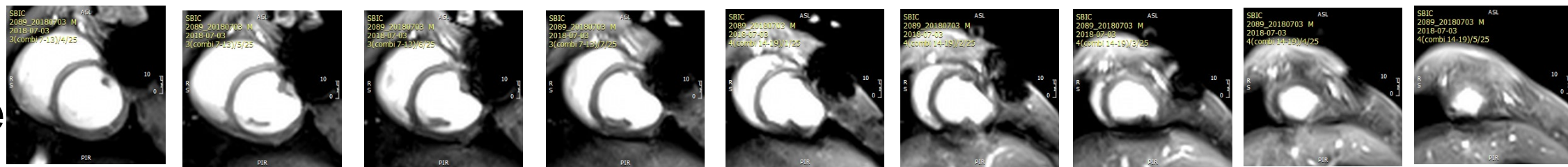
**Figures S5.** Representative images of short-axis left ventricular chamber at the end of systole and the end of diastole in the pig hearts of the CM Group at weeks-1 (**D1**) and -4 (**D2**) after MI and treatment.



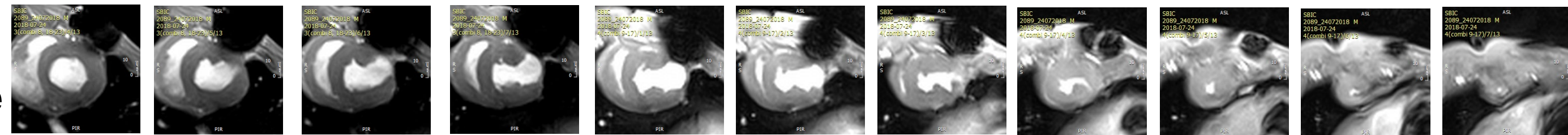
**E1**  
The end  
of systole



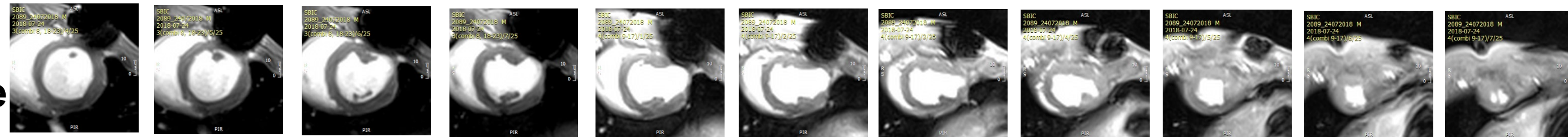
The end  
of diastole



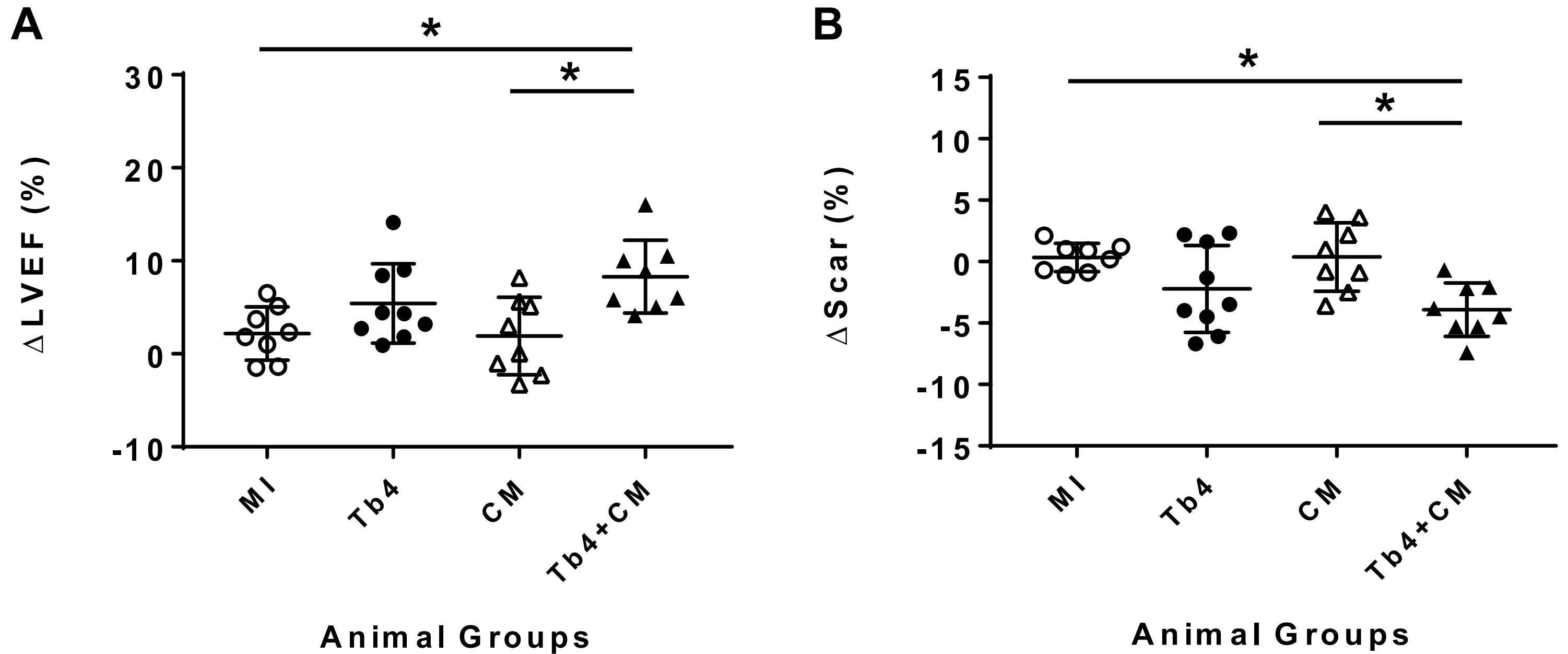
**E2**  
The end  
of systole



The end  
of diastole

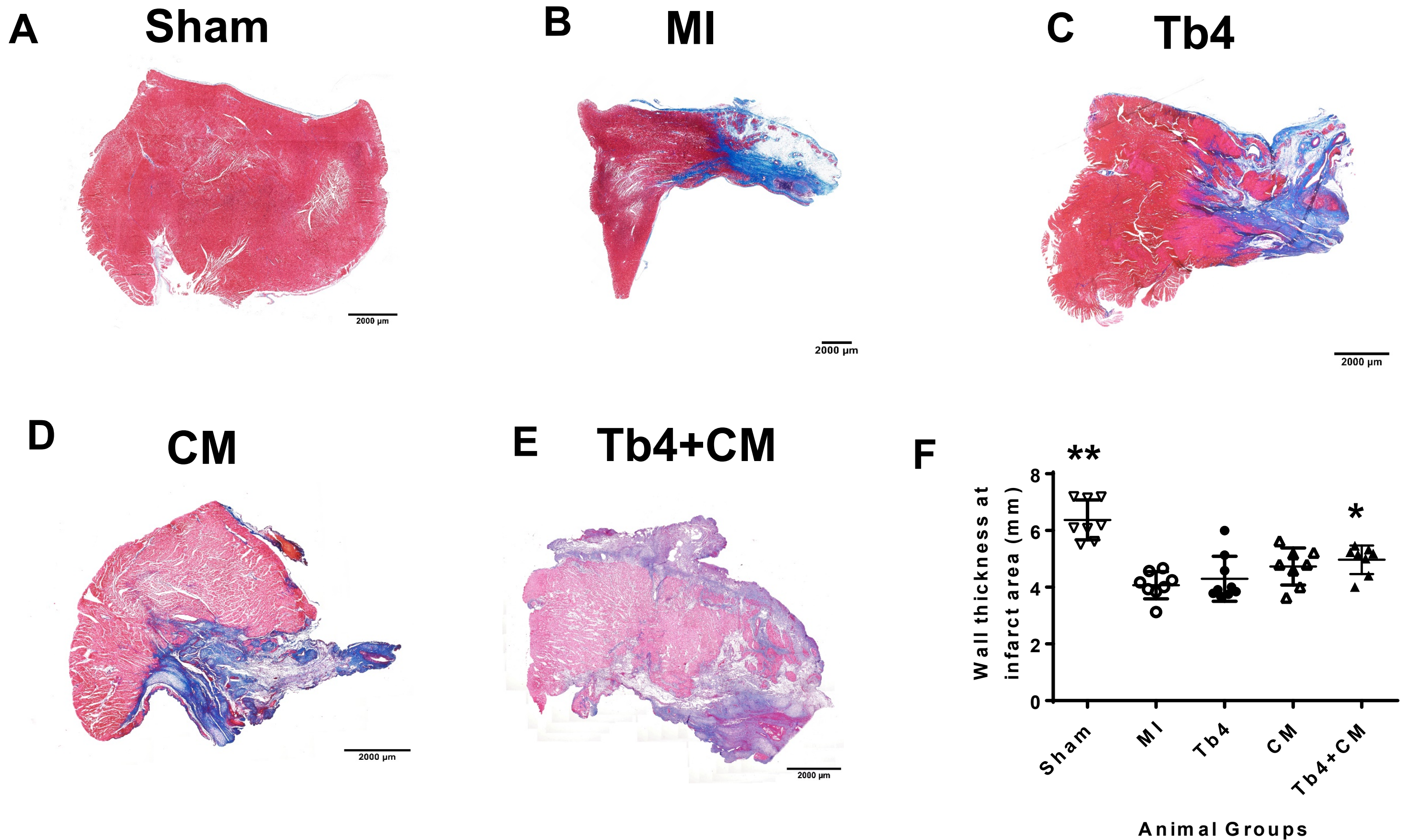


**Figures S5.** Representative images of short-axis left ventricular chamber at the end of systole and the end of diastole in the pig hearts of the Tb4 + CM Group at weeks-1 (**E1**) and -4 (**E2**) after MI and treatment.



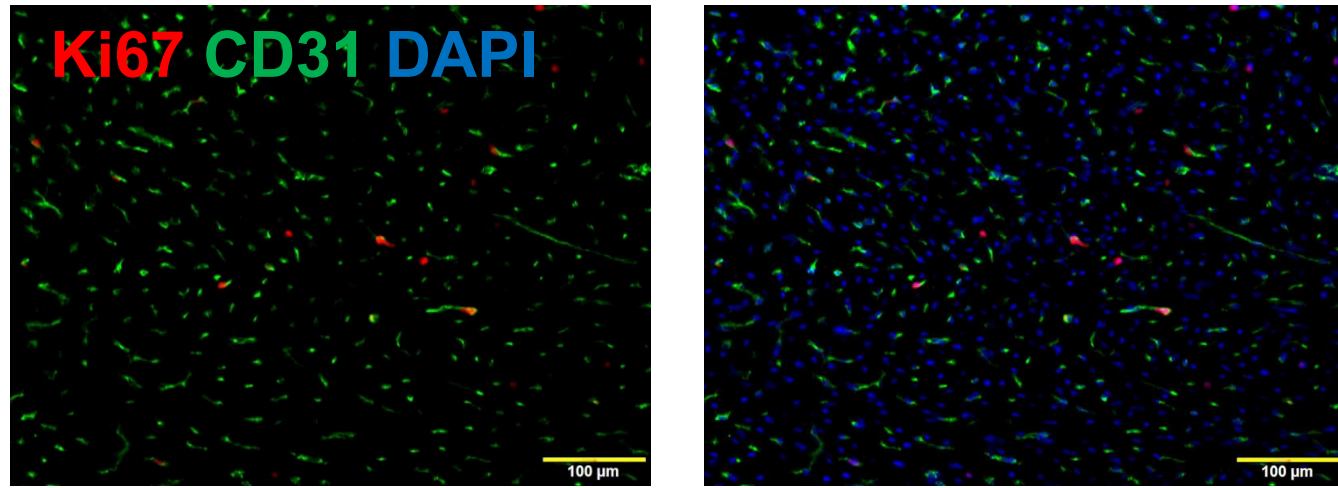
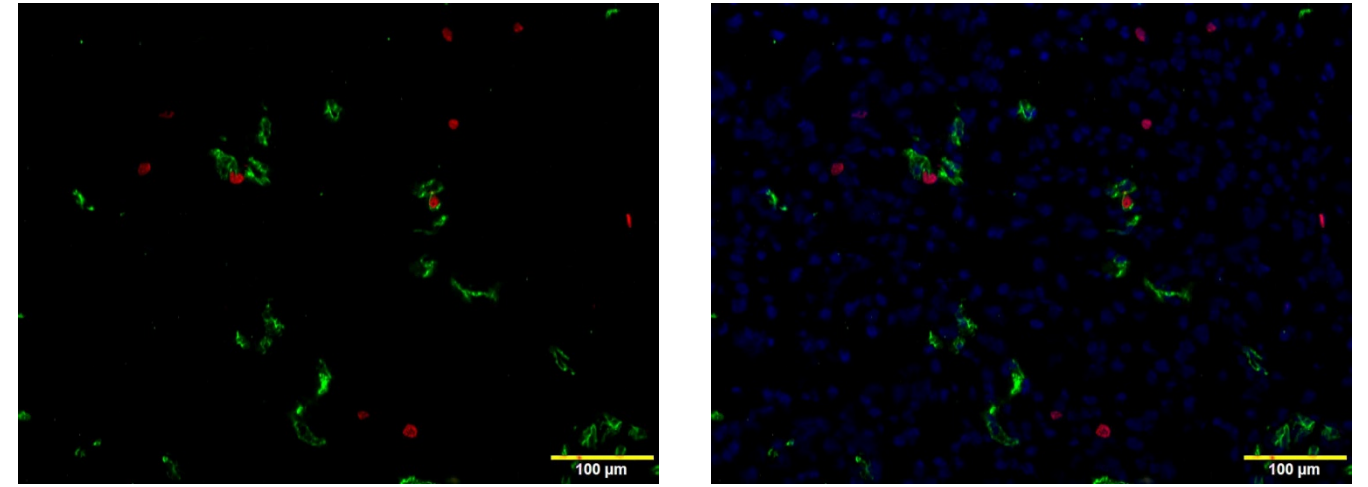
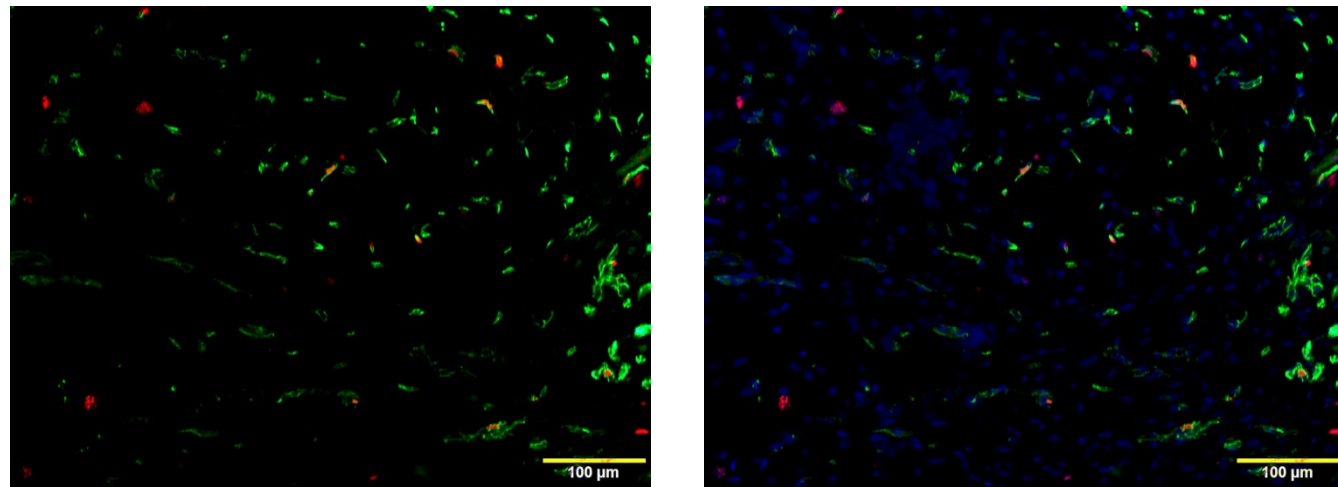
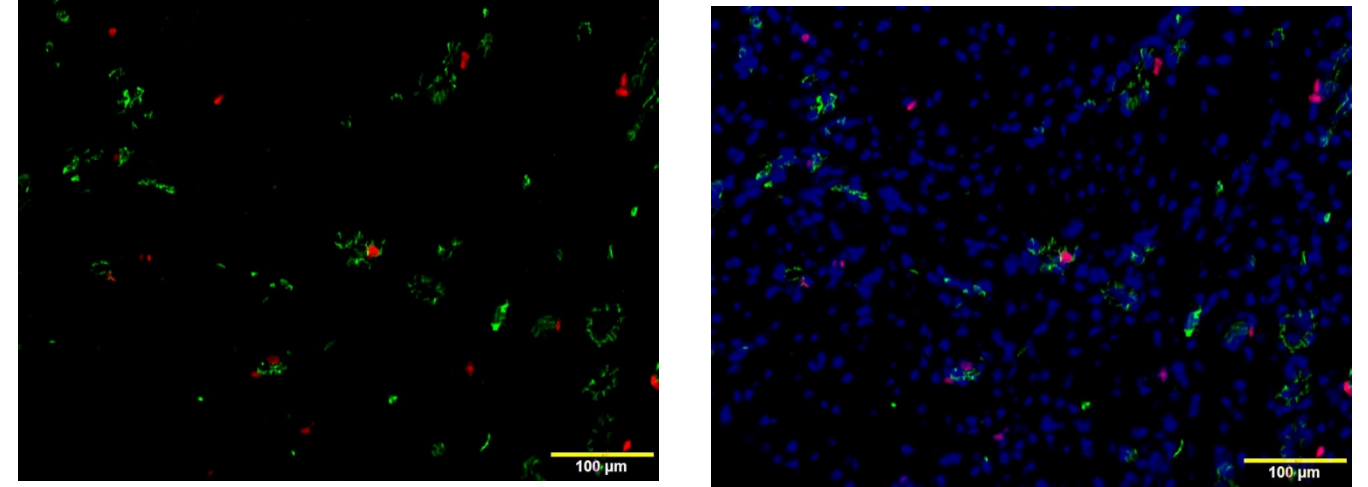
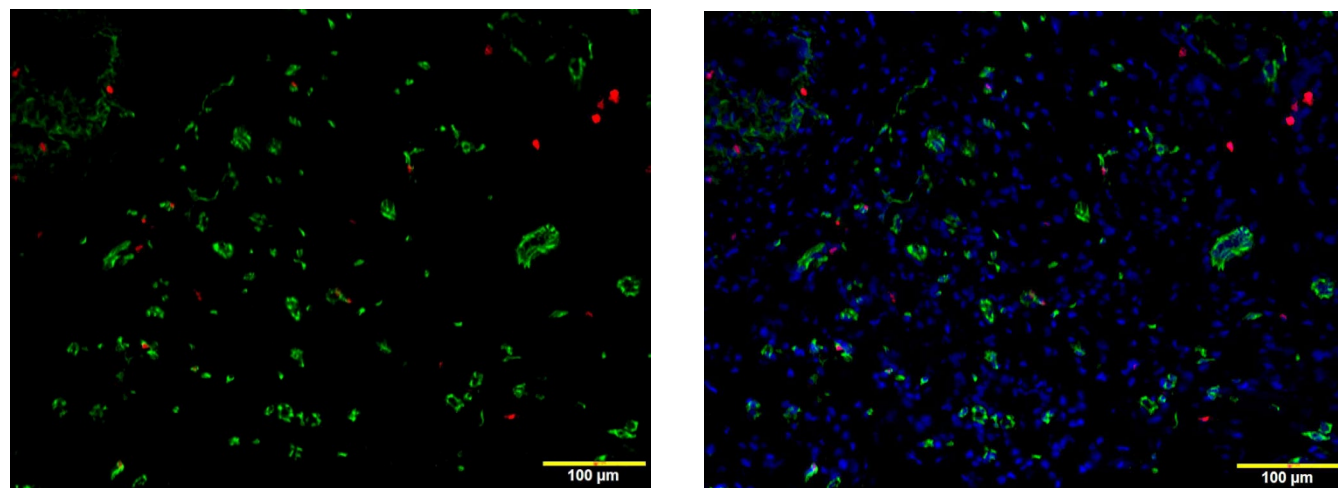
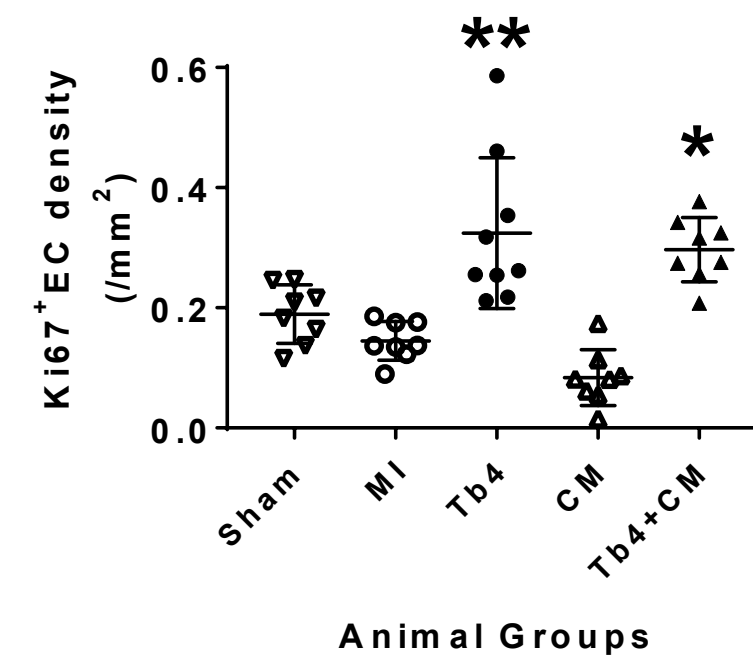
**Figure S6. Changes of LVEF ( $\Delta$ LVEF) and scar area ( $\Delta$ scar) in the pig hearts. (A)  $\Delta$ LVEF in each group is calculated by LVEF at week-4 minus LVEF at week-1. (B)  $\Delta$ scar in each group is calculated by scar area at week-4 minus scar area at week-1. (n = 8 - 9 for each group. One-way ANOVA: \*: P < 0.05). Values are presented as the means  $\pm$  SD.**





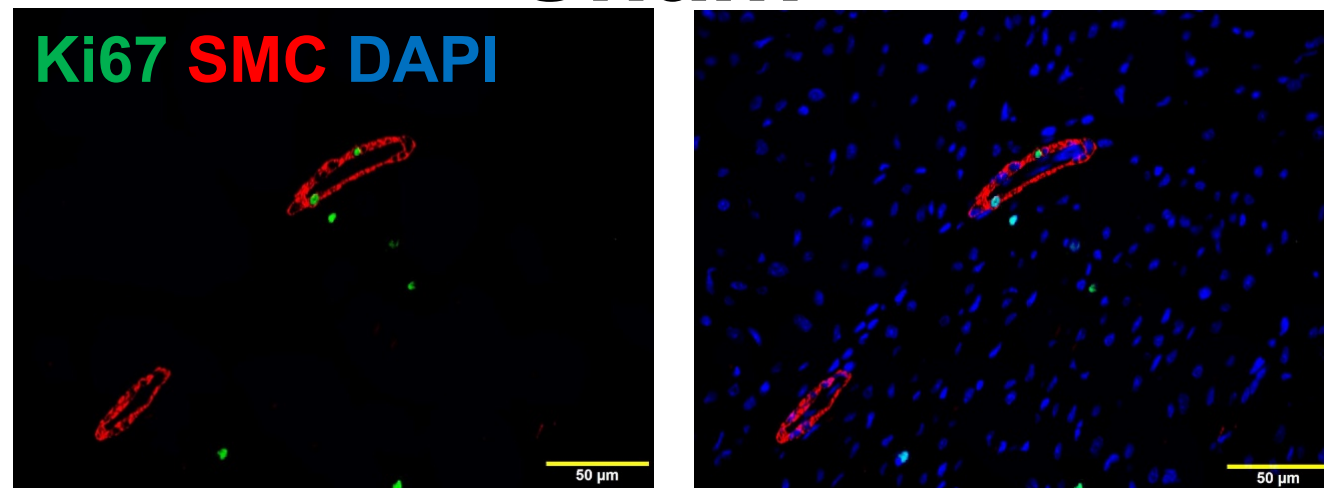
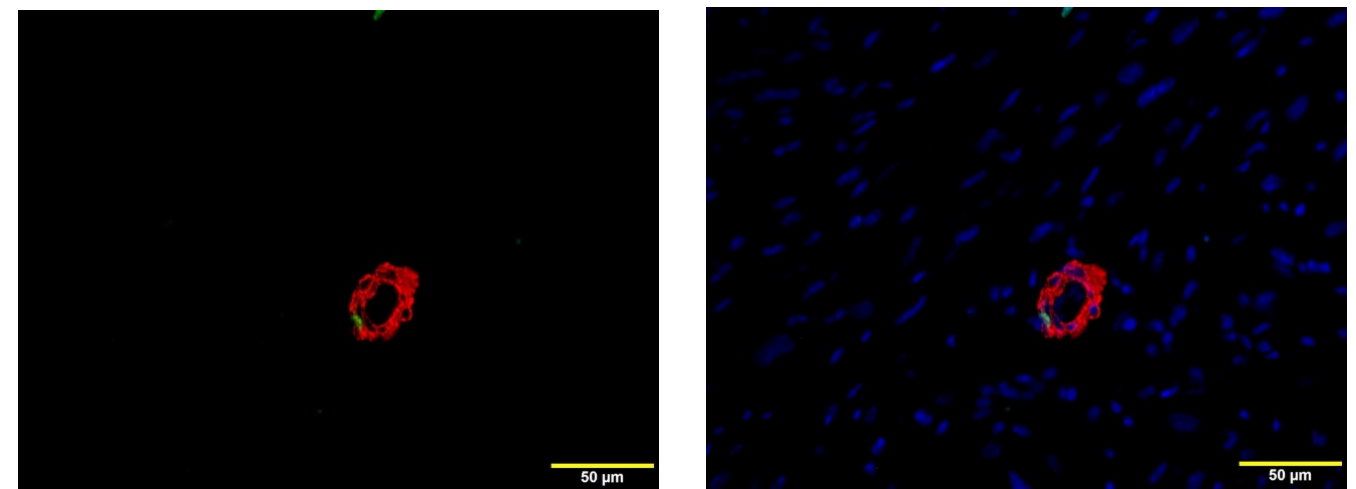
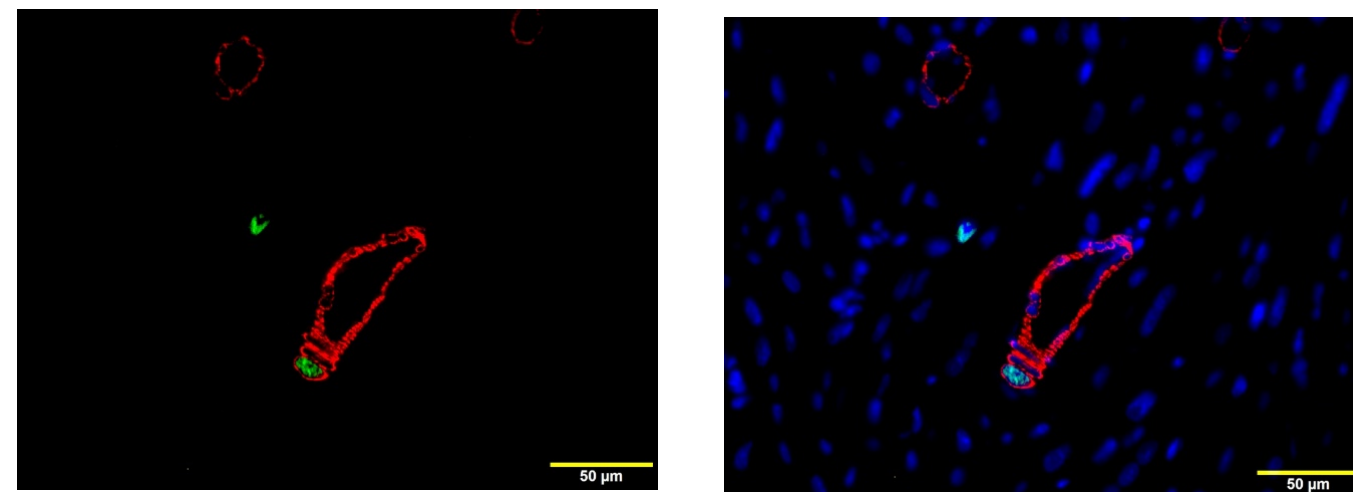
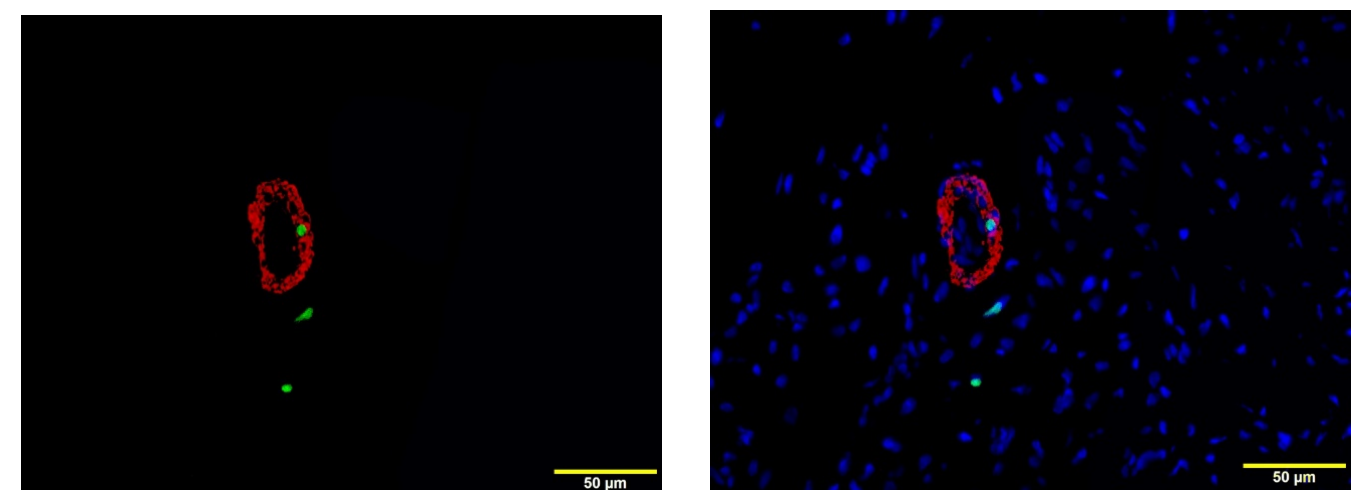
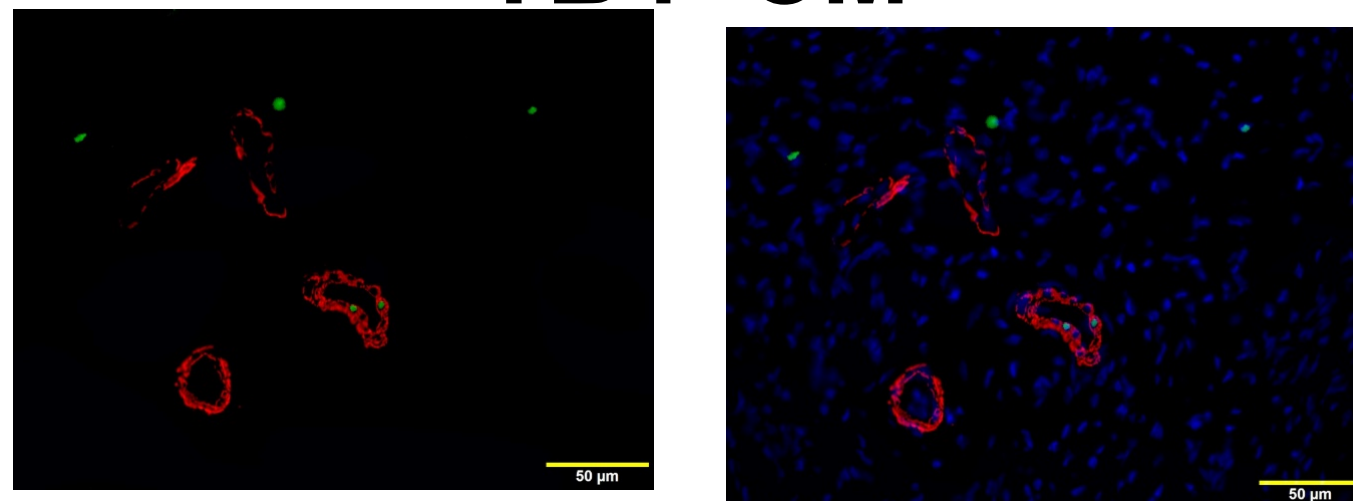
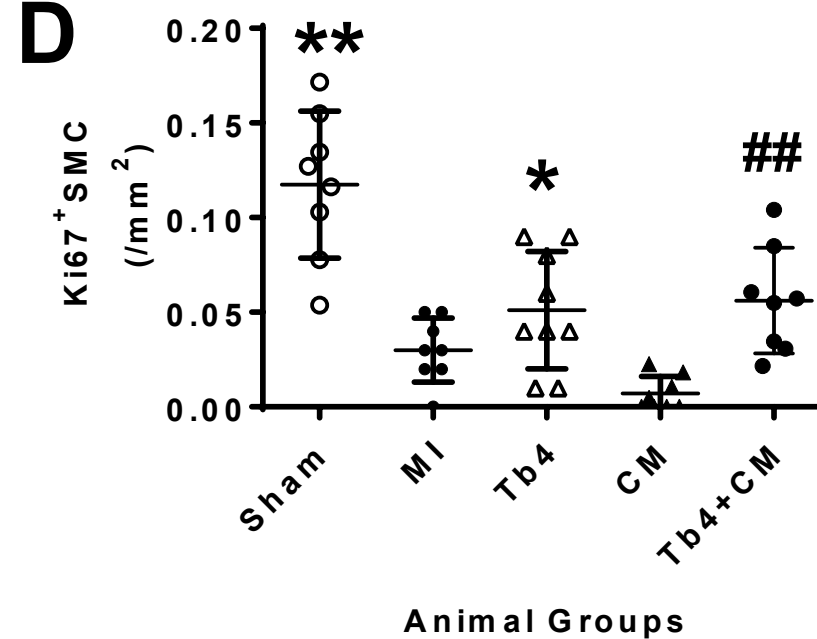
**Figure S7. Macro-images of infarct myocardium in the pig hearts using Masson's Trichrome staining.** Representative images of Masson's Trichrome stained pig heart tissue to visualize scar in the pig hearts of the Sham (A), MI (B), Tb4 (C), CM (D), and Tb4+CM (E) Groups at week-4 after MI and treatment. (F) Quantification of wall thickness at infarct area. (n=8 or 9 for each group. One-way ANOVA. \*\*: P < 0.01 vs every other group; \*: P < 0.05 vs the MI Group). Values are presented as the means  $\pm$  SD. Bar = 2000  $\mu$ m.



**A****Sham****MI****Tb4****CM****Tb4+CM****B**

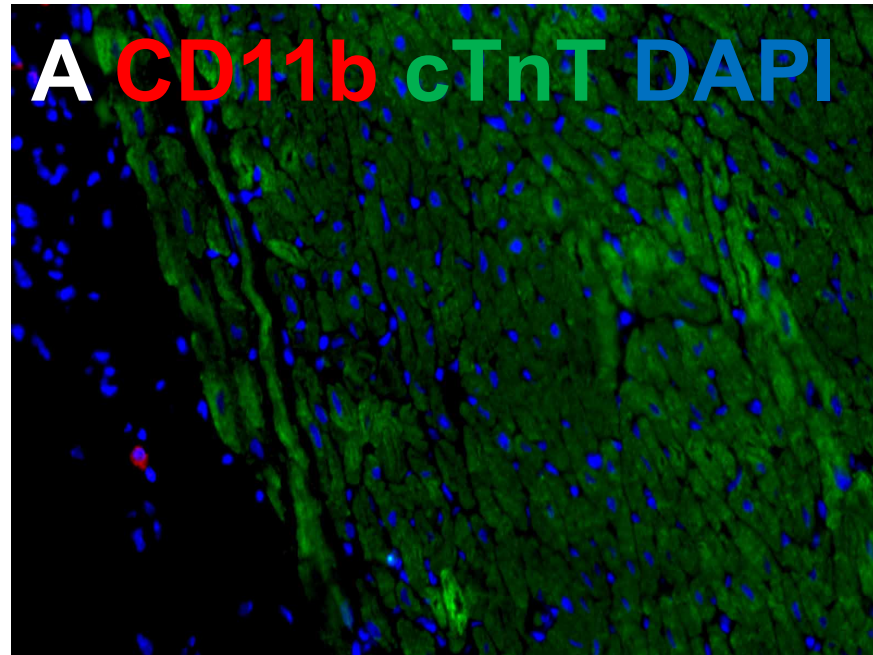
**Figures S8. Proliferation of endothelial cells (ECs) and smooth muscle cells (SMCs) in the pig hearts at week-4 after MI and treatment. (A)** Representative images of Ki67 expressing ECs in the Sham, MI, Tb4, CM, and Tb4 + CM Groups at Week-4 after MI and treatment. **(B)** Quantitative analysis of Ki67<sup>+</sup>ECs in all animal groups. (n = 8 or 9 for each group. One-way ANOVA. \*\*: P < 0.01 vs the Sham, MI, and CM Groups ; \*: P < 0.05 vs the Sham, MI, and CM Groups). Values are presented as the means ± SD. Bar = 100 μm.



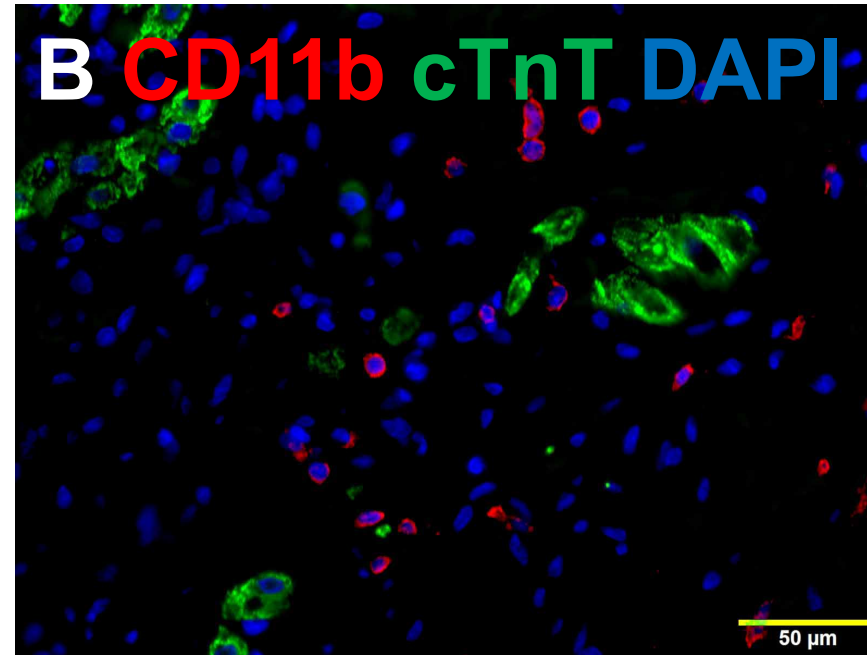
**C****Sham****MI****Tb4****CM****Tb4+CM****D**

**Figures S8. (C)** Representative images of Ki67 expressing SMCs in the Sham, MI, Tb4, CM, and Tb4 + CM Groups at Week-4 after MI and treatment. **(D)** Quantitative analysis of Ki67<sup>+</sup>SMCs in all animal groups. (n = 8 or 9 for each group. One-way ANOVA. \*\*: P < 0.01 vs every other group; ##: P < 0.01 vs the MI and CM Groups; \*: P < 0.05 vs the CM Group). Values are presented as the means ± SD. Bar = 50 μm.

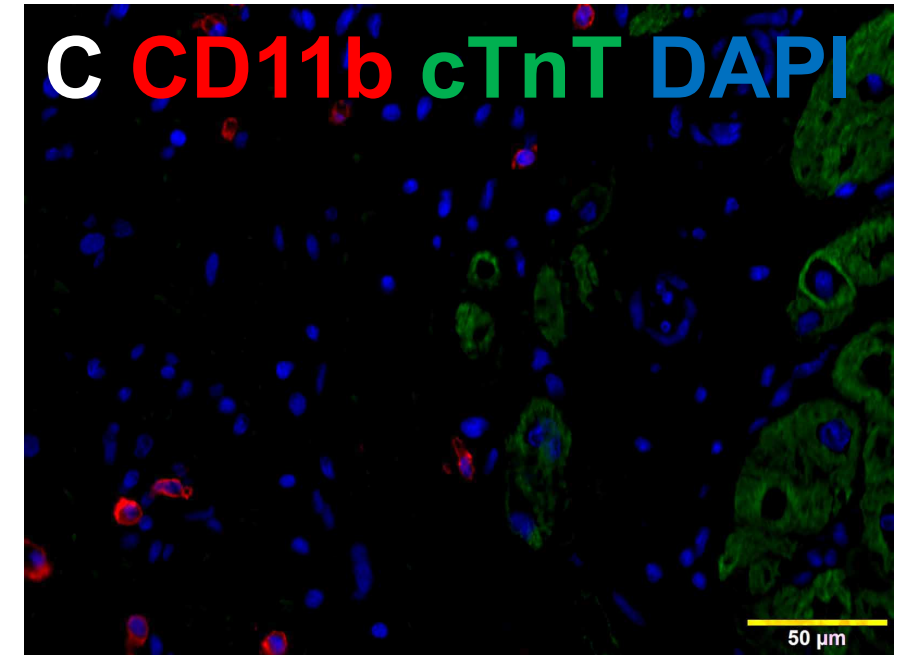
# Sham



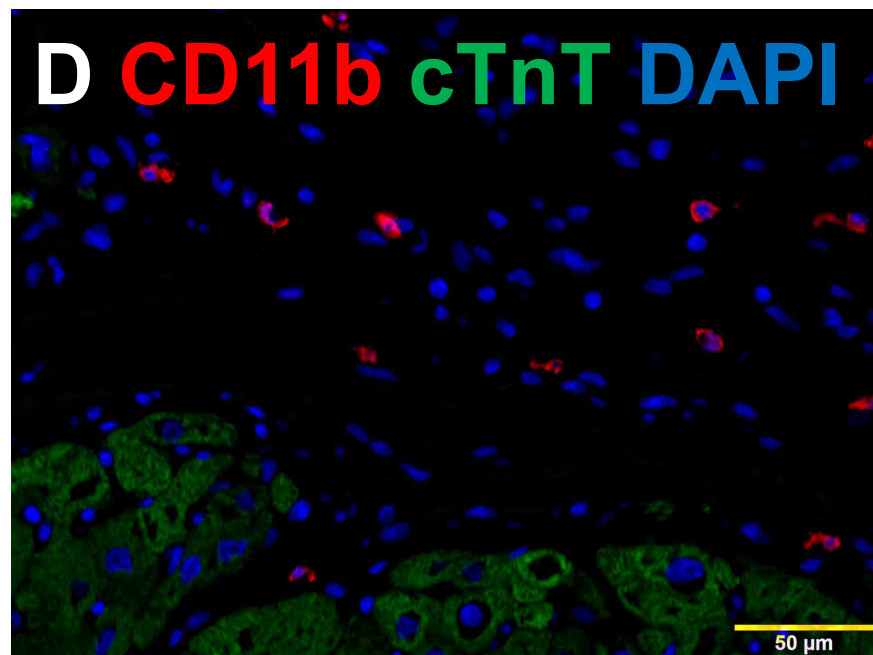
# MI



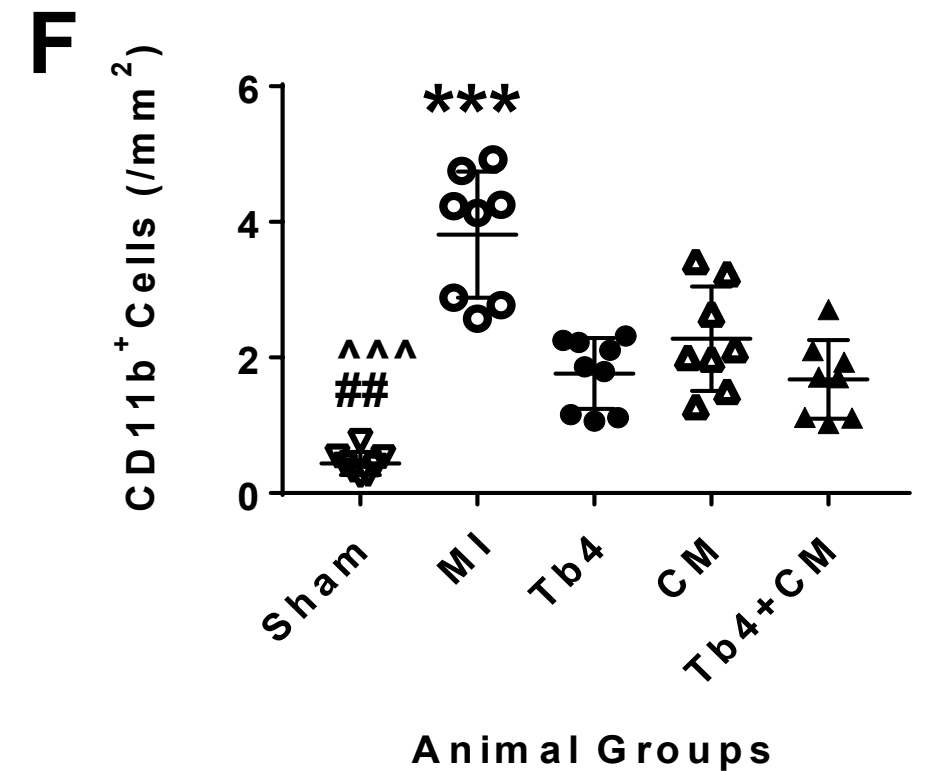
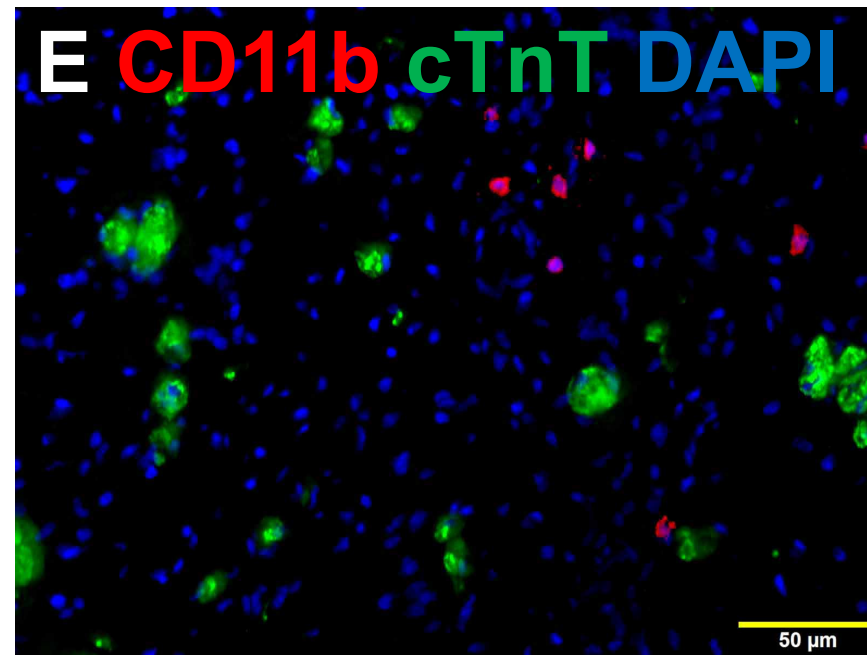
# Tb4



# CM



# Tb4 + CM



**Figure S9. Fluorescence immunostaining for detecting CD11b<sup>+</sup> cells.** Representative images of CD11b<sup>+</sup> cells in the Sham (A), MI (B), Tb4 (C), CM (D), and Tb4 + CM (E). (F) Quantitative analysis of CD11b<sup>+</sup> cells in all animal groups. (n = 8 or 9 for each group. One-way ANOVA. ^^^: p < 0.001 vs the MI and CM Groups; ##: p < 0.01 vs the Tb4 and Tb4 + CM Groups; \*\*\*: P < 0.001 vs every other group). Values are presented as the means ± SD. Bar = 50 μm.



**Table S1 . Number of animals in each group**

	<b>Sham Group</b>	<b>MI Group</b>	<b>Tb4 Group</b>	<b>hiPSC-CM Group</b>	<b>Tb4 + hiPSC-CM Group</b>
<b>4 weeks</b>	8	8	9	8	8
<b>12 weeks</b>	0	0	0	0	6

**Table S2. Human Angiogenesis Array Q2**

	hiPSC-CM	hiPSC-CM + Tb4
<b>Activin A</b>	30.16	21.90
<b>AgRP</b>	2.88	3.31
<b>Angiogenin</b>	1.34	1.30
<b>ANG-2</b>	1.00	10.17
<b>ANGPTL4</b>	0	0
<b>bFGF</b>	0	22.48
<b>ENA-78</b>	17.51	2.00
<b>GRO</b>	0	3.55
<b>HB-EGF</b>	0	0.35
<b>HGF</b>	0	0
<b>IFNg</b>	0.25	0
<b>IGF-I</b>	51.46	0
<b>IL-1a</b>	0	0
<b>IL-2</b>	3.04	1.26
<b>IL-6</b>	0.86	0
<b>IL-8</b>	0	0
<b>IL-17</b>	0	0
<b>IP-10</b>	0.29	0
<b>Leptin</b>	18.66	18.45
<b>LIF</b>	9.21	12.81
<b>MCP-1</b>	54.95	58.22
<b>PDGF-BB</b>	1.62	1.28
<b>PIGF</b>	0.73	2.48
<b>RANTES</b>	0	0.15
<b>TGFb1</b>	0	0
<b>TIMP-1</b>	7497.31	6579.71
<b>TIMP-2</b>	3233.89	2480.30
<b>TNFa</b>	0	0
<b>TNFb</b>	0	0
<b>TPO</b>	104.52	75.75

**Table S3. Human Angiogenesis Array Q3**

	hiPSC-CM	hiPSC-CM + Tb4
<b>ANG-1</b>	0	0
<b>Angiostatin</b>	4554.59	4568.78
<b>CXCL16</b>	1.37	0
<b>EGF</b>	0.12	0.05
<b>FGF-4</b>	25.98	151.24
<b>Follistatin</b>	7217.05	8028.29
<b>G-CSF</b>	0	0.44
<b>GM-CSF</b>	0.37	2.07
<b>I-309</b>	0	0
<b>IL-1b</b>	0	2.90
<b>IL-4</b>	0.28	1.16
<b>IL-10</b>	0	0
<b>IL-12p40</b>	9.56	10.38
<b>IL-12p70</b>	0.20	0.47
<b>I-TAC</b>	2.23	9.41
<b>MCP-2</b>	1.41	0.33
<b>MCP-3</b>	1.39	1.46
<b>MCP-4</b>	2.00	22.86
<b>MMP-1</b>	218.17	94.03
<b>MMP-9</b>	4.61	0
<b>PECAM-1</b>	25.08	2.27
<b>TGFa</b>	11.69	8.21
<b>TGFb3</b>	0.20	0.45
<b>Tie-1</b>	106.91	0
<b>Tie-2</b>	0	5.25
<b>uPAR</b>	309.60	197.61
<b>VEGF</b>	87.75	123.16
<b>VEGF R2</b>	7.74	2.44
<b>VEGF R3</b>	9.35	8.19
<b>VEGF-D</b>	9.51	0



**Video-1:** shows the upper abdomen to the pelvis, including part of the liver, small and large intestines, kidneys and urinary bladder at 1 week post cell implantation.

**Video-2:** shows the neck (larynx) to the upper abdomen, including the heart, lung, liver, gallbladder, stomach and part of the large bowel at 1 week post cell implantation.

**Video3:** shows the head (brain) to the upper chest at 1 week post cell implantation.

**Video-4:** shows Sagittal view of the thorax centered at the level of the heart at 1 week post cell implantation.

**Video-5:** shows Head and upper neck including the brain, larynx at 3 months post-cell implantation.

**Video-6:** shows upper neck (larynx) to the upper chest (mediastinum)\_ larynx, lungs, heart at 3 months post-cell implantation.

**Video-7:** shows the upper chest (mediastinum) to the upper abdomen, including the heart, lungs, part of the liver and gallbladder at 3 months post-cell implantation.

**Video-8:** shows the upper abdomen to the abdomen, liver, gallbladder, bowels, kidneys and urinary bladder at 3 months post-cell implantation.

**Video-9:** shows the abdomen to the pelvis - bowels, kidneys and urinary bladder at 3 months post-cell implantation.

**Video-10:** shows the lower pelvis, perineum area with partly visualised urinary bladder, rectum and part of the vagina at 3 months post-cell implantation.