Electric Supplementary Information for

Biodegradation of injectable silk fibroin hydrogel prevents negative left ventricular remodeling after myocardial infarction

Yusuke Kambe[a] and Tetsuji Yamaoka[*a]

[a]Department of Biomedical Engineering, National Cerebral and Cardiovascular Center (NCVC) Research Institute, 6-1 Kishibeshinmachi, Suita, Osaka 564-8565, Japan.

E-mail: yamtet@ncvc.go.jp; Tel: +81-6-6170-1070 (ext 31009); Fax: +81-6-6170-1702

MGGSHHHHHHGMASMTGGQQMGRDLYDDDDKDRW**GSGYEYAWSSESDFGTGSG AASGAGAGAGAGAGTGSSGFGPYVANGGYSG***REDVREDV*GPQGIWGQKLTWQEL YQLKYKGIKK

Figure S1 Amino acid sequence of the fusion peptide. Sequences of the FibH-derived peptide are in bold; sequences of the tandem repeat of cell-adhesive REDV are italicized; sequences of the MMP-cleavable peptide are in gray; and sequences of the vascular endothelial growth factor-mimicking QK peptide are underlined.

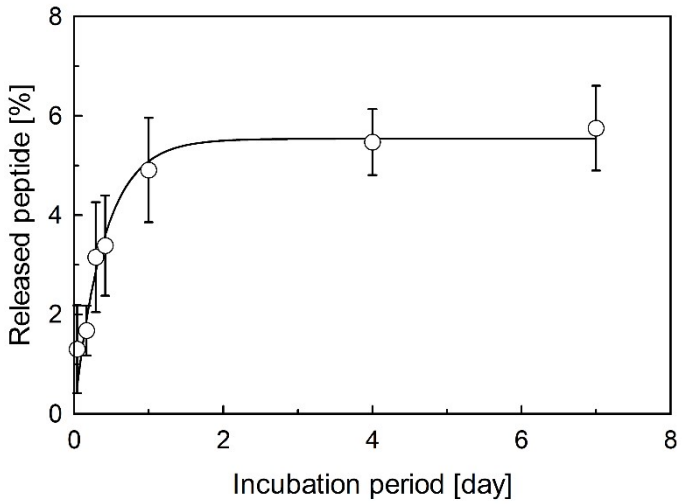

Figure S2 Release behavior of a tetramethylrhodamine (TAMRA)-labelled fusion peptide from SF hydrogels modified with the TAMRA-peptide in PBS at 37°C. Curve fitting was done using a single exponential association. Data are shown as mean ± SD (n = 4).

The TAMRA-peptide was prepared as previously described.[28] An SF aqueous solution with TAMRA-peptide was mixed with ethanol in a 1.5 ml-tube (total volume: 100 μL; final concentrations: SF, 20 mg mL^{-1} TAMRA-peptide, 10 μM [0.12 mg mL^{-1}]; and ethanol, 33 vol%). After incubation at room temperature for 15 min, 200 μL of PBS was added to the tube containing the hydrogel. After incubation at 37°C for 1, 4, 7, 10, 24, 96, and 168 h, the PBS was collected and replaced. The fluorescence (excitation 557, emission 576 nm) of the collected solution was measured using a plate reader (Varioskan^{TM}; Thermo Fisher Scientific, MA, USA). Cumulative release percentage was determined based on the feed amount of TAMRA-peptide in the SF hydrogels modified with the TAMRA-peptide.

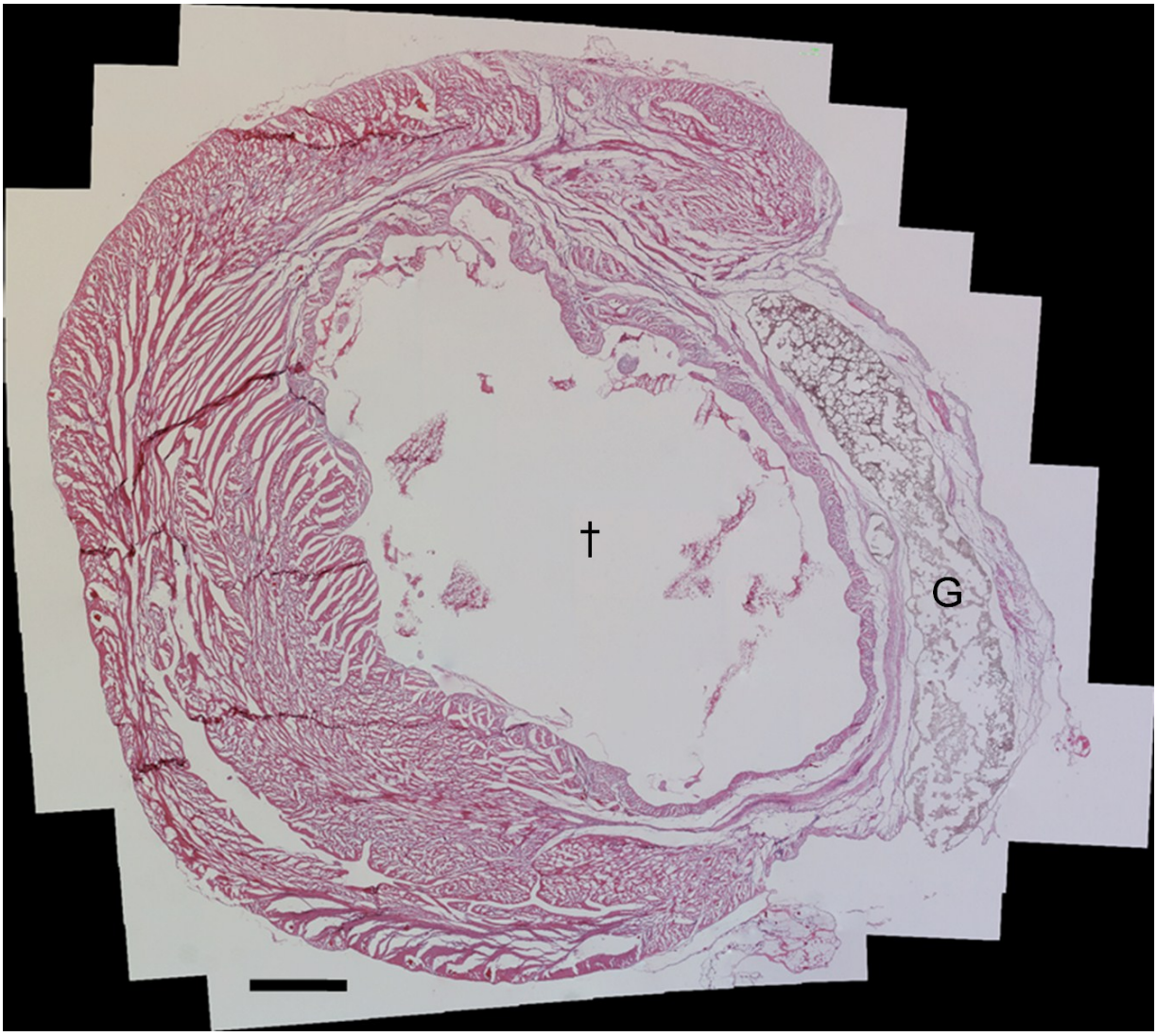

Figure S3. Photograph of the H&E-stained heart tissue section from a MI model rat with intramyocardial injection of SF hydrogel. The heart was harvested immediately after injection. Dagger indicates LV cavity. G indicates injected SF hydrogel, whose thickness was approximately 1 mm. Scale bar = 1 mm.

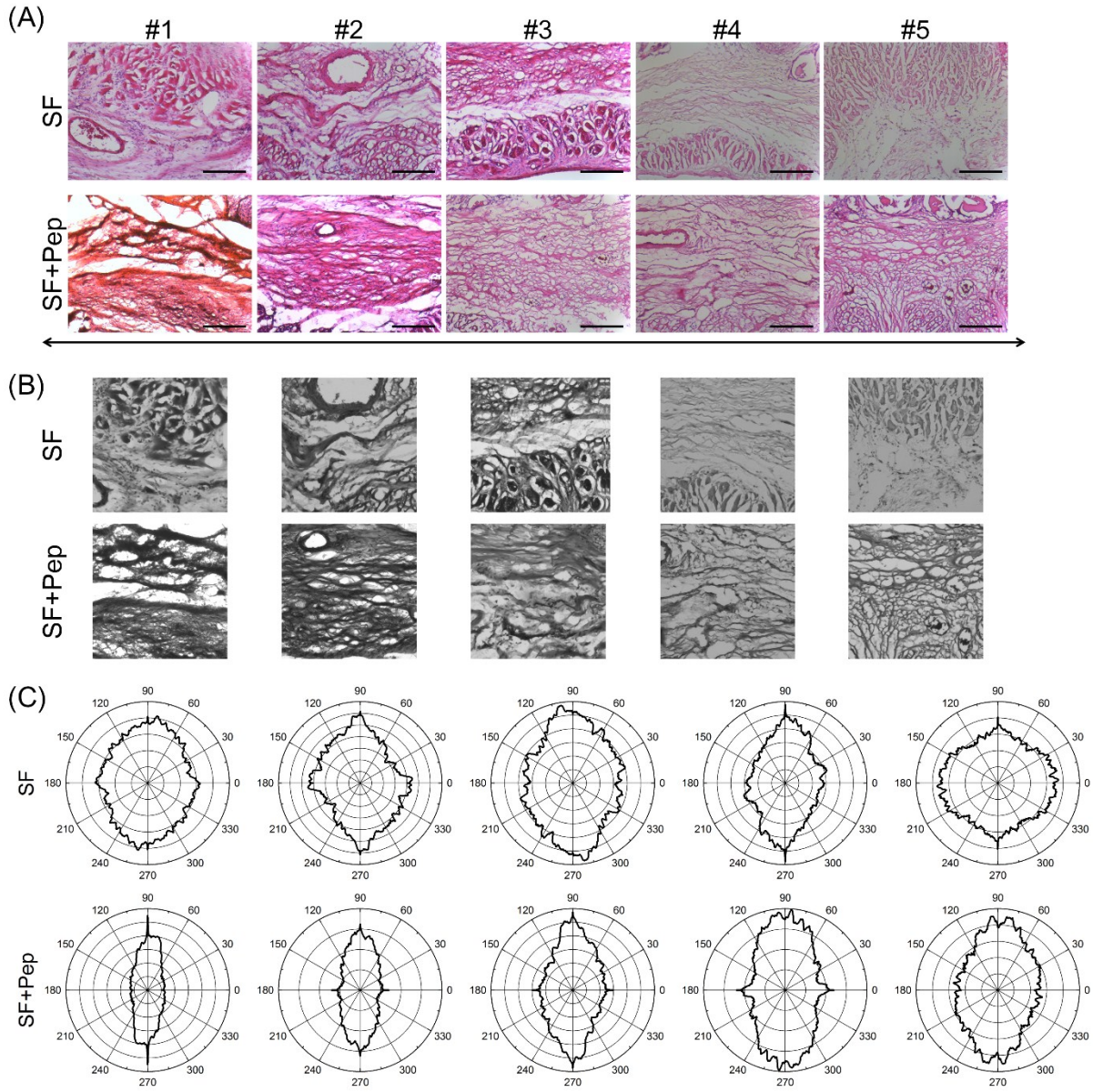

Figure S4. (A) Photographs of H&E-stained heart LV wall of MI model rats with intramyocardial injection of SF or SF+Pep hydrogel. The heart was harvested at 12 weeks post-gel injection. Double-headed arrow indicates the LV circumferential direction. Scale bar = 200 μm. (B) Photographs of the H&E-stained images converted to grayscale in the process of orientation intensity calculation. (C) Mean amplitude of the Fourier coefficient as a function of angle. The angles of 0° (180°) and 90° (270°) indicate the LV circumferential and radial directions, respectively. Higher mean amplitude indicates higher frequency of dark and light. Therefore fibers align in the direction with low mean amplitude.

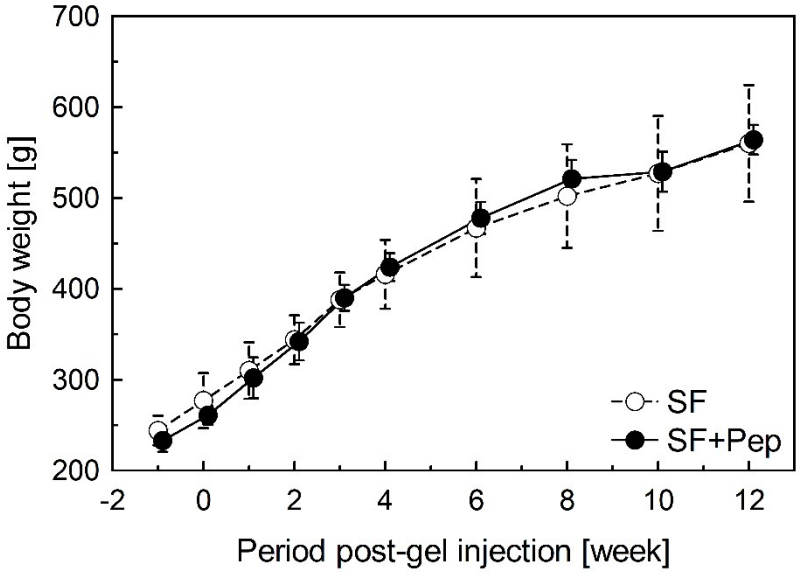

Figure S5. Time-dependent changes in body weight of MI model rats with intramyocardial injection of SF or SF+Pep hydrogel. Data are shown as mean ± SD (n = 5). There was no difference between the SF and SF+Pep groups (two-way ANOVA).

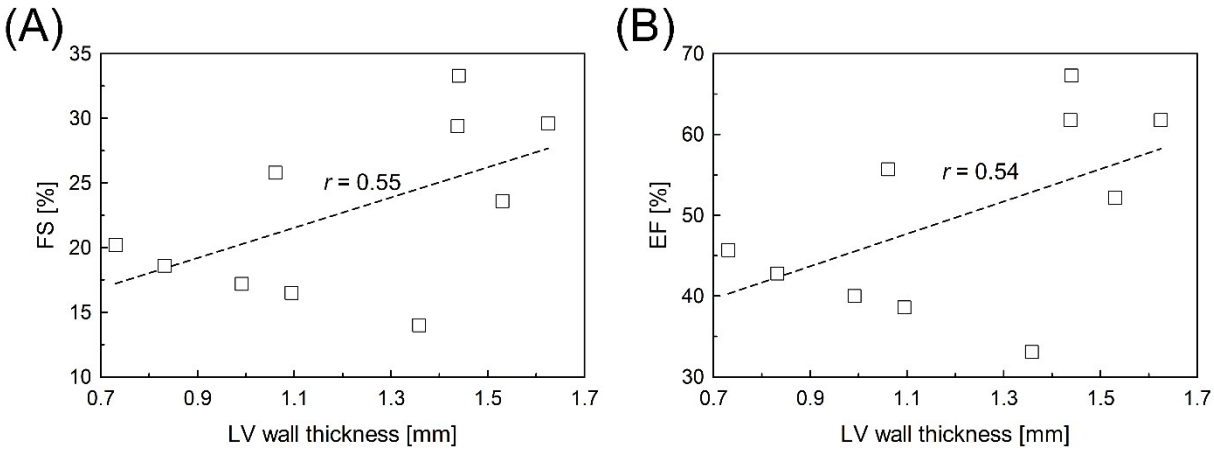

Figure S6. Correlations between LV wall thickness and cardiac function. (A) Correlation between LV wall thickness and FS (r = 0.55; p > 0.05 by simple regression analysis). (B) Correlation between LV wall thickness and EF (r = 0.54; p > 0.05 by simple regression analysis).

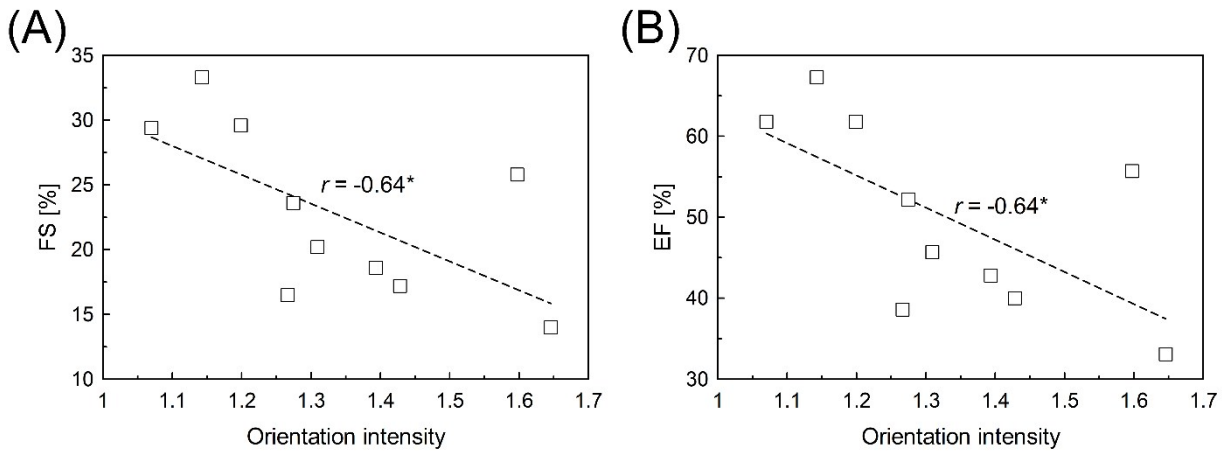

Figure S7. Correlations between orientation intensity of collagen fibers in LV wall and cardiac function. (A) Correlation between orientation intensity and FS ($r = -0.64$; $p < 0.05$ by simple regression analysis). (B) Correlation between orientation intensity and EF ($r = -0.64$; $p < 0.05$ by simple regression analysis).