

## Supplementary Materials for

### Cardiac cell–integrated microneedle patch for treating myocardial infarction

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Published 28 November 2018, *Sci. Adv.* **4**, eaat9365 (2018)  
DOI: 10.1126/sciadv.aat9365

#### The PDF file includes:

Fig. S1. Characterization of PVA MN.

Fig. S2. Characterization of NRCMs cultured with MN.

Fig. S3. Local T cell immune response in immunocompetent rat treated with a MN-CSC patch.

Fig. S4. MN-CSC therapy protects cardiac morphology and reduces fibrosis in a rat model of MI.

Fig. S5. Cardiac functions at baseline and 3 weeks after MI + No–MN-CSC or MI + MN-CSC treatment.

Fig. S6. Effects of PVA patches on kidney and liver functions 21 days after transplantation.

Fig. S7. Changes in ECG parameters from pre-LAD ligation to post-LAD ligation in swine study.

Legends for Movies S1 to S4

#### Other Supplementary Material for this manuscript includes the following:

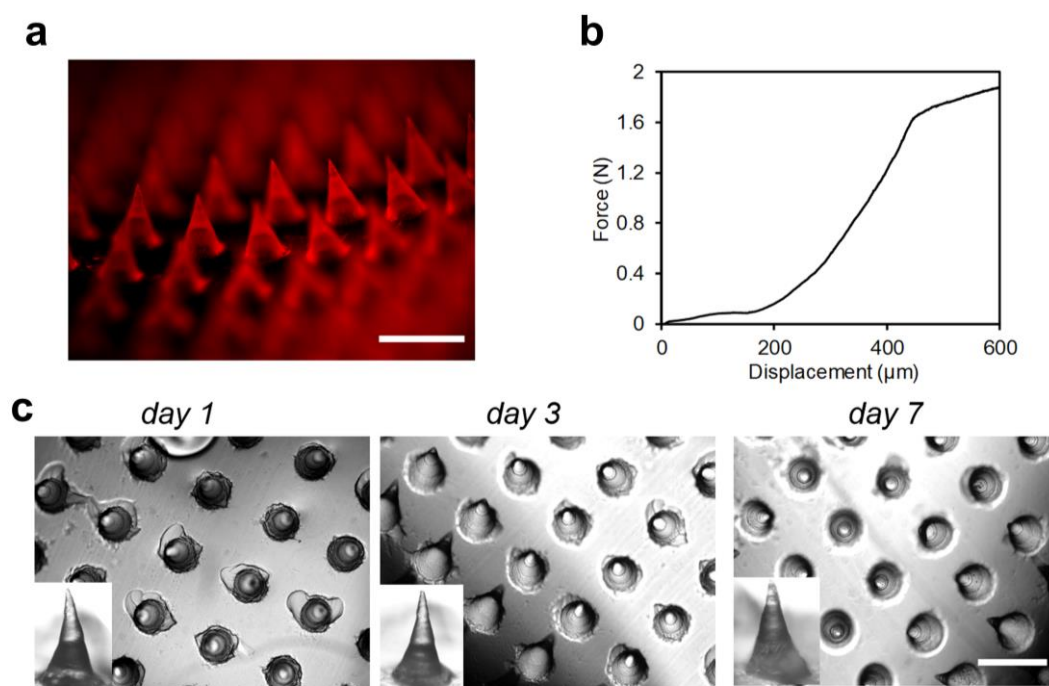
(available at [advances.sciencemag.org/cgi/content/full/4/11/eaat9365/DC1](https://advances.sciencemag.org/cgi/content/full/4/11/eaat9365/DC1))

Movie S1 (.mp4 format). Beating NRCMs cultured alone on TCP.

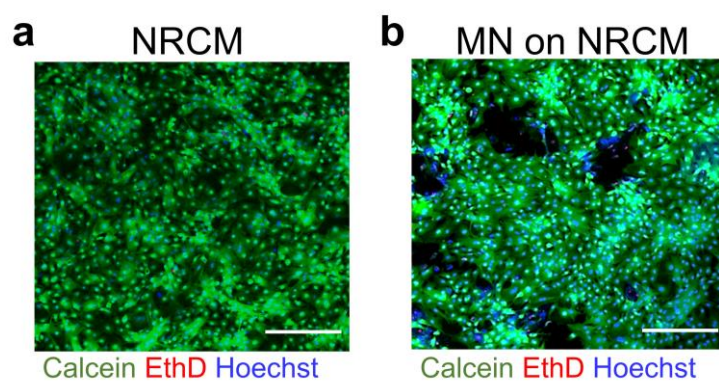
Movie S2 (.mp4 format). Beating NRCMs cultured with a MN patch on TCP.

Movie S3 (.mp4 format). Beating NRCMs cultured with a MN patch loaded with CSCs (MN-CSCs) on TCP.

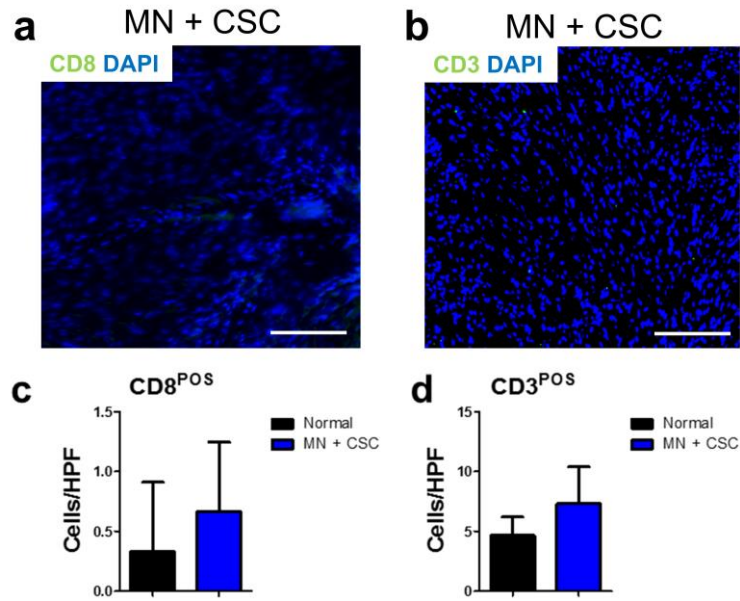
Movie S4 (.mp4 format). MN patch loaded with CSCs (MN-CSCs) placed on the surface of an infarcted rat heart.



**Fig. S1. Characterization of PVA MN.** (a) Representative fluorescent images of MN. (b) Mechanical strength of MN was determined as 2 N/needle. (c) Integrity of the PVA MN in PBS at day 1, day 3 and day 7. Scale bars, 600 μm.



**Fig. S2. Characterization of NRCMs cultured with MN.** (a) Calcein(live)/EthD(dead) staining revealed a distinct morphology of NRCMs grown on tissue culture plate after 3 days in culture. (b) Calcein(live)/EthD(dead) staining revealed a distinct morphology of NRCMs cultured with MN patch after 3 days. Scale bar, 200μm.



**Fig. S3. Local T cell immune response in immunocompetent rat treated with a MN-CSC**

**patch.** (a) Representative fluorescent images showing the presence of infiltrated CD8<sup>POS</sup> T cells

(green) in MN-CSC patched heart at Day 7. Scale bar, 200 μm. (b) Representative fluorescent

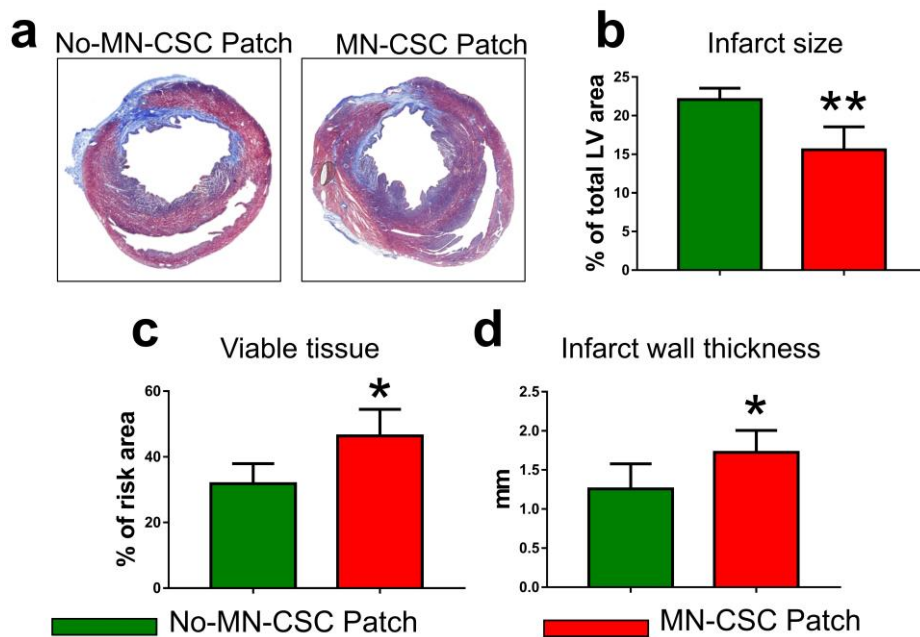
images showing the presence of infiltrated CD3<sup>POS</sup> T cells (green) in MN-CSC patched heart at Day

7. Scale bar, 200 μm. (c) Quantitative analysis of CD8<sup>POS</sup> T cells in MN-CSC patched heart or

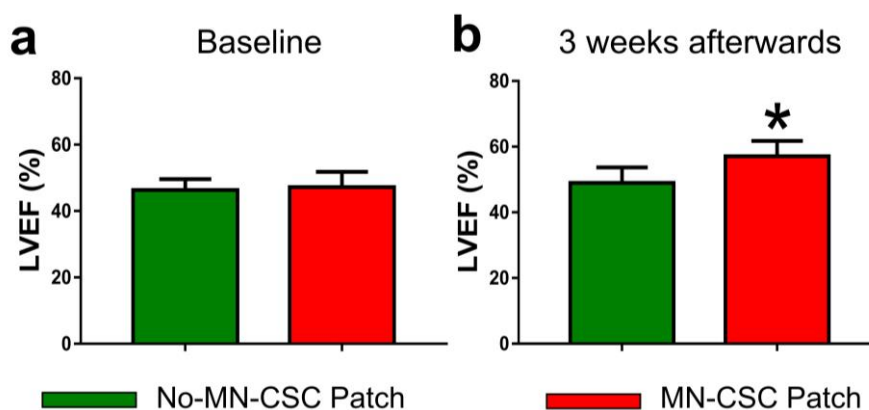
normal heart at day 7. n=3 animals per group. (d) Quantitative analysis of CD3<sup>POS</sup> T cells in

MN-CSC patched heart or normal heart at day 7. All data are mean ± s.d. Comparisons between

any two groups were performed using two-tailed unpaired Student's *t*-test.

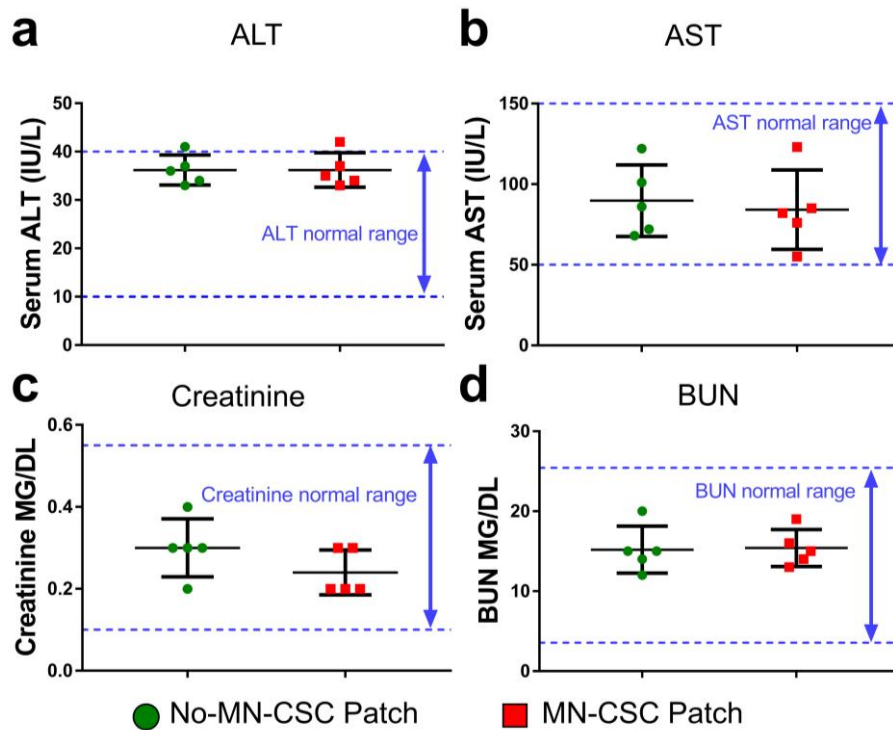


**Fig. S4. MN-CSC therapy protects cardiac morphology and reduces fibrosis in a rat model of MI.** (a) Representative Masson's trichrome-stained myocardial sections 3 weeks after treatment (blue = scar tissue and red = viable myocardium). (b,c,d) Quantitative analyses of infarct size (b), viable tissue in risk area (c), and infarct wall thickness (d) from the Masson's trichrome-stained images.  $n=5$  animals per group. All data are means  $\pm$  s.d. Comparisons between two groups were performed with two-tailed Student's *t*-test. \* indicated  $P < 0.05$ . \*\*indicated  $P < 0.005$ .



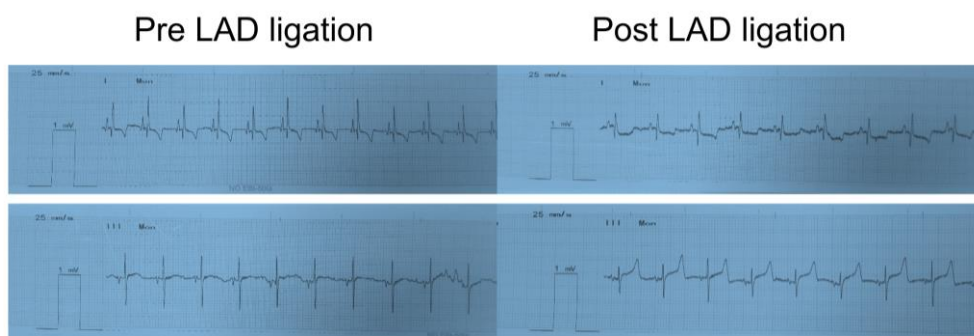
**Fig. S5. Cardiac functions at baseline and 3 weeks after MI + No-MN-CSC or MI + MN-CSC treatment.** LVEFs were measured by echocardiography at baseline (a) and 3 weeks (b) after

treatment.  $n=5$  animals per group. All data are means  $\pm$  s.d. Comparisons between two groups were performed with two-tailed Student's  $t$ -test. \* indicated  $P < 0.05$ .



**Fig. S6. Effects of PVA patches on kidney and liver functions 21 days after transplantation.**

Serum ALT (a), AST (b), Creatinine (c) and BUN (d) concentrations were measured 3 weeks after transplantation. All data are means  $\pm$  s.d.  $n=5$  animals per group. green = MI + No-MN-CSC group; red = MI + MN-CSC patch transplanted group. Blue dash line = normal range. Comparisons between two groups were performed with two-tailed Student's  $t$ -test.



**Fig. S7. Changes in ECG parameters from pre-LAD ligation to post-LAD ligation in swine**

**study.** Lead I (Top) and III (bottom) are shown for animals pre-LAD ligation and 20 mins post-LAD ligation. The ST segment elevation of the 20 min post LAD ligation confirms successful MI induction.

**Movie S1. Beating NRCMs cultured alone on TCP.**

**Movie S2. Beating NRCMs cultured with a MN patch on TCP.**

**Movie S3. Beating NRCMs cultured with a MN patch loaded with CSCs (MN-CSCs) on TCP.**

**Movie S4. MN patch loaded with CSCs (MN-CSCs) placed on the surface of an infarcted rat heart.**