## Supporting Information

Incorporation of small extracellular vesicles in sodium alginate hydrogel as a novel therapeutic strategy for myocardial infarction

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Figure S1. Identification of sEVs. (A) Transmission electron micrographs of sEVs displaying their morphology and size (bar = 100 nm). (B) ZetaView (Particle Metrix, Germany) was used to measure the particle size distribution of sEVs. (C) Western blotting was performed to characterize sEVs positive makers CD63, Alix and negative maker GM130.



Figure S2. Expression of miRNAs in sEVs from H9C2 cells and MSCs. Comparison of mirRNAs 19a-3p, 126a-3p, 29-3p, 21-5p, 210-3p, 132-3p in sEVs from H9C2 cells and MSCs. \*P < 0.05; \*\*P < 0.01; \*\*\*P < 0.001; \*\*\*\*P < 0.001.



Figure S3. Evaluation of the ratio of CD206 to CD68 in the infarct area at day 7. (A) Immunofluorescence staining of CD68- and CD206-positive macrophages at day 7. Bar = 50  $\mu$ m. (B) Quantitative analysis of the ratio of CD206 to CD68. n=3 for each group.



Figure S4. sEVs-Gel promotes the tube formation of HUVECs. (A) Representative tube formation ability of HUVECs with different pretreatments. Bar=100  $\mu$ m. (B) Quantitative analysis of tube formation length. n=3 per group. \*P < 0.05; \*\*\*P < 0.001.



Figure S5. The residual hydrogel in the infarct area 4 weeks after MI. Representative photomicrographs of HE staining showing residual hydrogel in the sEVs and sEVs-Gel groups. Arrows point to hydrogel. Bar=100  $\mu$ m.