Supplementary Information (ESI)

1. Molecular weight of PCL-OH (precursors for the synthesis of HA-g-PCL) based on NMR analysis

The molecular weight (~2.74 kDa) obtained by SEC (GPC) was confirmed by NMR, as shown below. Data analysis from the NMR spectrum revealed a molecular weight of 2.76 kDa, which was calculated based on the peak integral of "c" (45.10) ÷ the peak integral of "b" (2.0) × 114.14 + 186.34 = 2760.19.

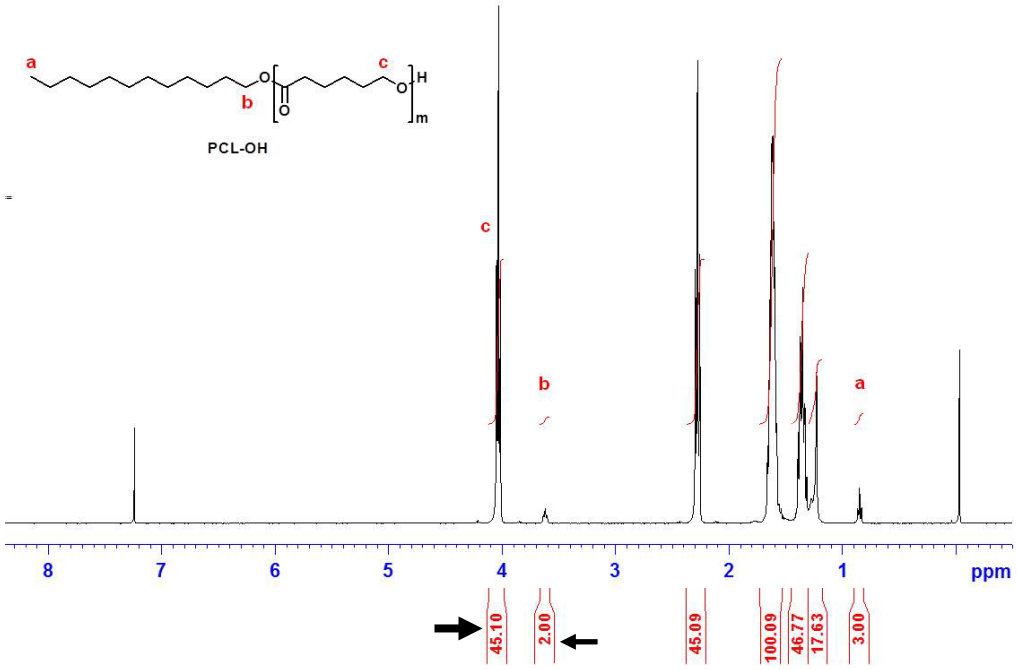

Figure S1. The ^{1}H NMR spectrum of mono-functional PCL (PCL-OH). The molecular weight can be estimated based on the integral ratios.

2. Infrared (IR) spectra of PCL-OH and HA used in the synthesis of HA-g-PCL

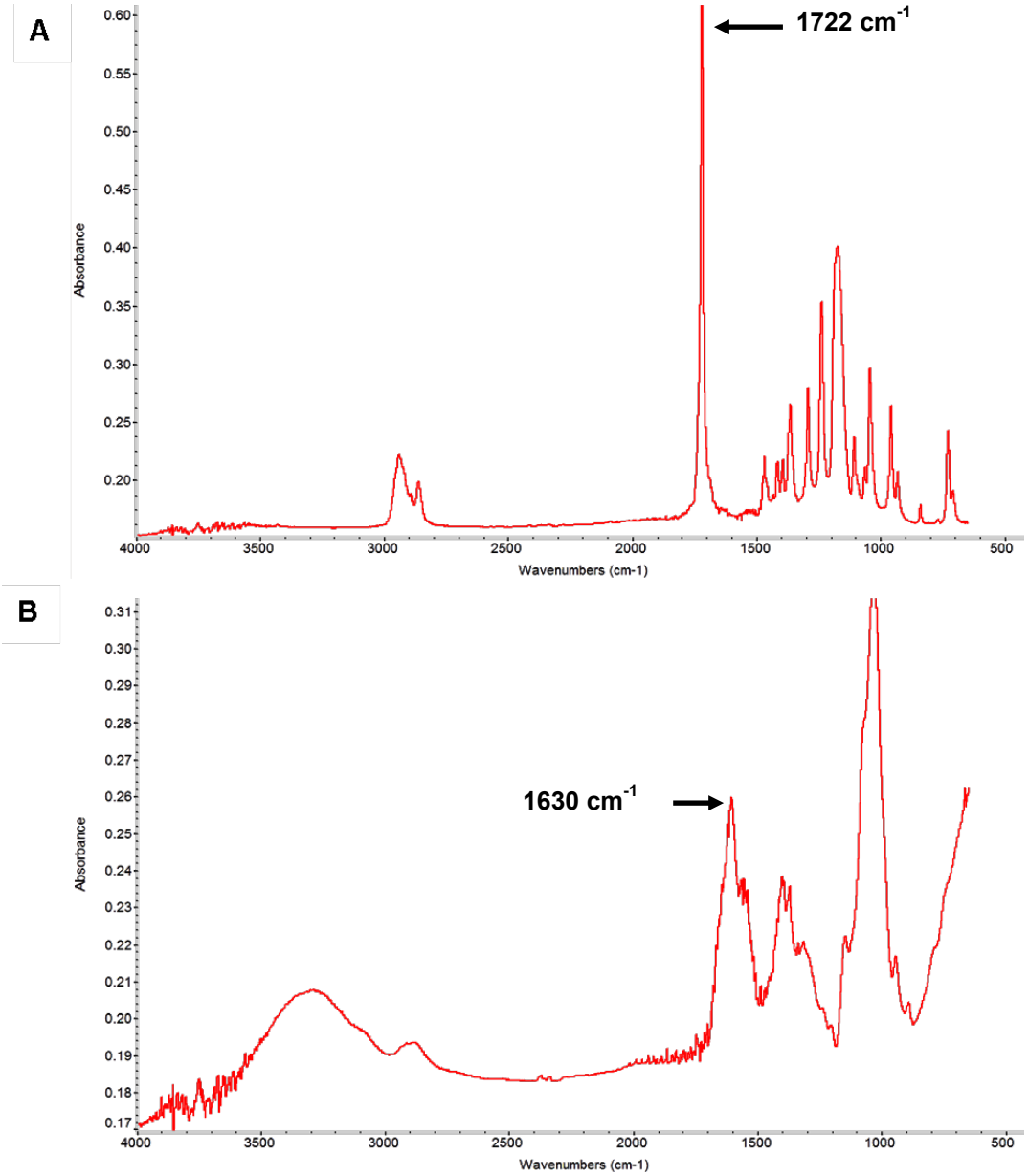

Figure S2. The IR spectra of (A) mono-functional PCL (PCL-OH, structure shown in Fig. 1A) and (B) HA used for the synthesis of HA-g-PCL. The peak at 1722 cm^{-1} in (A) is attributed to the ester linkage of PCL. The band around 1630 cm^{-1} in (B) is attributed the C=O carboxyl amide I group of HA.

3. FGF1 initially loaded and that remained after 21 days on micelles

Methods: The amount of FGF1 was verified by Western blot performed on the precipitates from each group. The precipitates after centrifugation were mixed with sample buffer and boiled at 95°C for 5 min. The resulting samples were loaded on gels and proteins were separated according to the molecular weights by 10% sodium dodecyle sulfate-polyacrylamide gel electrophoresis (400 mA, 4°C, 70 min). Proteins were transferred to polyvinylidene fluoride (PVDF) membranes by electroblotting. A primary antibody (Promega, USA) was diluted to 0.2 μg/mL with 5% bovine serum albumin (Invitrogen), incubated, and followed with a horseradish peroxidase (HRP)-conjugated secondary antibody (Jackson ImmunoResearch, USA, 1:5000 dilution). An Immobilon Western Chemiluminescent HRP Substrate (Millipore, USA) was used for antibody detection. The intensity of band was analyzed by the ImageJ software. The amount of FGF1 on micelles was determined based on band intensities vs. FGF1 standards by semi-quantification. **Note:** The method was based on the assumption that the treatment of the samples completely destroyed the micelles and quantitatively released the native conjugated protein. This method was not validated and may not unambiguously quantify the conjugated protein from the micelles.

Results: The loading amount of FGF1 on micelles was confirmed by Western blot results (Fig. S3A). The amount of FGF1 loaded to micelles by reaction with 0.1 mg/mL

EDC (EDC-M) was ~1174 ng based on band intensities, which was much higher than that without EDC (w/o EDC, by sonication only). The results also showed that the molecular weight of FGF1 did not change after 21 days compared with the FGF1 control groups (Fig. S3B). The actual amount of FGF1 remained on micelles after 21 days of release was ~450 ng (per mg of HA-g-PCL for micelles physically entrapping FGF1 and ~762 ng (per mg of HA-g-PCL) for EDC-M micelles, based on this method.

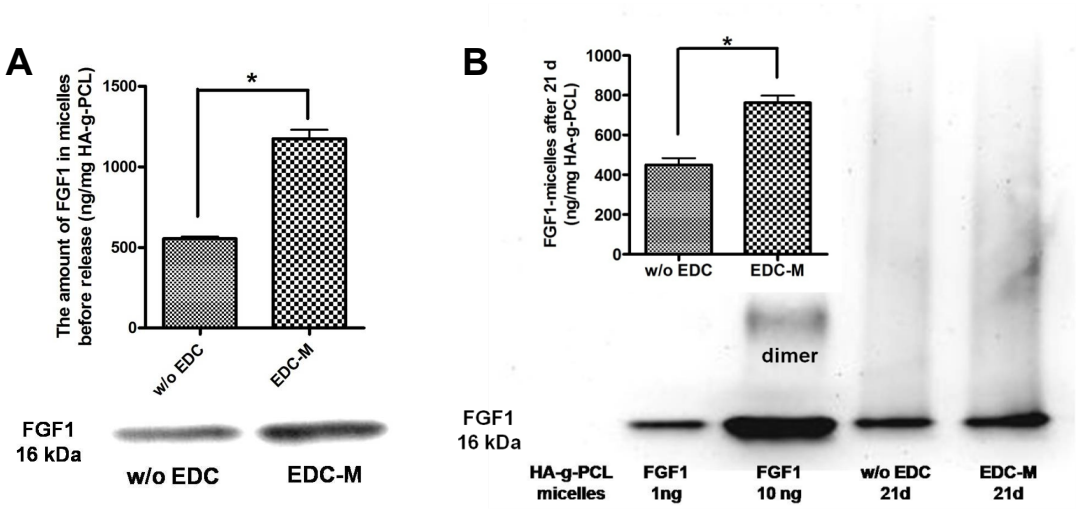

Figure S3. (A) Western blots were used to confirm the loading of FGF1 on micelles. The amount of FGF1 loaded on EDC-M was greater than that physically entrapped (w/o EDC). (B) The amount of FGF1 on micelles after release for 21 days (200× diluted). Based on semi-quantification, EDC-M micelles retained more FGF1 than micelles physical entrapping FGF1 (w/o EDC). * refers to $p < 0.05$.

4. Skin wound repair by FGF1 micelles combined with dressings (vs. Tegaderm)

Methods: The dorsum of Sprague Dawley rats 200-250 g was cut off the 1.5 × 1.5 cm^2 skin wound under anesthetized state by inhalational anesthesia with the mixture of oxygen and isoflurane. A gel membrane ("Gel") made from 4 mL of gelatin-poly(γ-glutamic acid) (γ-PGA) solution (10% type A bloom 300 gelatin and 1% γ-PGA) and 400 μL of 1.7% EDC (formula based on *Biorheology* 2007;44:17-28) was laid on the wound area. To prepare bulk gel containing FGF1, FGF1-loaded micelles (EDC-M with a nominal loading of 400 μg FGF1 on 2 mg HA-g-PCL micelles or the actual loading of ~350 μg FGF1) were added in the gelatin-γ-PGA solution (4 mL) before 400 μl of EDC was added. The bulk gel membrane was then cut to pieces in the size of 1.5 × 1.5 cm^2 for wound coverage (Fig. S4A). Each gel membrane had a dry weight 6.5 mg with/without 88.1 μg FGF1-loaded micelles (75 μg micelles and 13.1 μg FGF1; abbreviated as "Gel+FGF1-micelles").

Results: The effect of wound dressings supplemented with FGF1-loaded micelles is shown in Figures S4. All wounds contracted in similar rates (Fig. S4B, C). The histology of the wounds at 8 days showed that FGF1-loaded micelles (in the gel membrane) induced the formation of more blood capillaries (Fig. S4D, E). On the other hand, Tegaderm or the gel membrane with no FGF1 supplement showed less angiogenesis. This result suggested that the combination of FGF1-loaded micelles and

wound dressings may be another possible prototype.

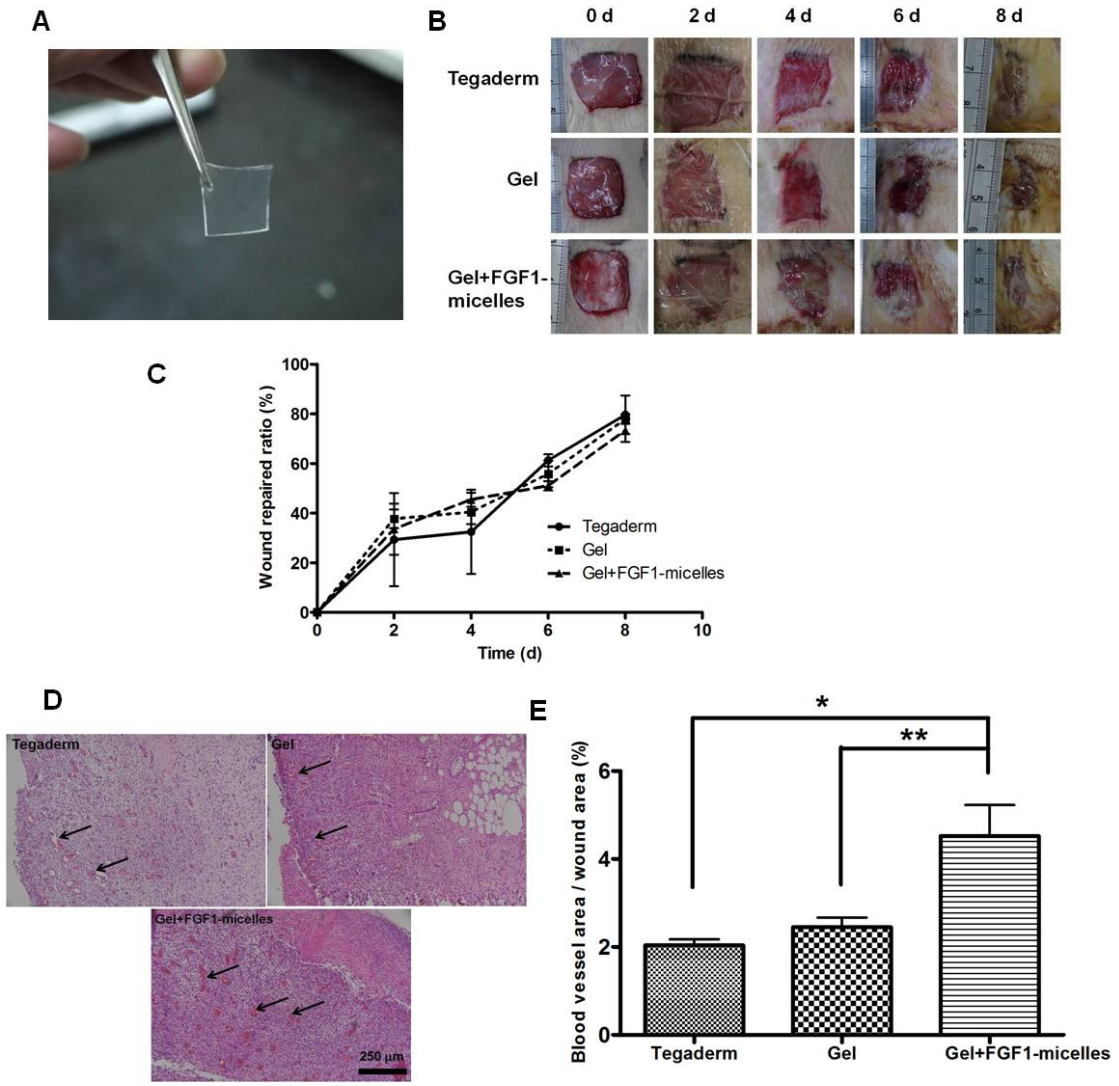

Figure S4. Rat skin wound healing. (A) The gel-like membranes used to carry micelles encapsulating FGF1. (B) The gross appearance of wound area contraction at different times. (C) The quantified wound areas. (D) Histology of the repairing wounds at 8 days, H&E stained. Black arrows indicate blood vessels. The long black arrow indicates the remains of the gel. (E) The area of blood vessels quantified based on histology.