Supporting Information

Sustained Protein Therapeutics Enabled by Self-healing Nanocomposite Hydrogels for Non-invasive Bone Regeneration

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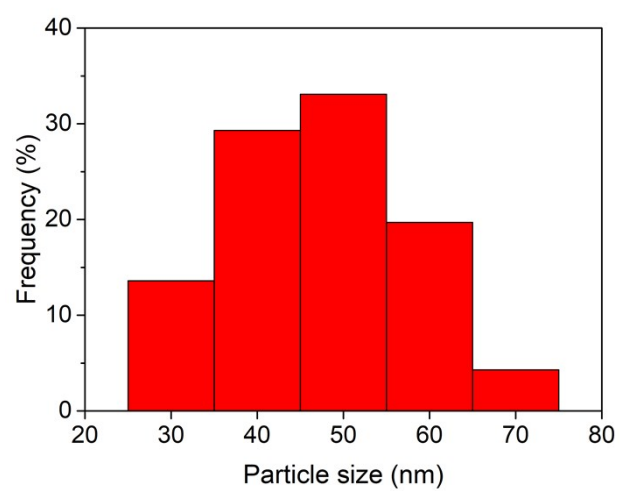
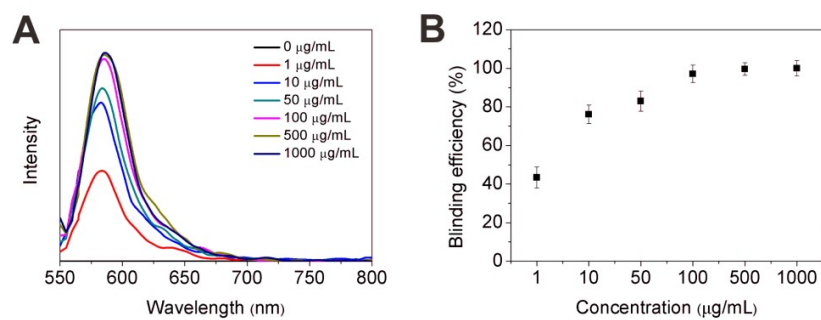**Fig.S1** The size distribution histogram of LAP nanoplatelets from TEM image.

Fig. S2 A) The fluorescence spectra of LAP@BSA complexes. B) The binding efficiency of BSA by LAP nanoplatelets.
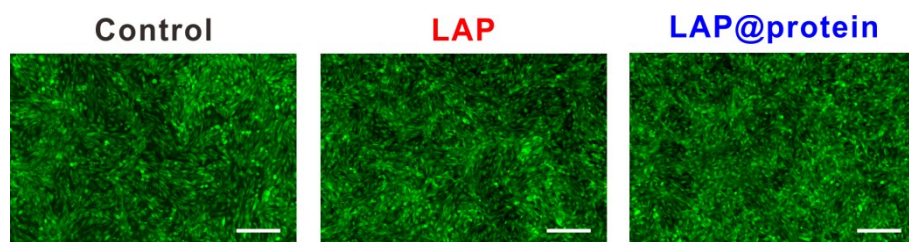
Fig. S3 The cell viability as incubated with LAP nanoplatelets and LAP@BSA complexes at concentration of 100 μg/mL. The scale bar is 500 μm.
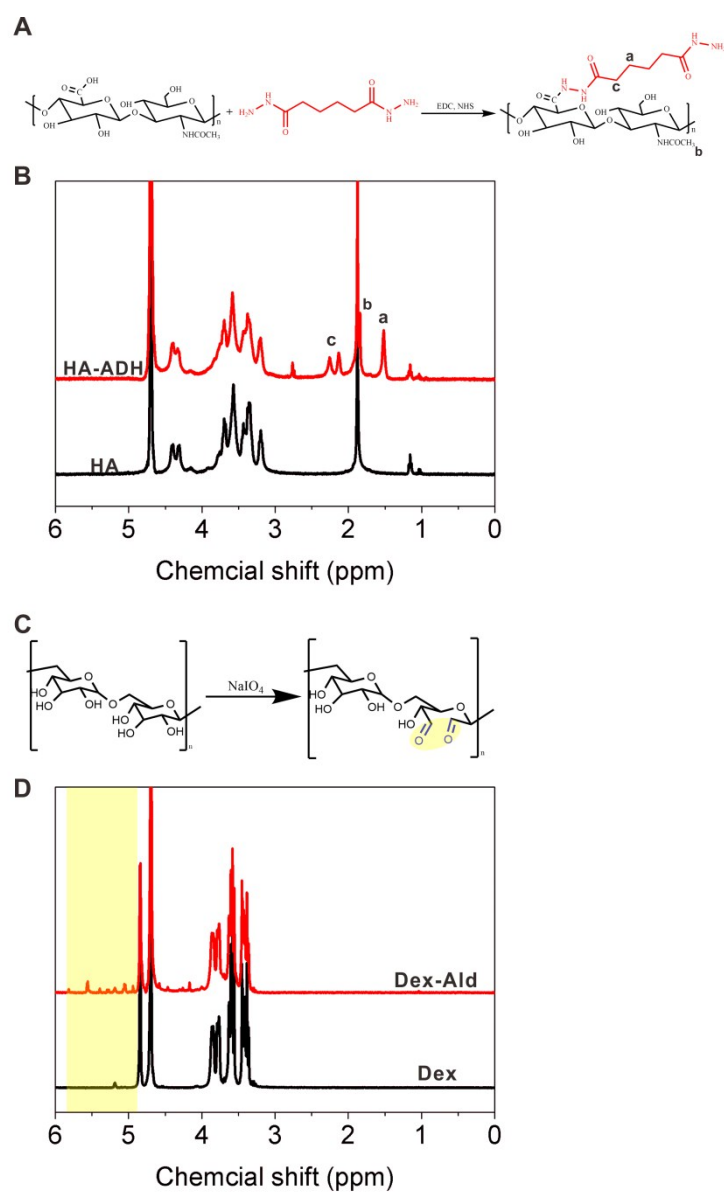
Fig. S4 A) The synthesis routine of HA-ADH. B) The ^{1}H-NMR spectra of HA and HA-ADH. The characteristic methyl peak of acetoamide group (b) appears at 1.9 ppm, while new peaks of methylene protons (a and c) appear at 1.5, 2.1 and 2.2 ppm. C) The preparation of oxidized Dex by NaIO$_4$. D) The ^{1}H-NMR spectra of Dex and Dex-Ald. The aldehyde group locates at 4.9-5.8 ppm (marked as yellow).
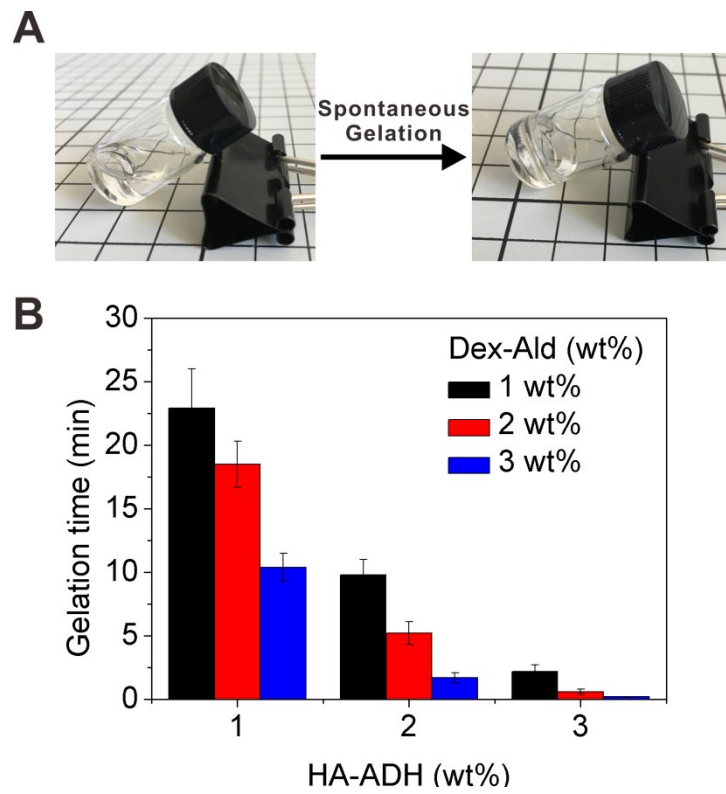
Fig. S5 A) The images of gelation process of hydrogels. B) The gelation time of hydrogels with orthogonal concentration of HA-ADH and Dex-Ald.
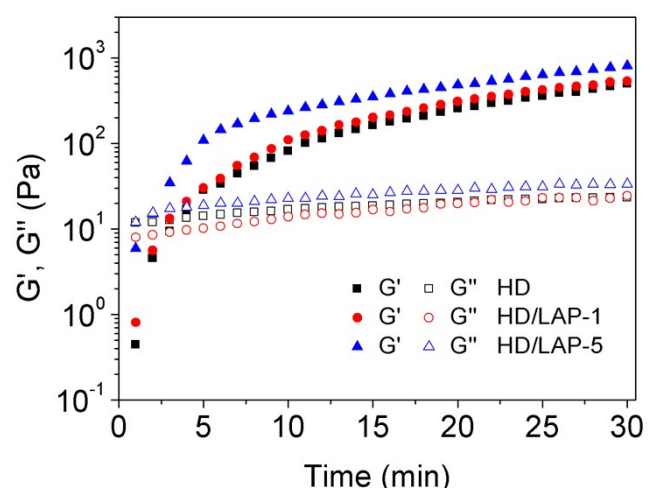
Fig. S6 The rheological tests of time sweep to evaluate the gelation process of hydrogels with various concentrations of LAP nanoplatelets.
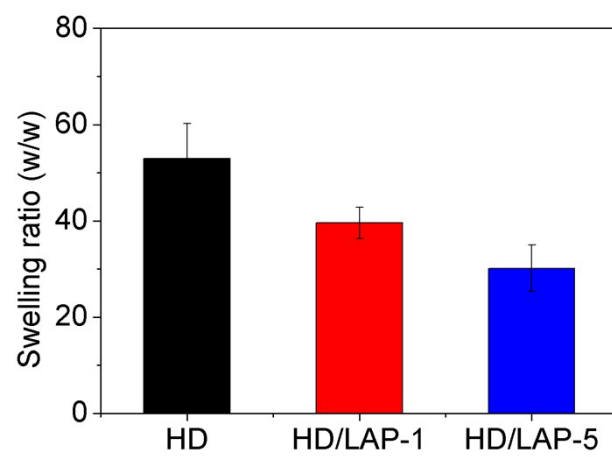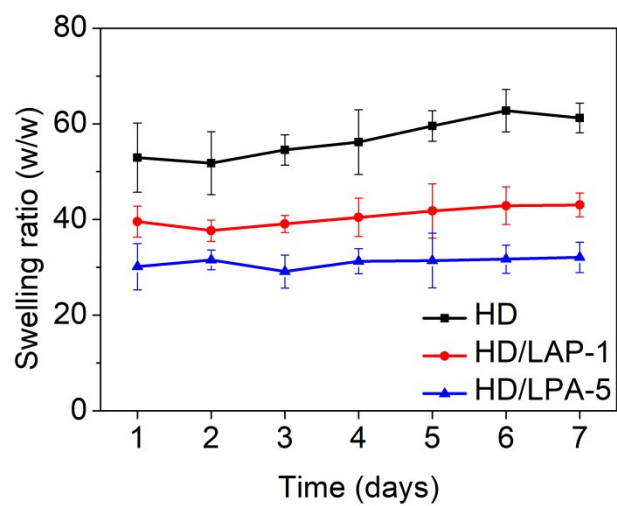
Fig. S7 The swelling behavior of HD/LAP hydrogels.

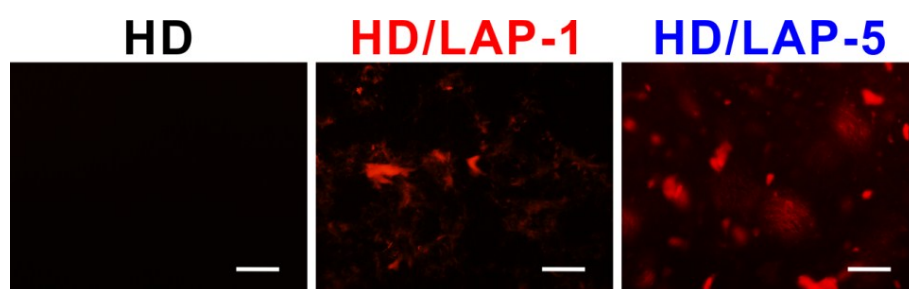**Fig. S8** The stability of hydrogels immersed in PBS for one week.

Fig. S9 The fluorescence image of HD/LAP hydrogel immersed in medium containing rhodamine-conjugated BMP-2. The scale bar is 100 μm.
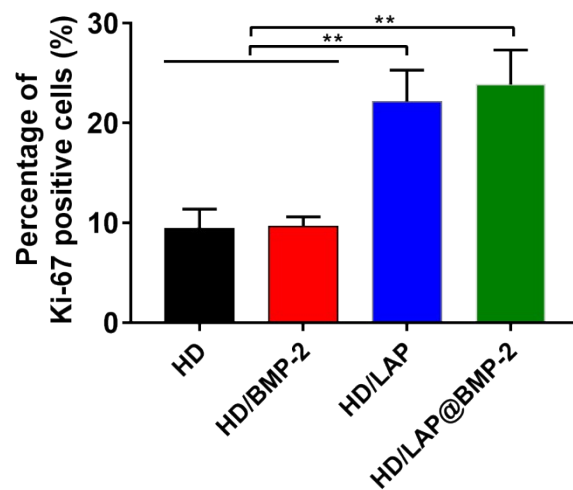
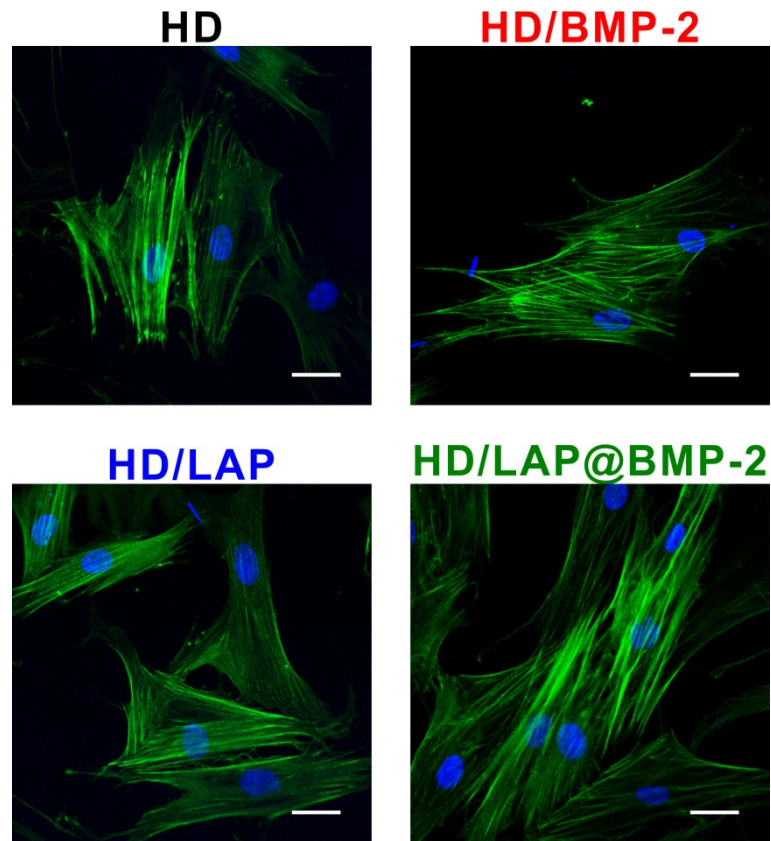**Fig. S10** The percentage of Ki-67 positive cells. *p < 0.05 and **p < 0.01.

Fig. S11 The morphology of rBMSCs incubated on 2D hydrogel surfaces. The scale bar is 25 μm.

Table S1 Primers and parameters used for the real-time PCR analysis

Gene Name	Accession No.	Primer sequence	Annealing temperature(℃)	Product size (base pairs)
ALP	NM_000478	Forward: 5'-GTGAACCGCAACTGGTACTC-3' Reverse: 5'-GAGCTGCGTAGCGATGTCC-3'	60	454
RUNX-2	NM_001015	Forward:5'-TGGTTACTGTCATGGCGGGTA-3' Reverse:5'- TCTCAGATCGTTGAACCTTGCTA -3'	60	101
OSX	NM_152860	Forward:5'-CCTCTGCGGGACTCAACAAC-3' Reverse:5'-AGCCCATTAGTGCTTGTAAAGG-3'	60	128
OPN	NM_001251	Forward:5'-CTCCATTGACTCGAACGACTC-3' Reverse:5'-CAGGTCTGCGAAACTTCTTAGAT-3'	60	230
GAPDH	NM_001256	Forward:5'-GGAGCGAGATCCCTCCAAAAT-3' Reverse:5'-GGCTGTTGTCATACTTCTCATGG-3'	60	197