

### Supporting information

#### **Enhanced regeneration of osteochondral defects by using an aggrecanase-1 responsively degradable and N-cadherin mimetic peptides-conjugated hydrogel loaded with BMSCs**

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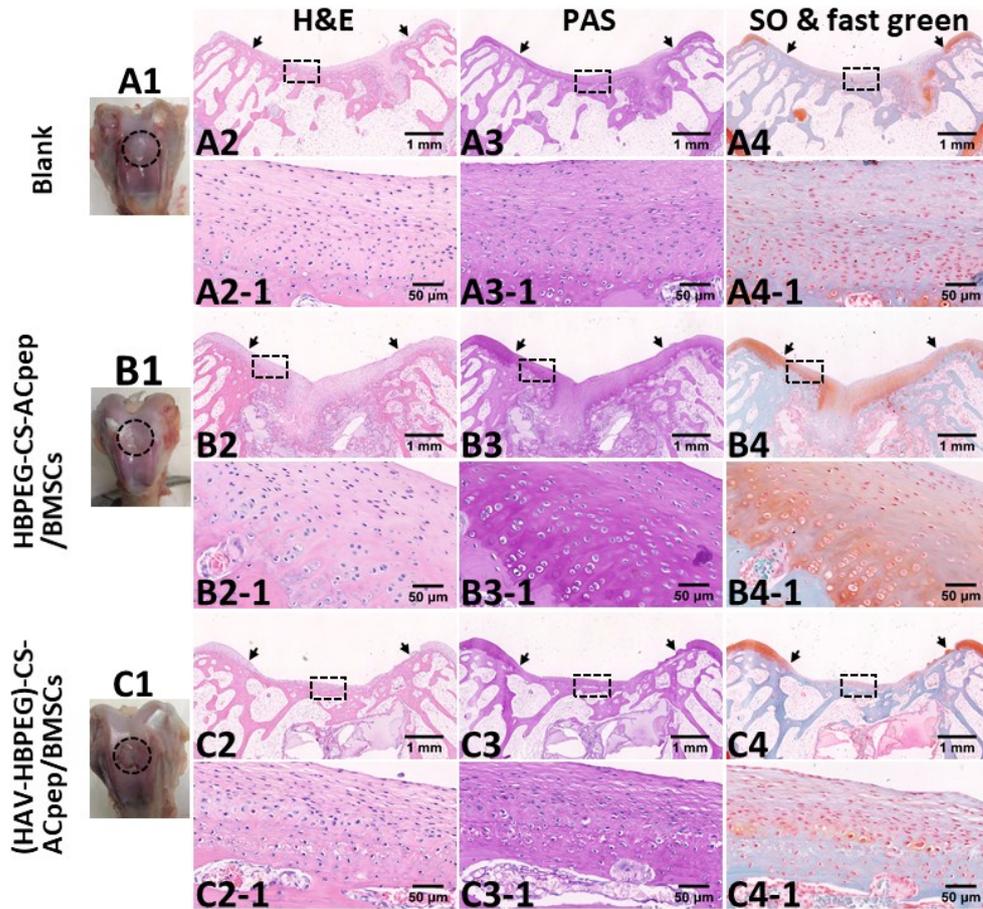


Figure S1 (A1, B1, C1) Gross view, and histological images by (A2, B2, C2) H&E staining, (A3, B3, C3) PAS staining and (A4, B4, C4) SO & fast green staining of neo-tissues at 12 w post-surgery. (A) Blank control group, (B) HBPEG-CS-ACpep/BMSCs hydrogel group and (C) (HAV-HBPEG)-CS-ACpep/BMSCs hydrogel group. The black circles in gross images indicate the location of neo-tissues. The black arrows in the histological images indicate boundaries between native tissues and neo-tissues. The regions marked with black boxes are magnified in the corresponding lower images labeled with “-1”.

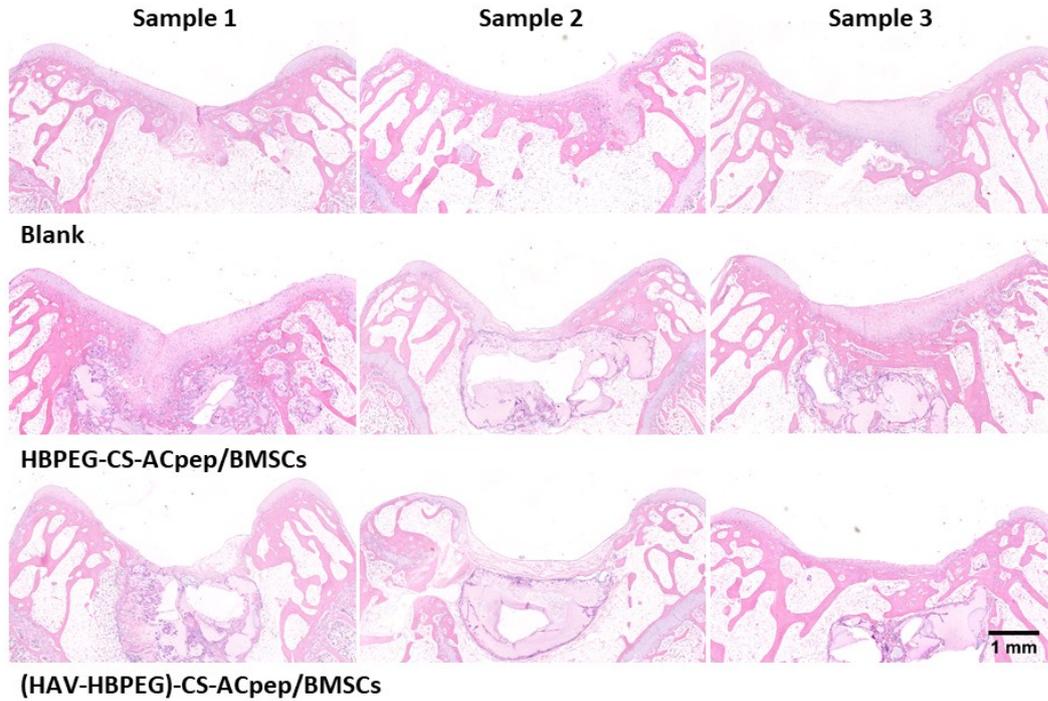


Figure S2 Neo-tissues formed within osteochondral defects without treatment (blank control) or implanted with HBPEG-CS-ACpep/BMSCs hydrogel and (HAV-HBPEG)-CS-ACpep/BMSCs hydrogel at 12 w post-surgery evaluated by histological H&E staining, respectively.

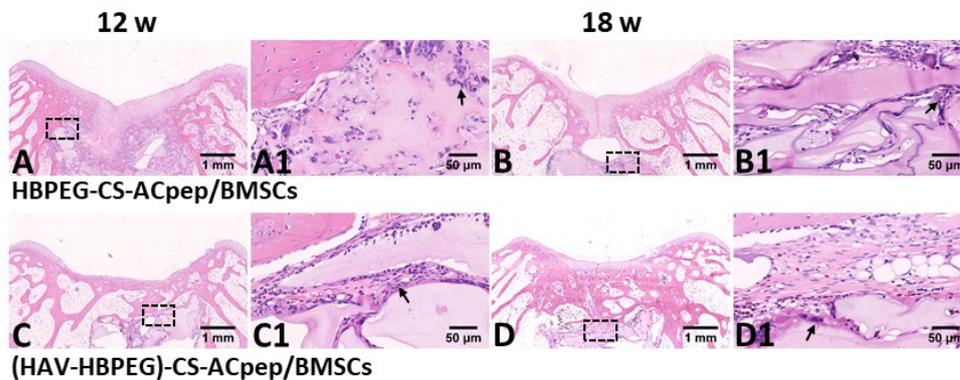


Figure S3 (A, B) Residual HBPEG-CS-ACpep/BMSCs hydrogel and (C, D) residual (HAV-HBPEG)-CS-ACpep/BMSCs hydrogel within the subchondral bone and bone marrow at (A, C) 12 w and (C, D) 18 w post-surgery. The regions marked with black boxes are magnified in the right adjacent images labeled with “1”, in which the black arrows indicate the endogenous immune cells invading into the hydrogels.

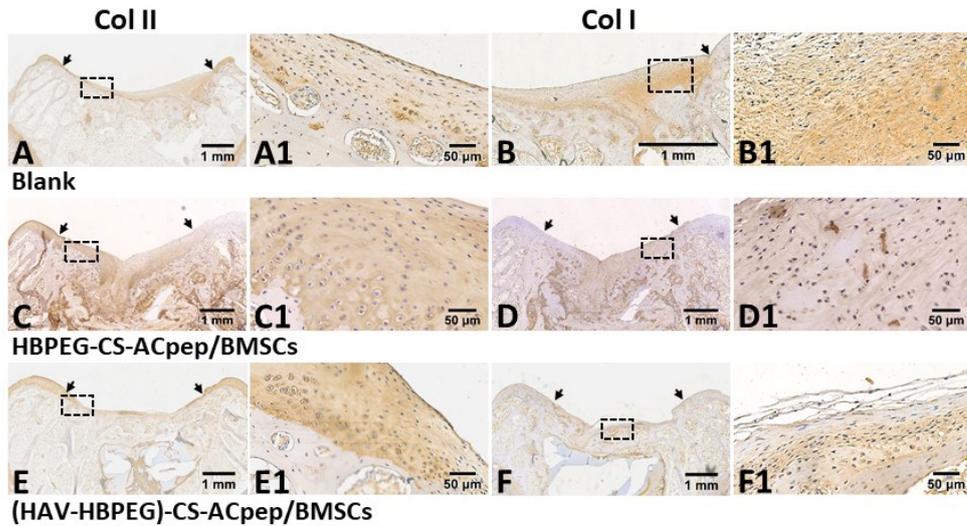


Figure S4 Immunohistochemical staining of (A, C, E) collagen II (Col II) and (B, D, F) collagen I (Col I) of neo-tissues at 12 w post-surgery. (A, B) Blank control group, (C, D) HBPEG-CS-ACpep/BMSCs hydrogel group and (E, F) (HAV-HBPEG)-CS-ACpep/BMSCs hydrogel group. The black arrows indicate boundaries between native tissues and neo-tissues. The regions marked with black boxes are magnified in the right adjacent images labeled with “1”.

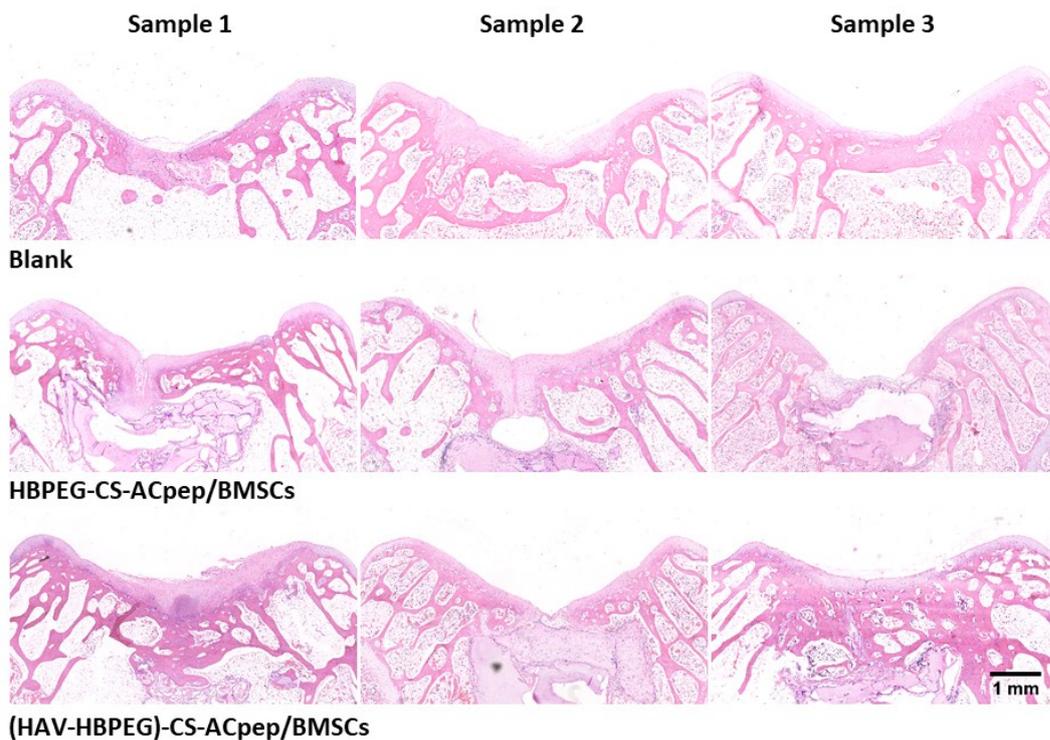


Figure S5 Neo-tissues formed within osteochondral defects without treatment (blank control) or implanted with HBPEG-CS-ACpep/BMSCs hydrogel and (HAV-HBPEG)-CS-ACpep/BMSCs hydrogel at 18 w post-surgery evaluated by histological H&E staining, respectively.

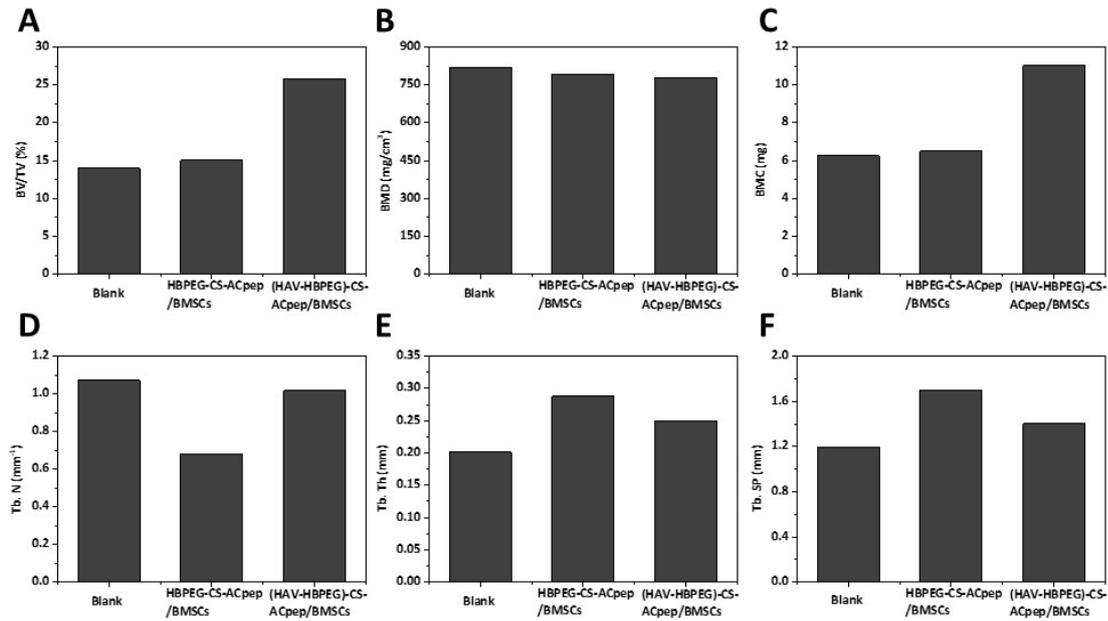


Figure S6 Quantitative analysis for (A) bone volume (BV)/total volume (TV), (B) bone mineral density (BMD), (C) bone mineral content (BMC), (D) trabecular number (Tb. N), (E) trabecular thickness (Tb. Th) and (F) trabecular space (Tb. SP) of neo-subchondral bone within the osteochondral defects without treatment (blank control) or implanted with HBPEG-CS-ACpep/BMSCs hydrogel and (HAV-HBPEG)-CS-ACpep/BMSCs hydrogel at 18 w post-surgery respectively. Data were obtained by  $\mu$ -CT.