

# **Black phosphorus thermosensitive hydrogels loaded with bone marrow mesenchymal stem cells-derived exosomes synergistically promote bone tissue defect repair**

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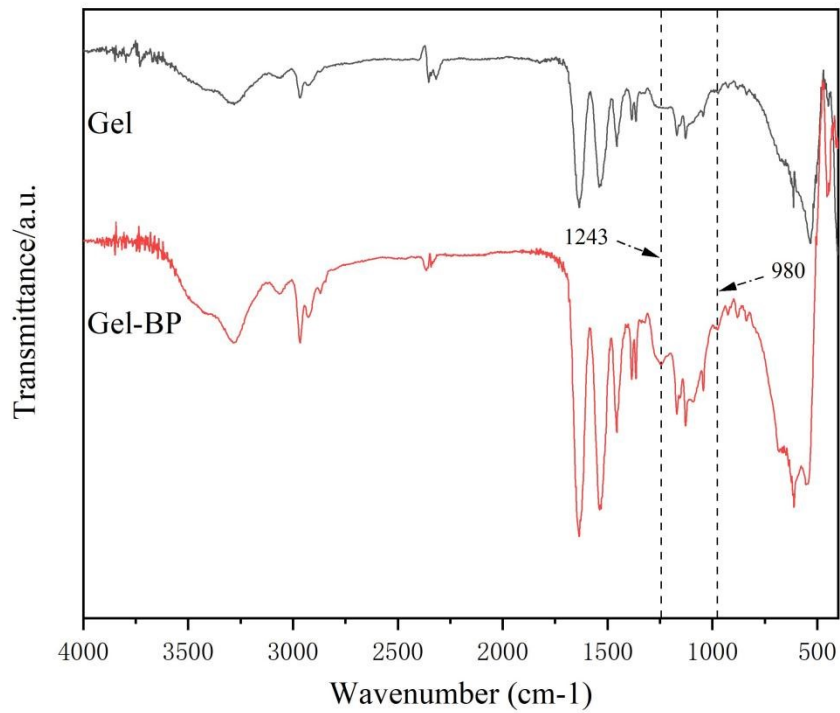
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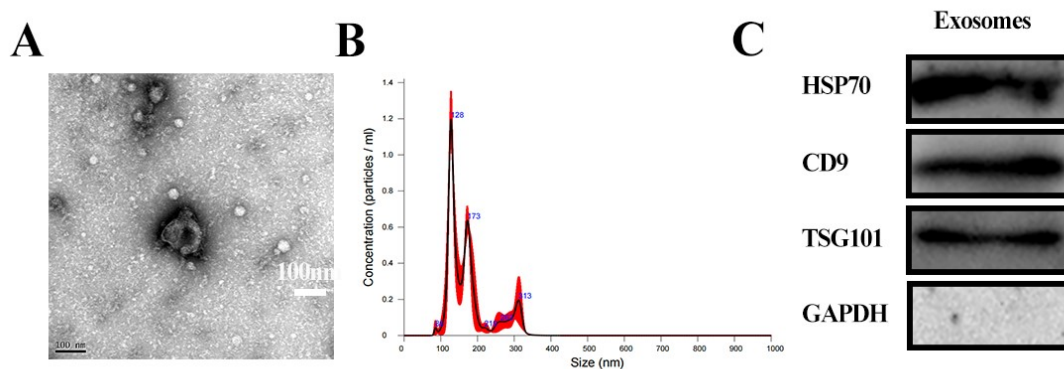
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**Table S1.** Primers used for the target genes

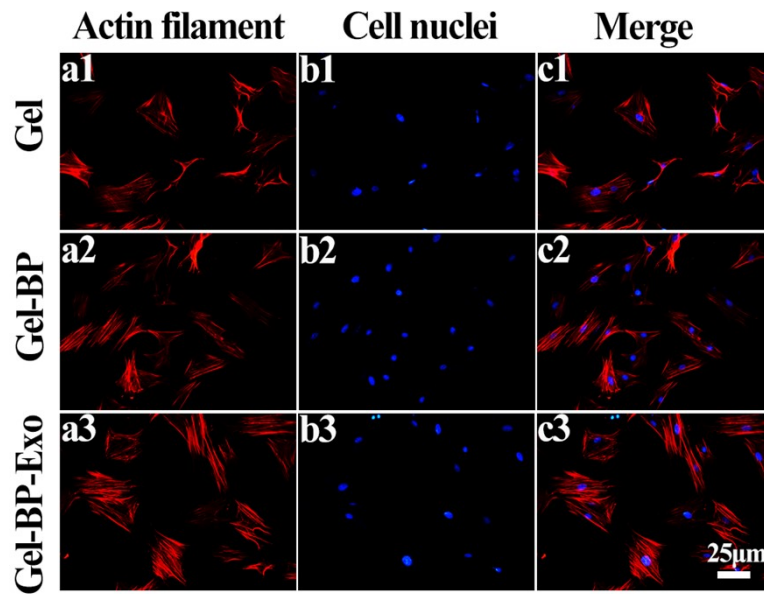
Gene	Primer (F = forward; R = reverse)
<i>Alp</i>	F: 5'AACGTGGCCAAGAACATCATCA3' R: 5'TGTCCATCTCCAGCCGTGTC3'
<i>Runx-2</i>	F:5'CACAAGTGCGGTGCAAACCTT3' R:5'AAGAGGCTGTTTGACGCCAT3'
<i>Opn</i>	F:5'AGACTGGCAGTGGTTTGCTT3' R:5'AGTGTTTGCTGTAATGCGCC3'
<i>Colla1</i>	F:5'CCGCTGTCTTCTAGTGTTGCT3' R:5'GGATAAGGGGCGCGATGC3'
<i>Gapdh</i>	F:5'GGCACAGTCAAGGCTGAGAATG3' R:5'ATGGTGGTGAAGACGCCAGTA3'



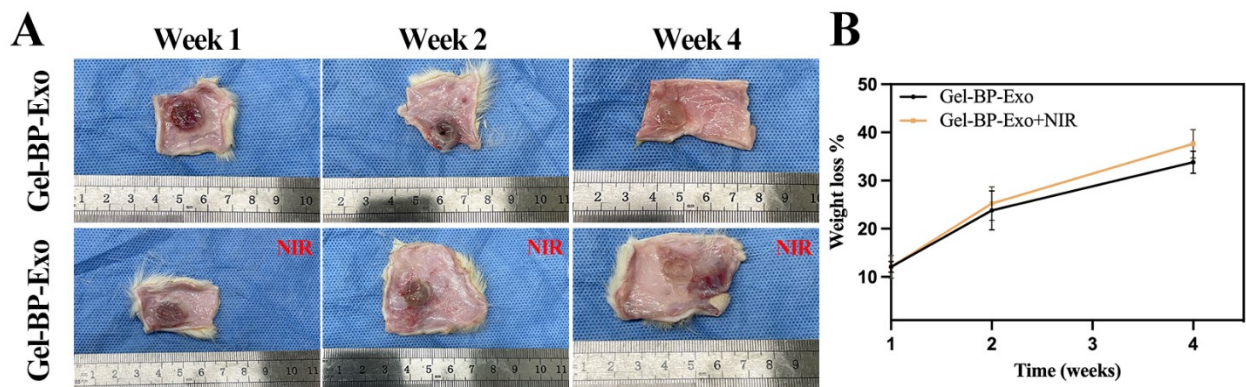
**Figure S1:** FTIR spectrum of Gel and Gel-BP.



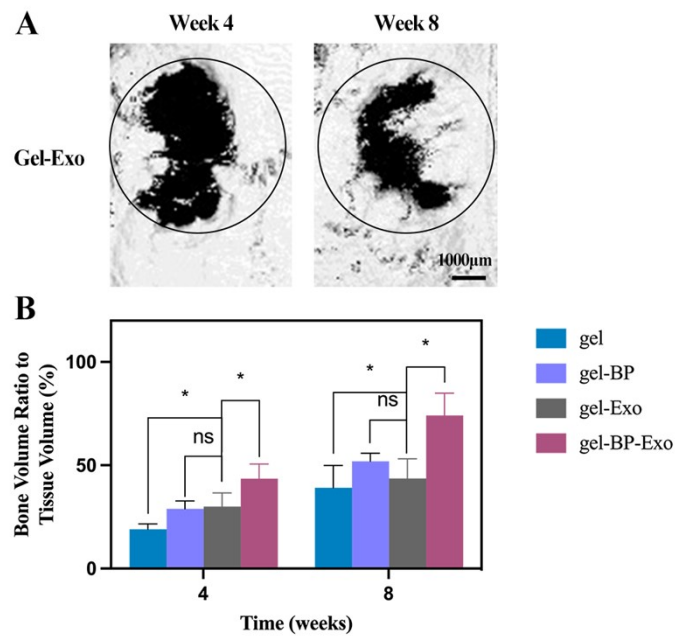
**Figure S2:** Characterization and identification of exosomes. (A) Image of exosomes morphology under TEM. (B) NTA of exosomes. (C) Western blotting of exosome specific protein markers.



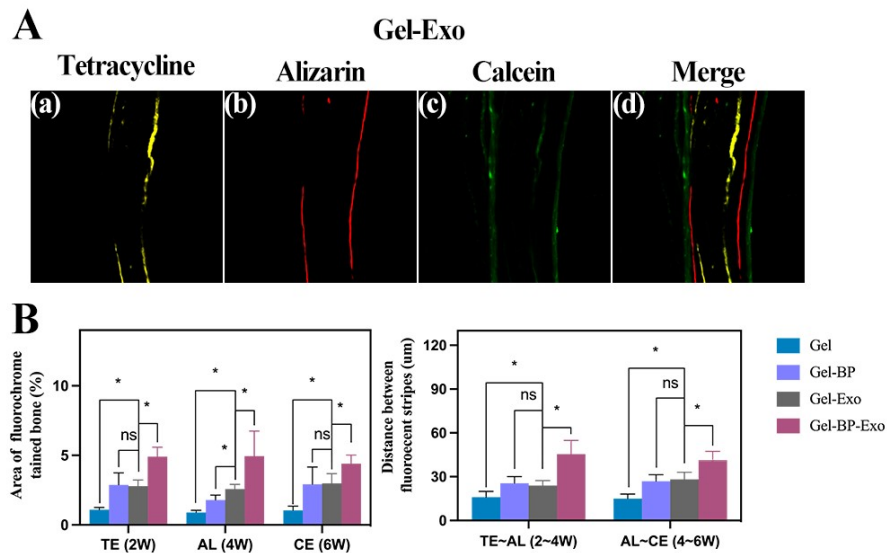
**Figure S3:** BMSCs were cultured on the surface of the Gel, Gel-BP, and Gel-BP-Exo groups for 24 hours. Red: actin (a1, a2, a3), blue: nucleus (b1, b2, b3), merged: actin and nucleus (c1, c2, c3).



**Figure S4:** *In vivo* degradation following subcutaneous implantation of the Gel-BP-Exo. (A) Gross view of the hydrogels after 1, 2, and 4 weeks of subcutaneous implantation. (B) Change of hydrogel weight for the remaining hydrogel during *in vivo* degradation.

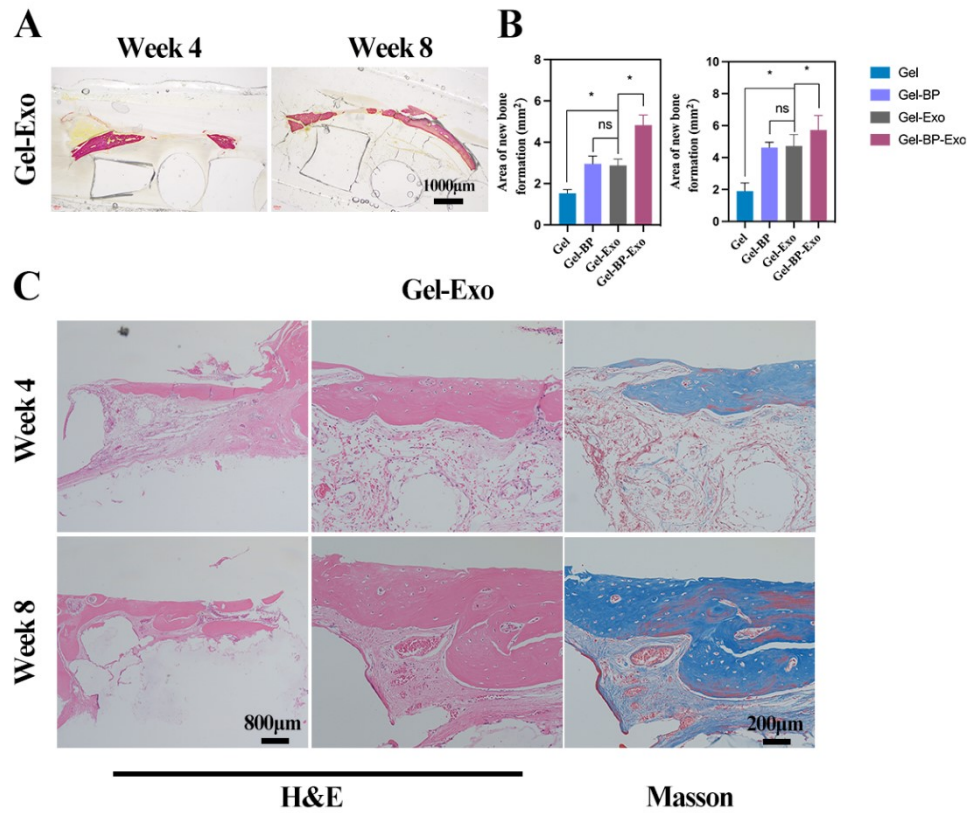


**Figure S5:** Analysis of bone tissue regeneration *in vivo* by micro-CT. (A) 3D reconstruction images of the defects area after implanting Gel- Exo for 4 and 8 weeks. (B) Quantitative analysis of the bone volume ratio to tissue volume based on micro-CT data. (\* indicates significant difference compared to Gel-Exo group,  $P < 0.05$ )

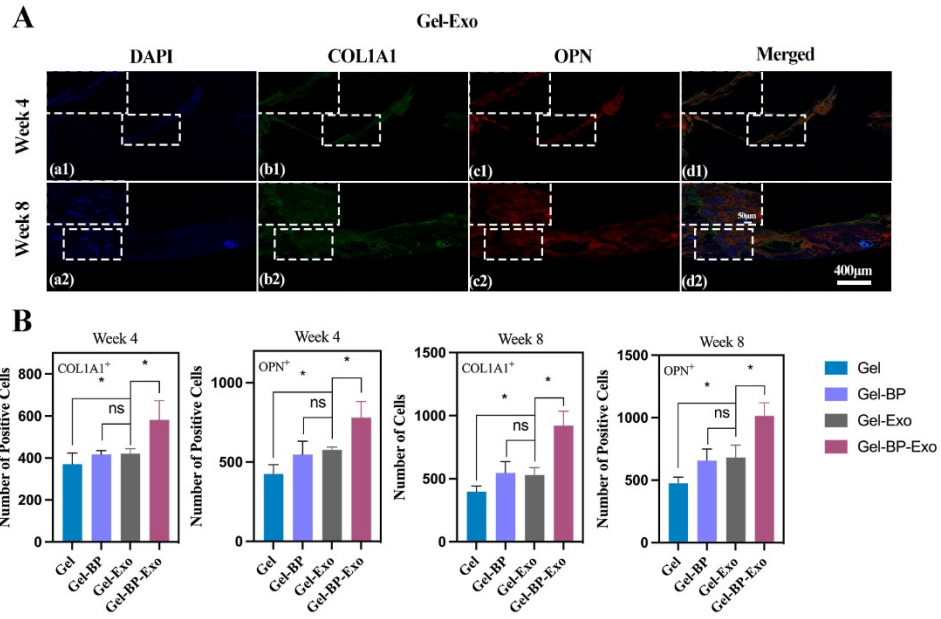


**Figure S6:** (A) Sequential fluorescent labeling images of four groups implanted *in vivo* for 8 weeks. (B) Quantitative analysis of the area of new formed bone tissue by fluorescent staining and the distance between fluorescent bands of new bone. (\* indicates significant difference compared to Gel-Exo group,  $P < 0.05$ )

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**Figure S7:** Histological staining analysis of bone tissue regeneration *in vivo*. (A) Van Gieson-stained images of new bone for the Gel-Exo group and (B) corresponding quantitative analysis. (C) Histological images of H&E stained and Masson's trichrome stained bone tissue sections of the Gel-Exo group (\* indicates significant difference compared to Gel-Exo group,  $P < 0.05$ )



**Figure S8:** Immunofluorescence staining analysis of bone tissue regeneration *in vivo*. (A) Representative immunofluorescence staining of COL1A1 and OPN in defect areas of Week 4 and Week8. (B) Semi-quantification of positively stained cells in (A). (\* indicates significant difference compared to Gel-Exo group,  $P < 0.05$ )