

SUPPORTING INFORMATION

Bioinspired nano-micron hydrogel microspheres for periodontitis therapy through synergistic multi-targeted remodeling of microenvironment

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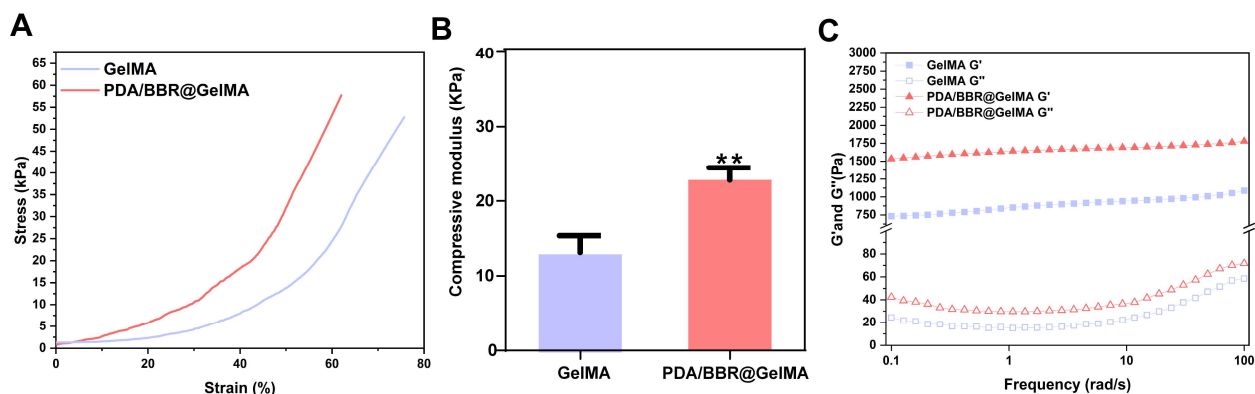


Figure S1. Mechanical properties of GelMA and PDA/BBR@GelMA hydrogels. (A) Representative compressive stress-strain curves. (B) Compressive modulus of the hydrogels (n=3). (C) Storage modulus (G') and loss modulus (G'') between 0.1-100 angular frequencies.

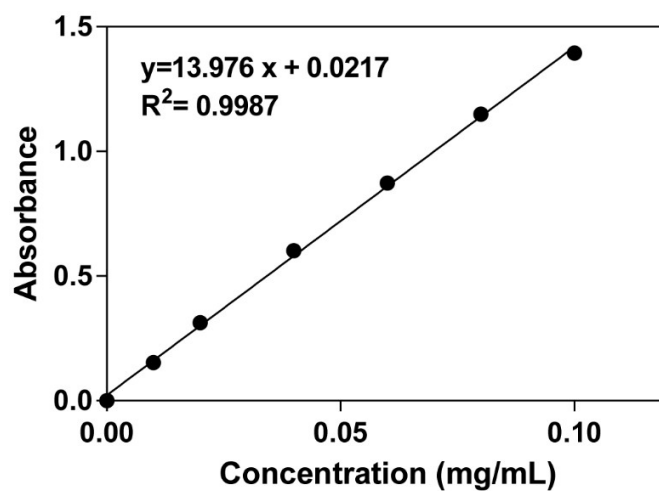


Figure S2. Standard curve of absorbance and concentration of BBR.

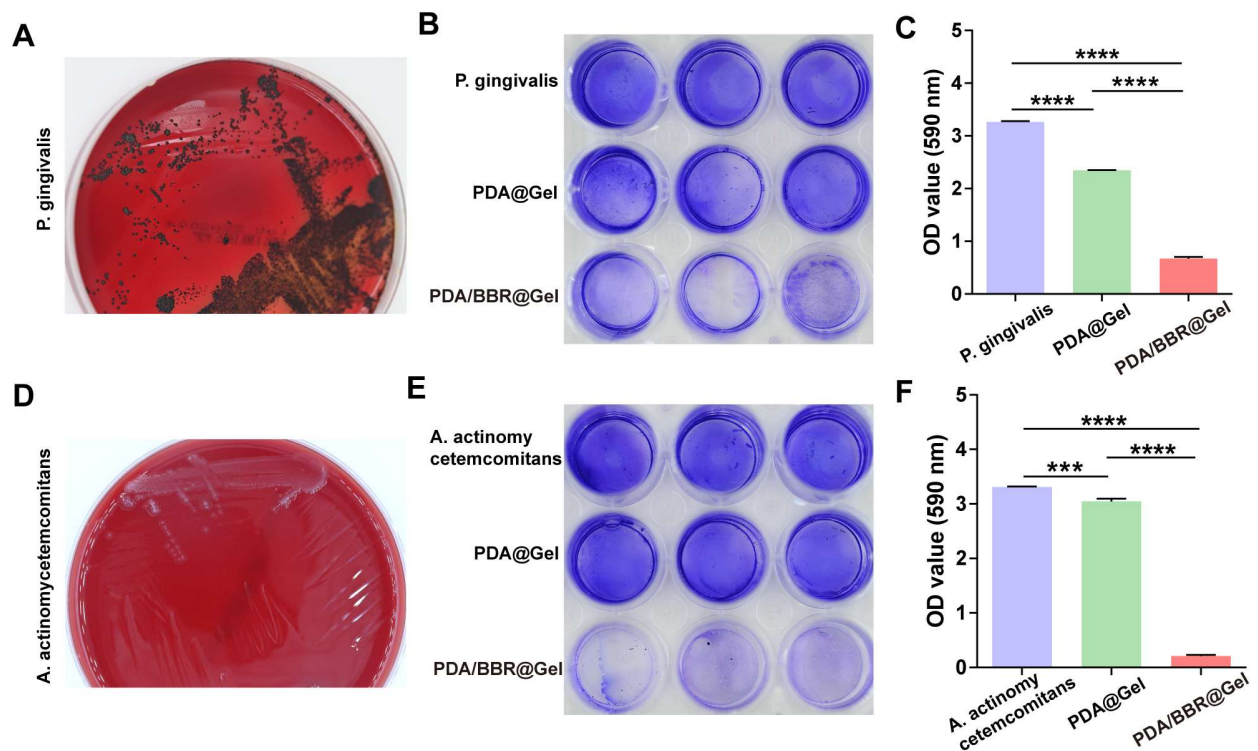


Figure S3. (A) *P. gingivalis* colonies on Columbia blood agar plate. (B) Crystal violet staining of *P. gingivalis* biofilms co-cultured with PDA/BBR@Gel microspheres for 5 days. (C) Relative quantitative crystal violet staining results for *P. gingivalis* biofilms co-cultured with PDA/BBR@Gel microspheres for 5 days. (D) *A. actinomycetemcomitans* colonies on Columbia blood agar plate. (E) Crystal violet staining of *A. actinomycetemcomitans* biofilms co-cultured with PDA/BBR@Gel microspheres for 3 days. (F) Relative quantitative crystal violet staining results for *A. actinomycetemcomitans* biofilms co-cultured with PDA/BBR@Gel microspheres for 3 days. (***) $p < 0.001$, (****) $p < 0.0001$

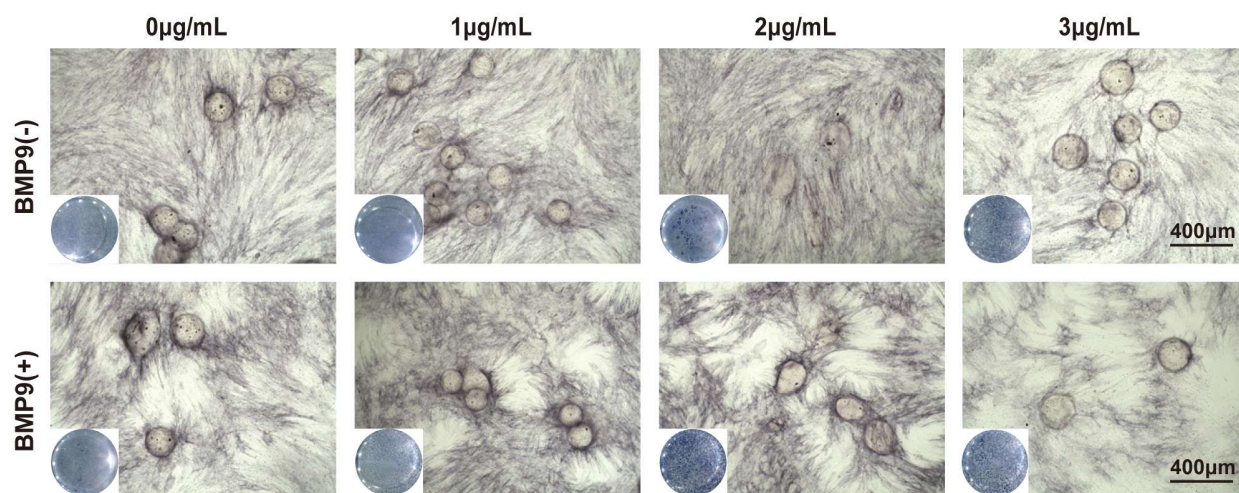


Figure S4. The results of ALP staining after 7 days of co-culture.

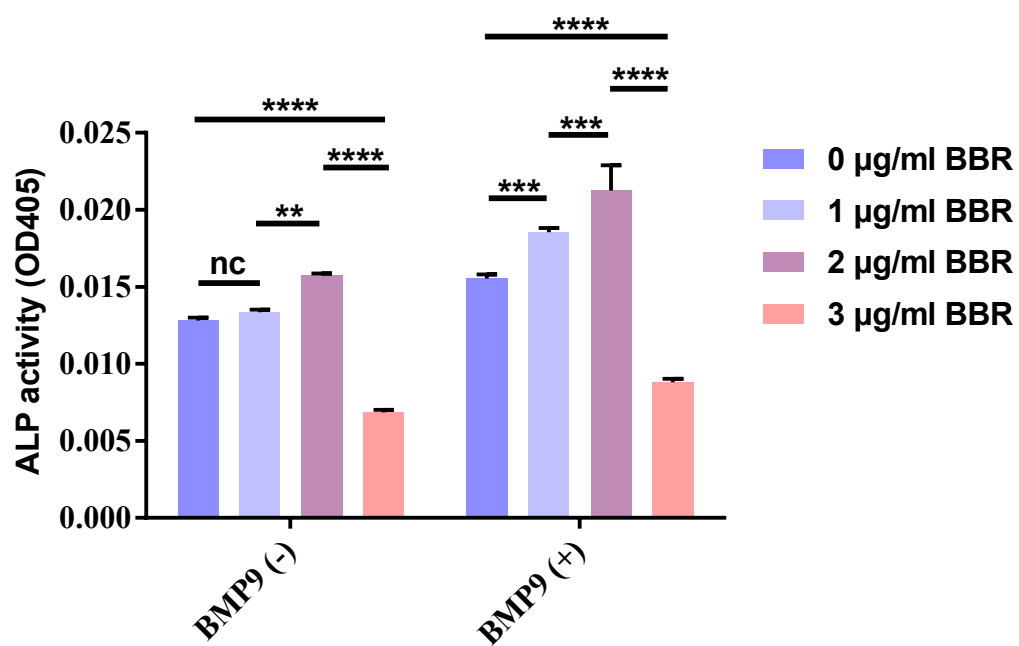


Figure S5. Quantitative results of ALP activity assay after 7 days of co-culture.

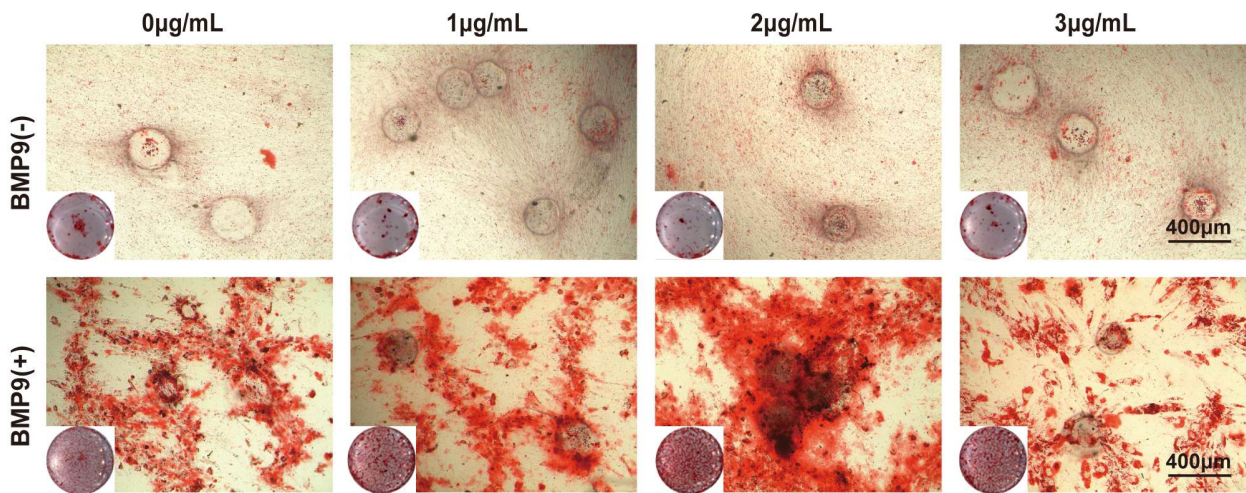


Figure S6. The results of alizarin red staining after 21 days of co-culture.

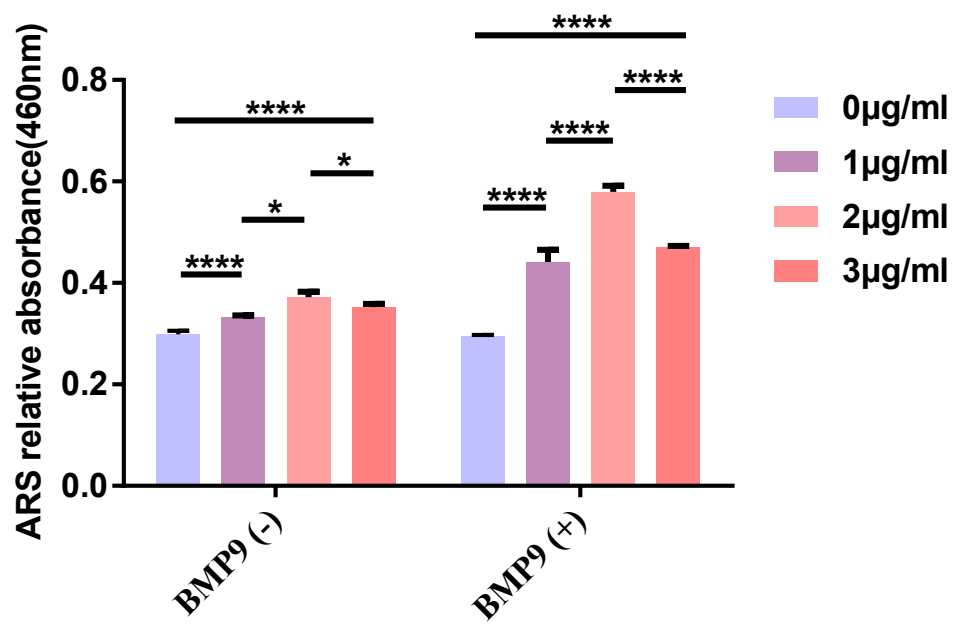


Figure S7. Quantitative results of alizarin red after 21 days of co-culture.

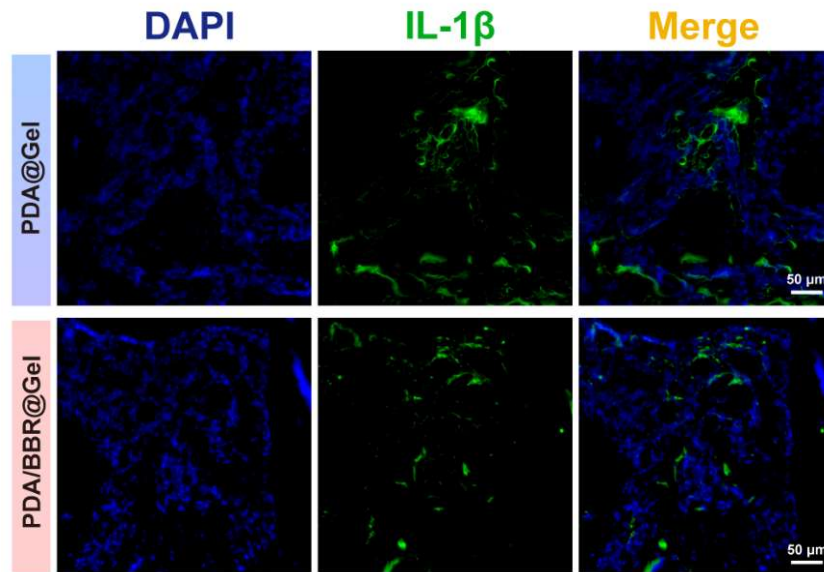


Figure S8. Immunofluorescence staining of the periodontal tissues, showed the distribution of IL-1 β positive cells (green). Nucleus were stained by DAPI (blue).

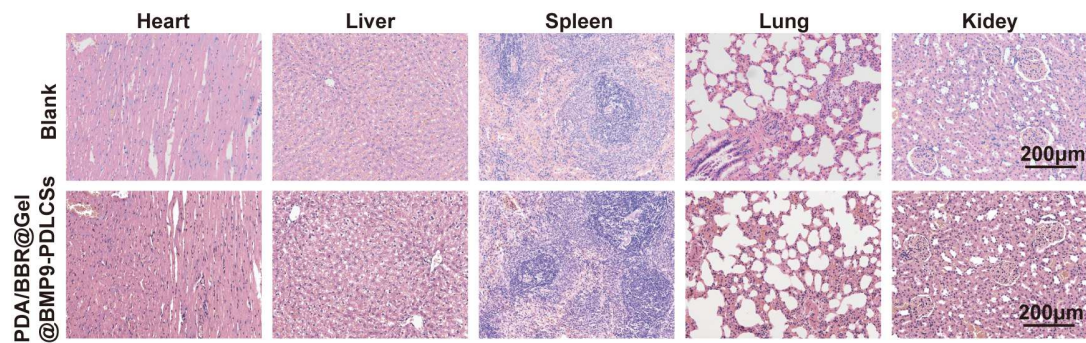


Figure S9. H&E staining of heart, liver, spleen, lung, and kidney in rats 4 weeks after implantation of PDA/BBR@Gel@BMP9-PDLCs engineered microspheres.

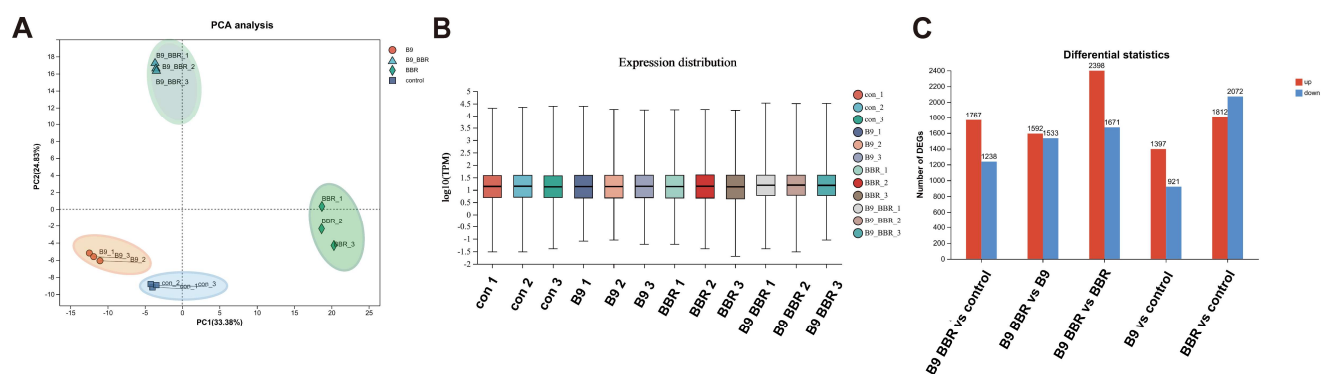


Figure S10. (A) PCA analysis of all samples. (B) Box plot of gene expression distribution of the dataset after normalization. (C) Histogram of significant difference statistics.

Table S1. List of qPCR primers of hPDLSCs

Gene Name	Direction	Sequence
GAPDH	Forward	GGAGTCCACTGGCGTCTTCA
	Reverse	GTCATGAGTCCTTCCACGATACC
ALP	Forward	CTTGACCTCCTCGGAAGACAC
	Reverse	CAGACCAAAGATAGAGTTGCCAC
RUNX2	Forward	GAACTGGGCCCTTTTTCAGA
	Reverse	CGGGGTGTAAGTAAAGGTGG
OPN	Forward	GCTTGGCTTATGGACTGAGG
	Reverse	GCTTGGCTTATGGACTGAGG
IL-4	Forward	TCTCACCTCCCAACTGCTTC
	Reverse	GTGTTCTTGGAGGCAGCAAA
IL-6	Forward	AAATTTCGGTACATCCTCGACGG
	Reverse	GGAAGGTTTCAGGTTGTTTTCTGC
IL-10	Forward	CCCTGTGAAAACAAGAGCAAGG
	Reverse	ACCCTGATGTCTCAGTTTCGT
TNF-α	Forward	GCCCATGTTGTAGCAAACCC
	Reverse	TATCTCTCAGCTCCACGCCA

Table S2 List of qPCR primers for mouse genes

Gene Name	Direction	Sequence
Gapdh	Forward	TGACCACAGTCCATGCCATC
	Reverse	GACGGACACATTGGGGGTTAG
IL-1β	Forward	ATGCCACCTTTTGACAGTGATG
	Reverse	TGATGTGCTGCTGCGAGATT
Tnf-α	Forward	GGTGCCTATGTCTCAGCCTCTT
	Reverse	GCCATAGAACTGATGAGAGGGAG

IL-6	Forward	TGATGGATGCTACCAAACCTGGA
	Reverse	TCTGTGACTCCAGCTTATCTCTTG
IL-10	Forward	GCAGCCTTGCAGAAAAGAGA
	Reverse	CTGGGAAGTGGGTGCAGTTA
Tgf-β	Forward	GACCTGGGTTGGAAGTGGAT
	Reverse	TTGGTTGTAGAGGGCAAGGA
Ym-1	Forward	AGAAGGGAGTTTCAAACCTGGT
	Reverse	CTCTTGCTGATGTGTGTAAGTGA