

Supporting Information

Tailorable Hierarchical Structures of Biomimetic Hydroxyapatite micro/nano Particles Promoting Endocytosis and Osteogenic Differentiation of Stem Cells

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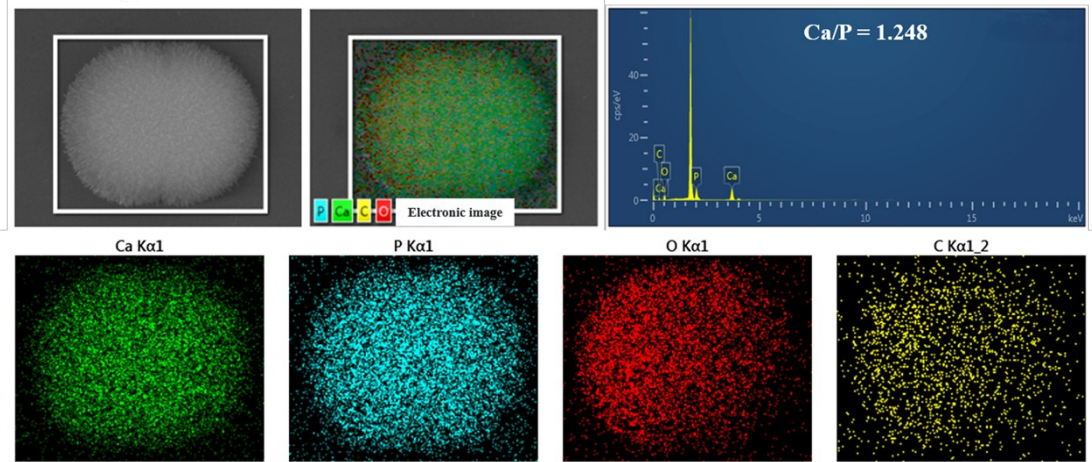


Fig. S1. The element compositions of the microspheres were analyzed by SEM-EDS.

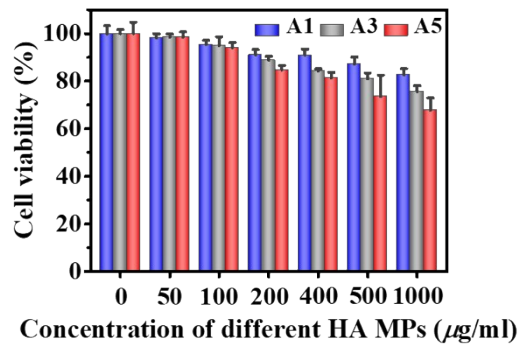


Fig. S2. Evaluation of mBMSCs viability after co-culture with different HA MPs, n=6.

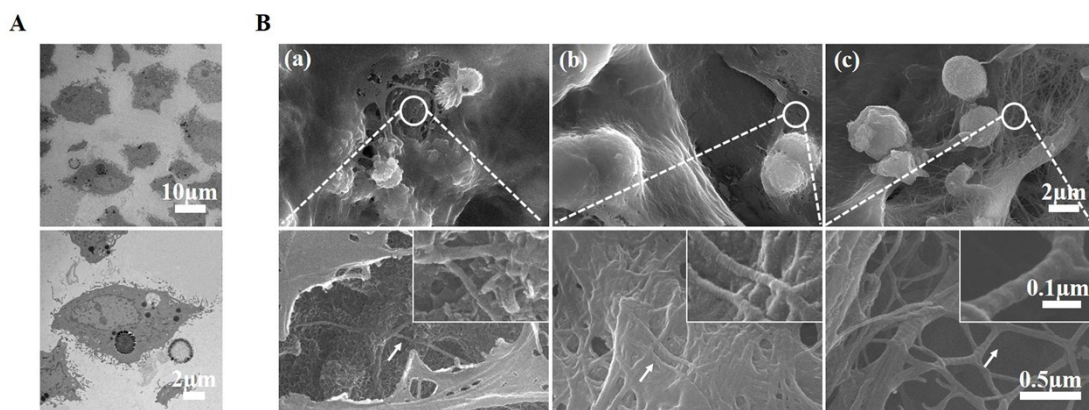


Fig. S3. Cells interaction with diverse microspheres after 21days of co-culture. (A) TEM images show that only a few A5 HA MPs residues were observed. (B) The SEM images taken at different magnifications. (a) A1 HA MPs. (b) A3 HA MPs. (c) A5 HA MPs.

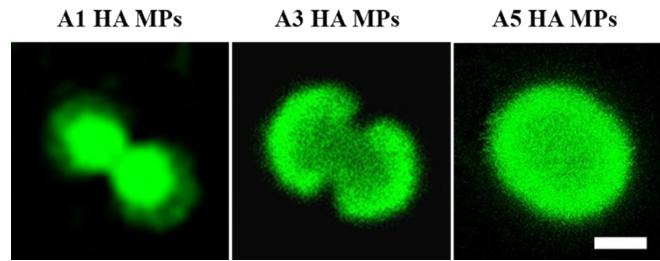


Fig. S4. Fluorescence images of three microspheres with different morphology labeled by FITC molecule, bar = 1 μ m.

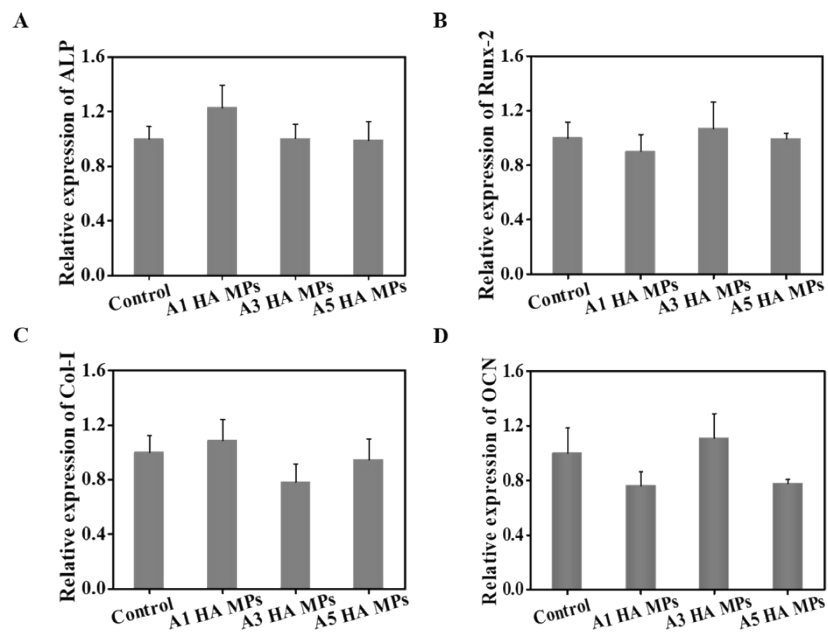


Fig. S5. Effect of leaching liquor from different HA MPs on the expression of osteogenic genes in mBMSCs of 7 days culture. (A) ALP, (B) Runx-2, (C) Col-I, (D) OCN.

Table S1. Primer sequences of genes related to osteogenic differentiation, including ALP, Runx-2, Col-I, OCN, and GAPDH, were used for the qRT-PCR.

Primer	Forward	Reverse
ALP	F:5'-TGCCTACTTGTGTGGCGTGAA-3'	R:5'-TCACCCGAGTGGTAGTCACAATG-3'
Runx2	F:5'-CACTGGCGGTGCAACAAGA-3'	R:5'-TTTCATAACAGCGGAGGCATTTC-3'
Collagen-I	F:5'-ATGCCGCGACCTCAAGATG-3'	R:5'-TGAGGCACAGACGGCTGAGTA-3'
OCN	F:5'-AGCAGCTTGCCCCAGACCTA-3'	R:5'-TAGCGCCGGAGTCTGTTCACTAC-3'
GAPDH	F:5'-GATTTGGTCGTATTGGGCG-3'	R:5'-CTGGAAGATGGTGATGG-3'

Table S2. Summary of the properties of HA MPs. The stoichiometric ratio of Ca/P, crystallinity, specific surface area and average pore size.

	Ca/P ratio	Crystallinity (%)	specific surface area	average pore size
			m ² /g	nm
A1	1.24±0.08	65	48.581	21.50
A2	1.24±0.03	57	64.838	16.68
A3	1.21±0.08	38	74.832	8.77
A4	1.21±0.03	16	85.826	7.75
A5	1.23±0.05	11	106.697	7.32
A6	1.20±0.03	9	120.195	7.74

Table S3. Relative expression of mBMSCs markers associated with osteogenic differentiation induced by A1 A3 and A5 HA MPs.

gene_name	A1 HA MPs vs A3 HA MPs		A1 HA MPs vs A5 HA MPs		A3 HA MPs vs A5 HA MPs	
	logFC	FDR	logFC	FDR	logFC	FDR
Alpl	1.01E-01	7.54E-01	7.98E-01	4.77E-05	7.09E-01	3.47E-04
Runx-2	1.93E-01	4.97E-01	3.50E-01	1.36E-01	1.67E-01	7.02E-01
Col1a1	3.60E-02	9.20E-01	1.24E+00	1.96E-11	1.22E+00	4.38E-11
Bglap	4.19E-01	8.71E-02	2.59E+00	1.15E-07	2.18E+00	7.58E-06
Bmp2	7.98E-01	1.39E-03	1.22E+00	1.67E-06	4.30E-01	2.09E-01
Camkmt	3.93E-01	6.28E-01	1.06E+00	2.23E-02	6.78E-01	3.50E-01
Ackr4	4.75E-01	5.47E-01	3.08E+00	3.70E-18	2.62E+00	5.08E-14
Sacs	3.91E-01	2.19E-01	1.03E+00	4.18E-02	6.48E-01	3.66E-01
Scamp5	8.29E-01	1.35E-01	8.94E-01	5.10E-02	7.68E-02	9.62E-01
Rapgef4	5.00E-01	3.47E-01	1.47E+00	2.82E-05	9.80E-01	2.26E-02
Rap1gap	6.82E-01	4.60E-02	8.02E-01	1.28E-02	1.31E-01	8.79E-01
Rapgef1	3.35E-01	1.97E-01	6.85E-01	3.34E-02	3.60E-01	4.43E-01
Rassf2	4.14E-02	9.46E-01	8.25E-01	4.79E-03	7.94E-01	1.41E-02
Raf1	-1.09E-01	8.11E-01	3.03E-01	3.03E-01	4.21E-01	3.11E-01
Smek2	-1.96E-01	4.89E-01	4.57E-03	9.98E-01	2.12E-01	5.98E-01
Cerk	1.38E-01	7.79E-01	7.88E-01	6.12E-03	6.61E-01	4.23E-02