Supporting Information

Macrophage-targeting bioactive glass nanoparticles for the treatment of intracellular infection and subcutaneous abscess

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1. Characterizations of nanoparticles

The morphology and elemental mapping of particles were characterized by scanning electron microscopy (SEM) coupled with an energy dispersive spectroscopy analysis system (Gemini 500, Zeiss, Germany) under an accelerating voltage of 5 kV. The surface zeta potential, polydispersity index (PDI), and particle size (1.0 mg/mL of particles in PBS, pH=7.4) were measured using a Zetasizer Nano ZS instrument (Malvern, UK) with the light scattering detector positioned at 90°. The thermogravimetric analysis (TGA) of particles was performed using a TGA/DSC 1 instrument (Mettler Toledo, Switzerland) with the N_2 flow rate of 50 mL/min and the heating rate of 10 °C/min over a temperature range of 25-800 °C. X-ray powder diffraction (XRD) was performed using the supernova XRD instrument (Rigaku, Japan) with a Cu Kα radiation in the 2θ range of 20-80° and the scan step size of 0.02°. The X-ray photoelectron spectroscopy (XPS) was performed using a ESCALAB 250 instrument (Thermo-VG Scientific, USA). XPSPEAK41 software was used for the deconvolution of S and Ag core level. The particles were mixed with KBr at a weight ratio of 1:100 and characterized by Fourier transform infrared spectroscopy (FTIR, Nicolet6700, Thermo Scientific, USA) in the range of 500-4000 cm^{-1}. The UV-vis absorption spectra of particles were analyzed using a DU730 instrument (Backman, UK) at a concentration of 1.0 mg/mL (PBS, pH=7.4) in the range of 200-800 nm.

2. Release of ions

5.0 mg of BGNs-Man/Ag was immersed in 10 mL of PBS (pH=5.0 or pH=7.4) and incubated at 37℃. At predetermined time points (0.5, 1, 2, 3, 4, 5, 6, 7 days), 1.0 mL

of the supernatant was taken out after centrifugation and diluted to 10 mL using 5% HNO_3. The concentrations of Ca^{2+}, silicate, and Ag^{+} were measured by inductively coupled plasma-mass spectrometry (ICP-MS) using iCAP Qc instrument (Thermo Scientific, USA).

3. Cytocompatibility evaluation

5×10^4 RAW264.7 macrophages were seeded in each well of the 96-well plate, and the cells were incubated for 24 hours. After that, the culture medium was removed, 100 μL of fresh medium containing BGNs-Man/Ag (0, 6, 12, 25, 50, 100, 200 μg/mL) was added for another 24 hours of incubation. Then, the culture medium was replaced by 100 μL of fresh medium containing 10% Cell Counting Kit-8 reagent (CCK-8, Beyotime, Shanghai, China) and incubated for one hour. Cells without any treatment served as control. The absorbance was measured at 450 nm, and the cell viability was calculated according to the following formula:

Cell viability%=$(A_{sample}-A_{background})\times100\%/(A_{control}-A_{background})$.

Where A_{sample} is the absorbance of cells treated with BGNs-Man/Ag, $A_{background}$ is the absorbance of culture medium containing 10% CCK-8, and $A_{control}$ is the absorbance of control group.

Table S1. Nominal and calculated compositions of BGNs determined by EDS.

Sample	Nominal Composition (mol%)		Calculated Composition (mol%)	
	SiO2	**CaO**	**SiO2**	**CaO**
BGNs	85	15	87.98	12.02

Table S2. Physicochemical characterization results of BGNs, BGNs-SH, BGNs-Man, and BGNs-Man/Ag.

Sample	PDI	Size (nm)	Z-potential (mV, pH=5.0)	Z-potential (mV, pH=7.4)
BGNs	0.126±0.21	277.5±8.0	-4.70±0.32	-11.0±0.79
BGNs-SH	0.143±0.44	293.2±4.2	-13.36±0.87	-19.1±0.64
BGNs-Man	0.336±0.13	290.6±3.3	-5.38±0.49	-7.70±0.35
BGNs-Man/Ag	0.282±0.17	335.3±7.3	-11.7±0.43	-14.97±0.52

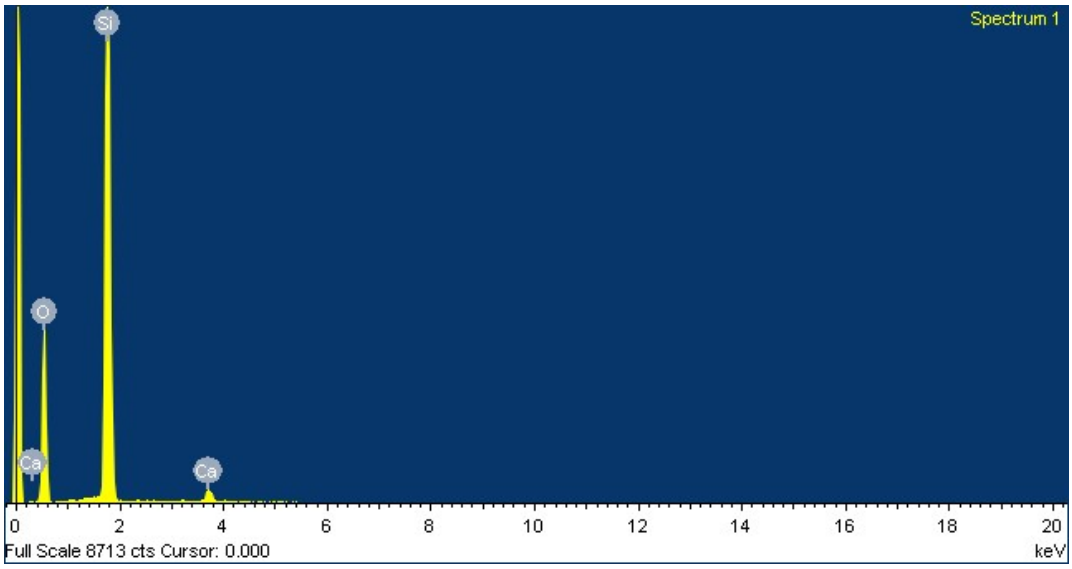

Figure S1. EDS spectrum of BGNs.

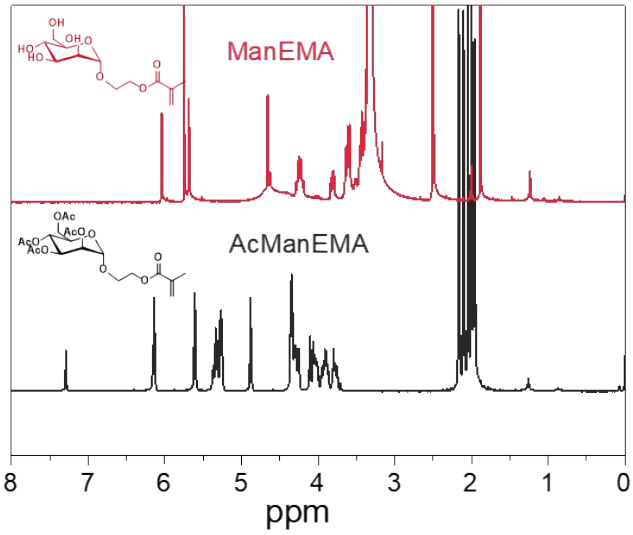

Figure S2. ^{1}H NMR spectra of ManEMA and AcManEMA.

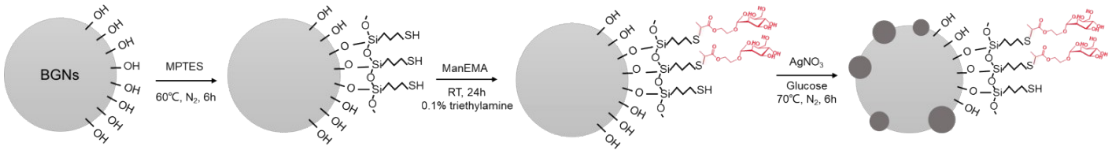

Figure S3. Chemistry of the functionalization process of BGNs.

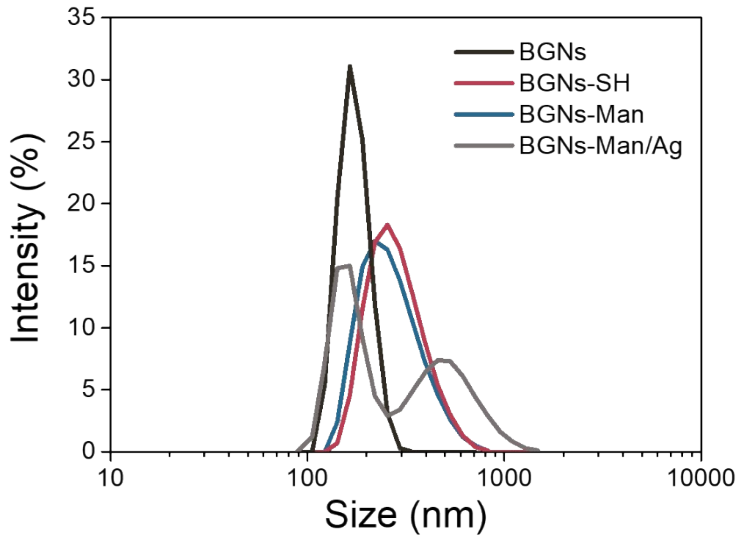

Figure S4. Size distribution of BGNs, BGNs-SH, BGNs-Man, and BGNs-Man/Ag.

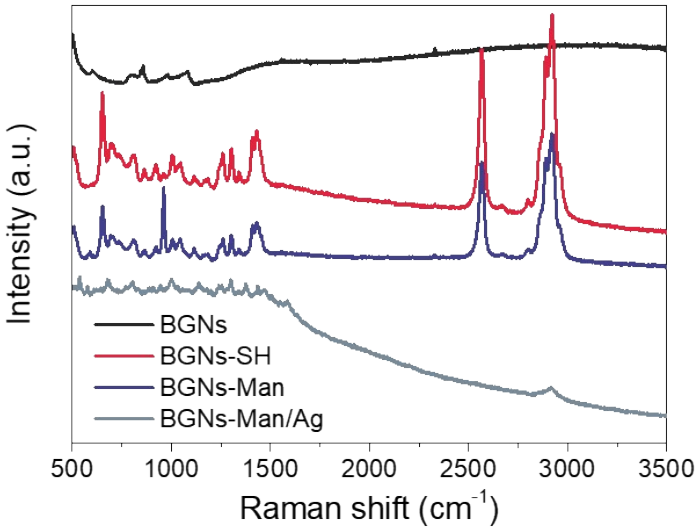

Figure S5. Raman spectra of BGNs, BGNs-SH, BGNs-Man, and BGNs-Man/Ag.

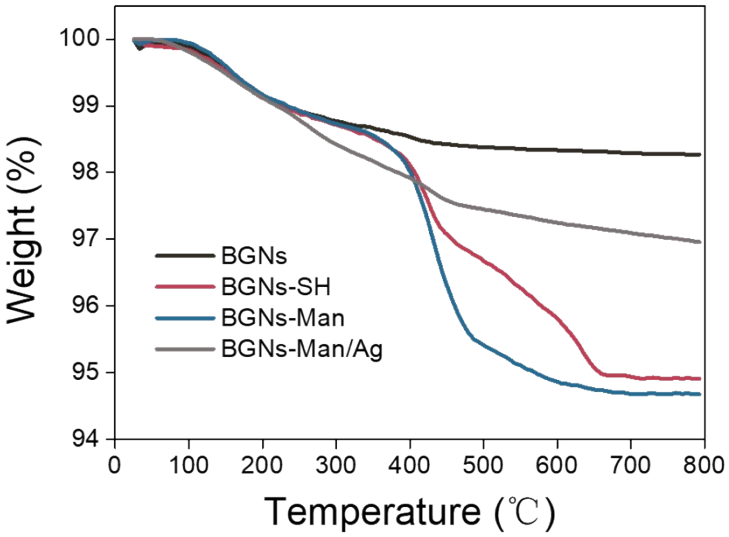

Figure S6. TGA curves of BGNs, BGNs-SH, BGNs-Man, and BGNs-Man/Ag.

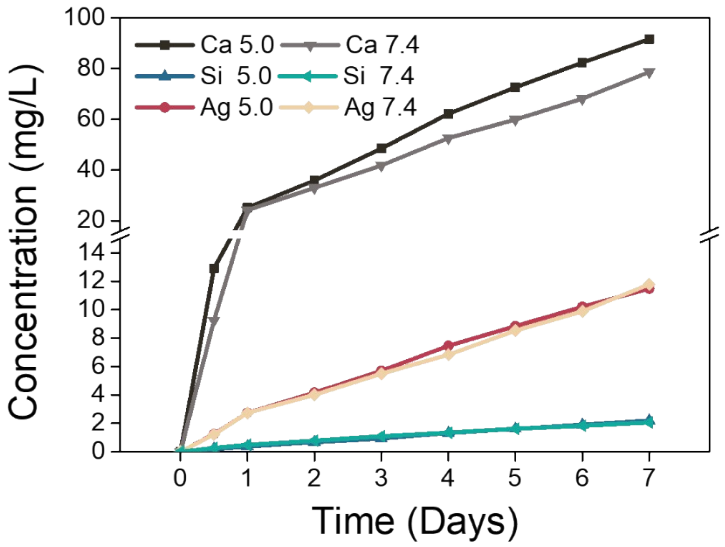

Figure S7. Ion release from BGNs-Man/Ag at pH=5.0 or pH=7.4.

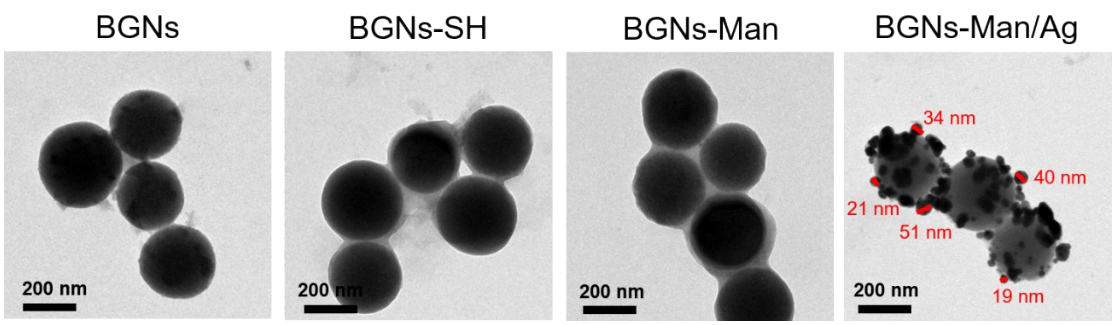

Figure S8. TEM images of BGNs, BGNs-SH, BGNs-Man, and BGNs-Man/Ag.

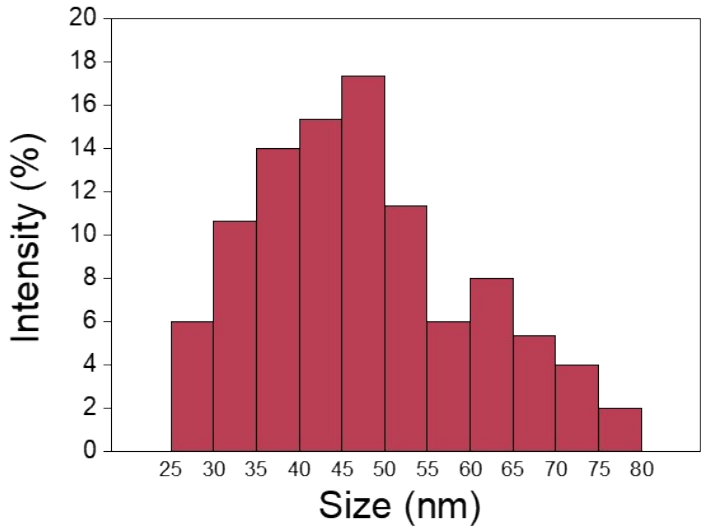

Figure S9. Size distribution of Ag nanoparticles on the surface of BGNs-Man/Ag.

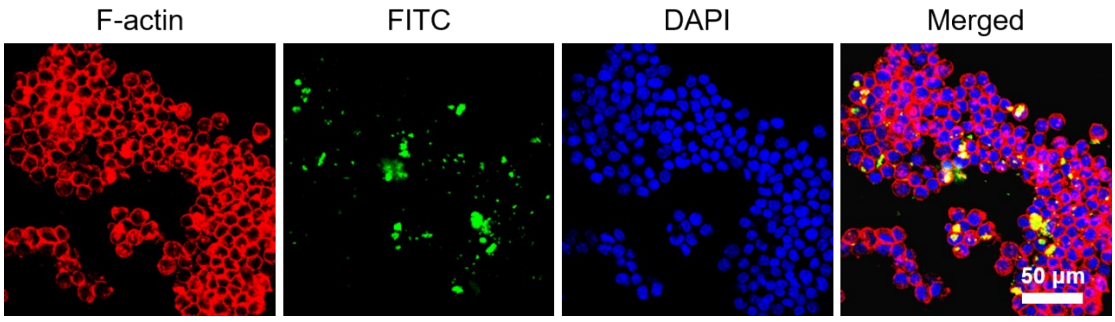

Figure S10. Images of the cellular uptake of BGNs-Man/Ag at low magnification.

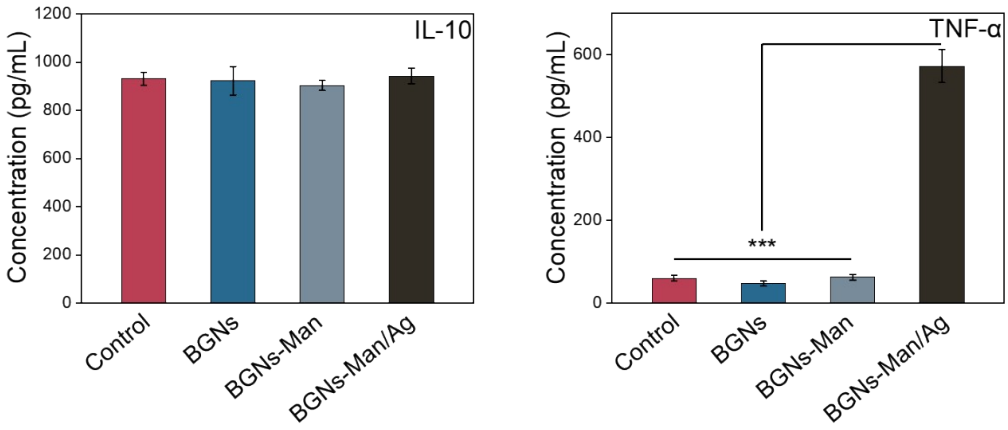

Figure S11. The production of IL-10 and TNF-α in the BGNs-Man/Ag treated macrophages

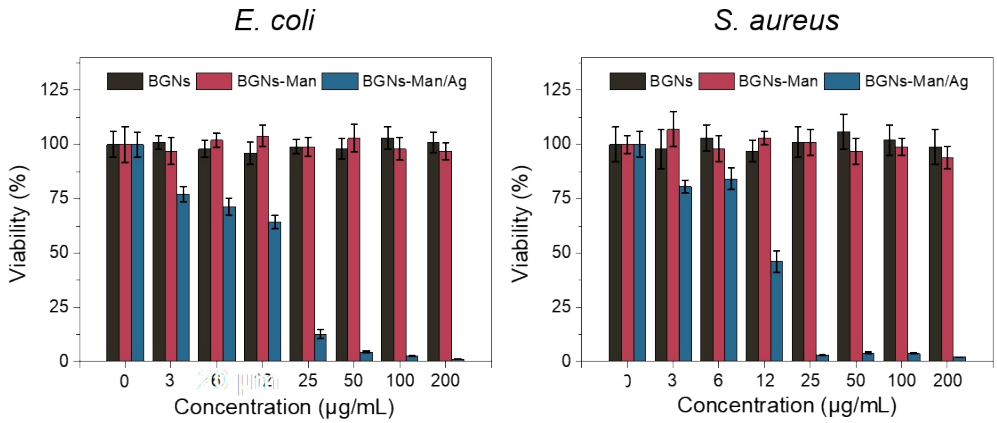

Figure S12. Minimum inhibitory concentration of BGNs, BGNs-Man, and BGNs-Man/Ag against *E. coli* and *S. aureus*, respectively.

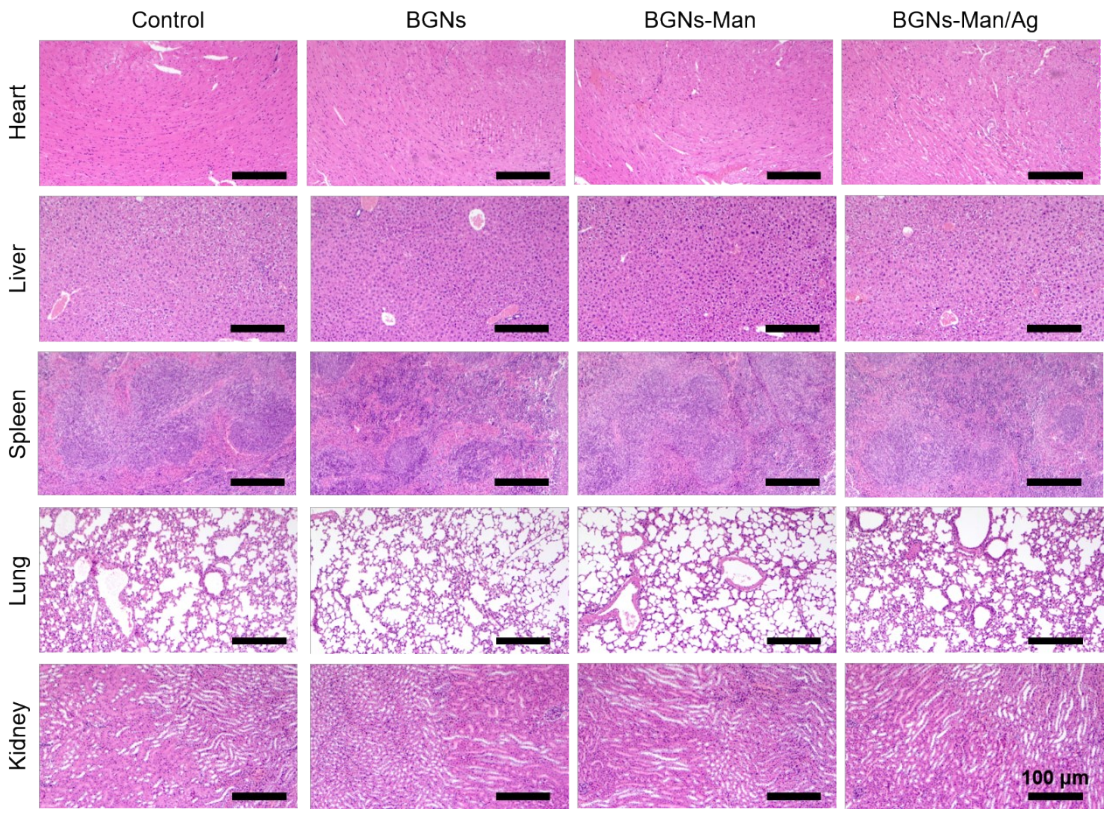

Figure S13. H&E staining of major organs.