

## Supplementary materials

### Myocardial perfusion

Sonovue, a clinical ultrasound contrast agent, was used to evaluate myocardial perfusion by echocardiography. HT model rats were administrated sonovue by tail injection on postoperative day 3. Heartbeat and myocardial perfusion were performed with a commercial ultrasound system IU22 (Philips Medical Systems, Amsterdam, Netherlands) using an L12-5 linear array transducer.

### Characterization of GM

The extractive GM was characterized by Fourier transform infrared (FTIR) (VERTEX70, Bruker Optik, Ettlingen, Germany) with the wavelength region ranging from  $4000\text{ cm}^{-1}$  to  $500\text{ cm}^{-1}$ . The spectra of GM obtained in a resolution of  $4\text{ cm}^{-1}$  by potassium bromide pellet technique. Thermogravimetric analyzer (TGA 800, PerkinElmer, Waltham, MA, USA) was used to assess GM. The samples were heated under the protection of nitrogen flow ( $20\text{ mL min}^{-1}$ ) from  $30\text{ °C}$  to  $800\text{ °C}$  at  $20\text{ °C min}^{-1}$ .

### SEM of GM at various pH

The morphologies of GM at various pH were determined by scanning electron microscopy (SEM, Hitachi SU8010, Tokyo, Japan). GM suspension ( $0.5\text{ mg/mL}$ ) incubated at  $37\text{ °C}$  in a shaking air bath (TS-110X30, TENSUC, Shanghai, China) under 100 rpm for 1 h. Then the samples were dried and placed on tin foil and coated with platinum using an ion sputter (EM ACE 200, Leica, Germany) for SEM.

### Bio-distribution of GM at HT model

Quantum dot (QD) as a conventional fluorescent dye was used to track the distribution of GM, QD-labelled GM was prepared in the same method as GM-FK506. Rats were received QD-loaded GM seven days after surgery. Then the allograft heart and LNs were harvested at 24 h after administration to appraise the bio-distribution of GM using a small animal imaging system (In-Vivo FX PRO, BRUKER).

### Effect of GM on LN cells

To evaluate the effect of GM on LN cells, Lewis rats received  $500\text{ mg/kg}$  of GM by gavage for five consecutive days, which is a 5-fold augmentation for GM compared with the GM dose in HT model. The rats were euthanized at 6 days, and the representative LNs (ALNs, MLNs, DLNs) were harvested for evaluation. Lymphocyte in LNs was assessed through H&E and Immunohistochemical staining. IL-2 and IFN- $\gamma$ , which secreted by T lymphocytes, were evaluated by immunofluorescence.

### Safety assessment of GM

The study examined the 14-day toxicity of GM in Lewis rats with 5-folds augmentation dose of GM, which was used in HT model rats. The rats were administrated  $500\text{ mg/kg}$  of GM by gavage for fourteen consecutive days, and they were daily monitored for weight gain and changes in behavior or appearance (i.e., feeding, ruffled fur, mobility, etc.). PBS served as a control group. Blood biochemistry indicators of the liver (AST, ALT) and kidney (BUN, CR) were examined by the automatic biochemical analyzer (Chemray-240, Shenzhen, China). The number of immune cells in the blood was measured with an automatic animal blood cell analyzer (BC-2800vet, Shenzhen, China). And the pathological features of the main organs were evaluated by H&E staining after treatment.

### TEM of phagocytic GM in macrophage

GMs were suspended cell culture medium and diluted to a concentration of  $2\times 10^8$  particles per mL, then co-incubation with macrophage at  $37\text{ °C}$  for 12 h. The cell samples were washed with PBS, then fixed with 2.5% glutaraldehyde for TEM. The representative structure was observed by TEM after a series of disposal.

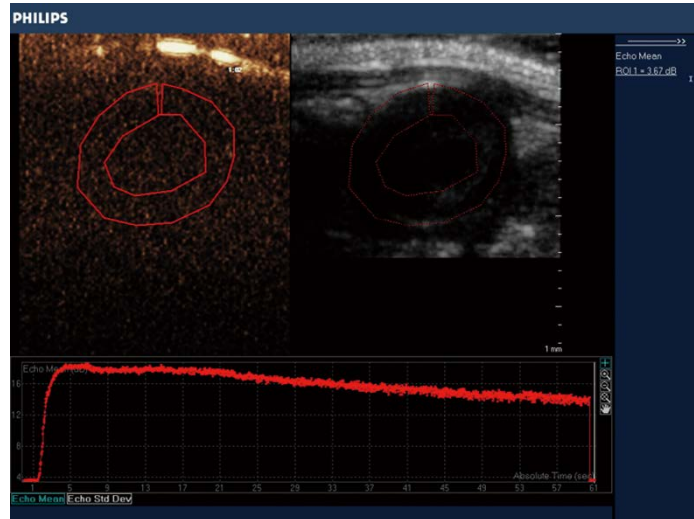


Fig S1 Myocardial perfusion after 3 d transplantation.

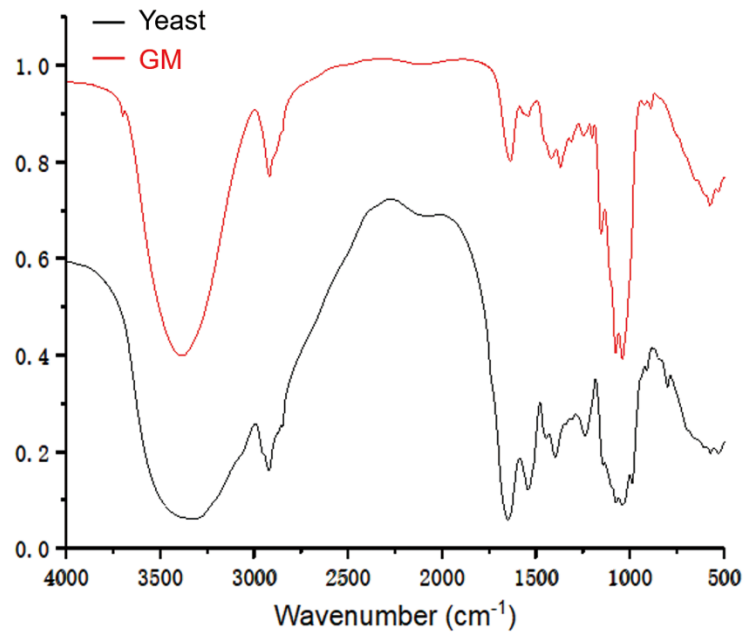


Fig S2 The FTIR spectra of yeast and GM.

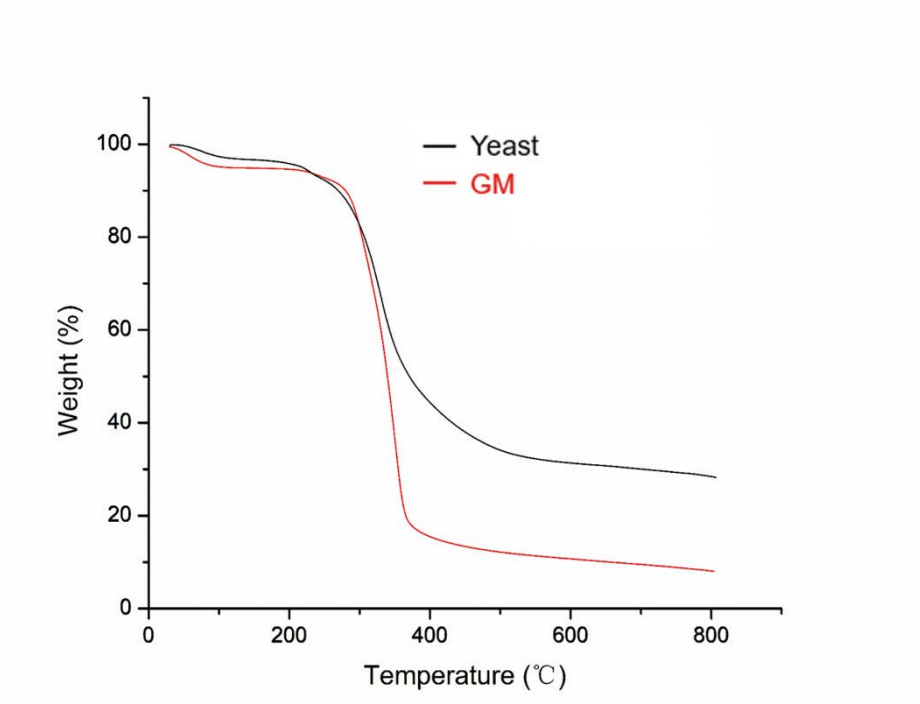


Fig S3 The thermogravimetric curve of yeast and GM.

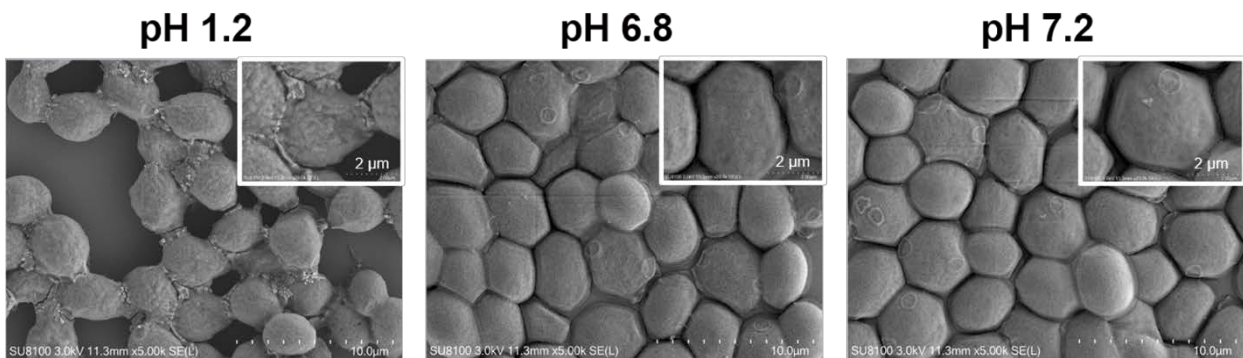


Fig S4 The scanning electron microscope (SEM) image of GM after incubation at various pH (pH 1.2, pH 6.8, pH 7.2) for 1 h.

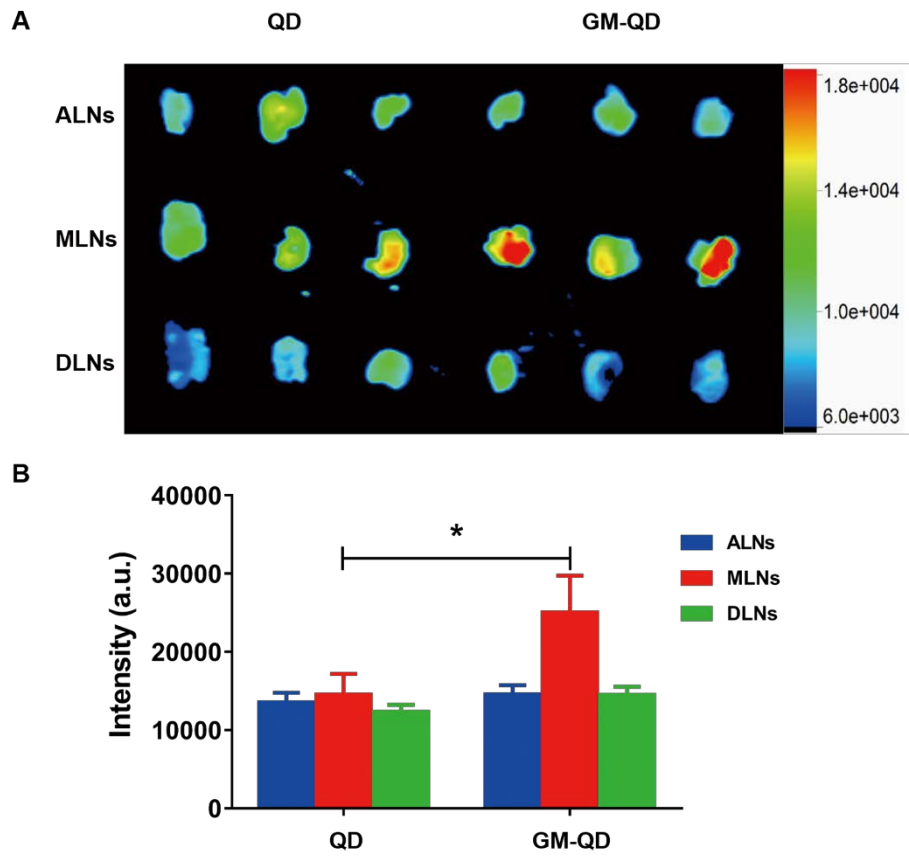


Fig S5 Ex vivo fluorescence image of LNs at 24 h after oral administration of QD and GM-QD.

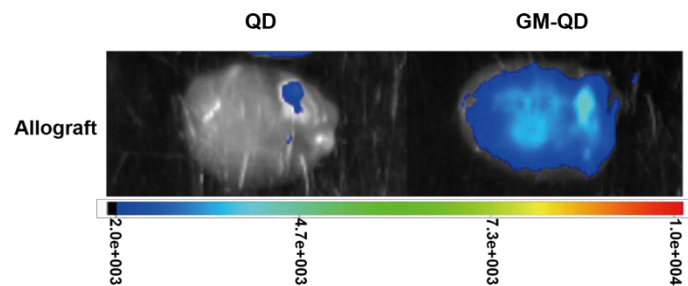


Fig S6 Ex vivo fluorescence image of allografts at 24 h after oral administration of QD and GM-QD.

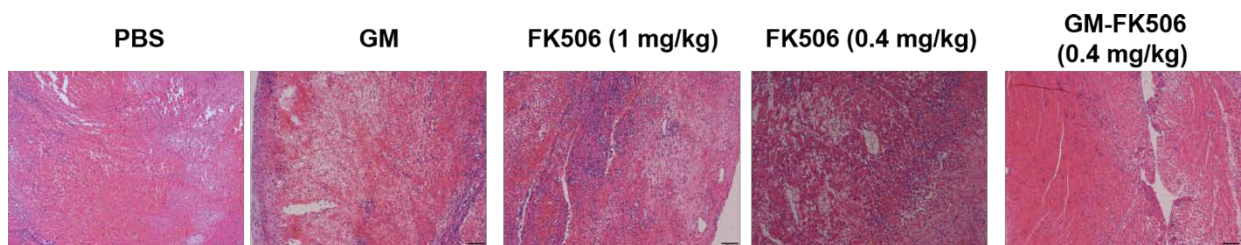


Fig S7 The H&E staining of end-stage allograft, scale bar = 100  $\mu$ m.

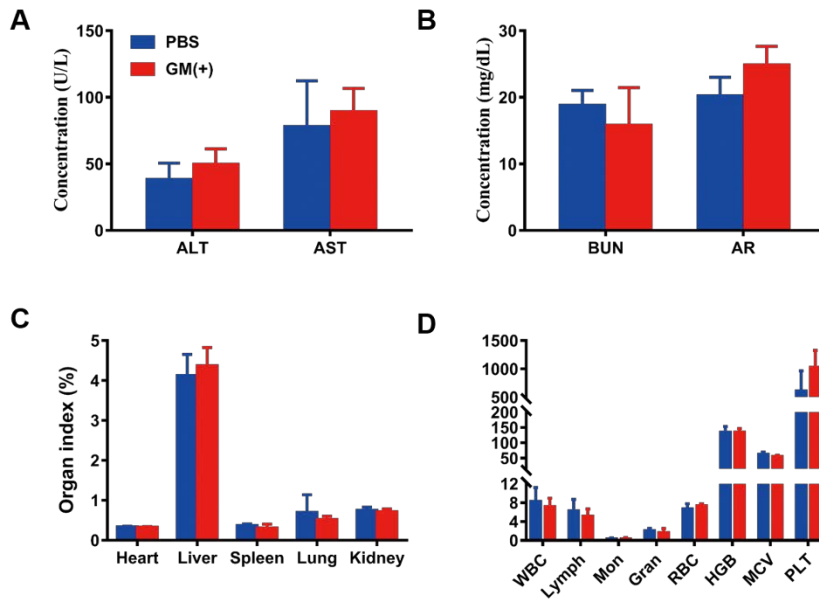


Fig S8 Safety evaluation of yeast microcapsules after 14 days treatment with PBS and GM. A. The liver function. B. The renal function. C. The organ index (%). D. Biochemical analysis of blood.

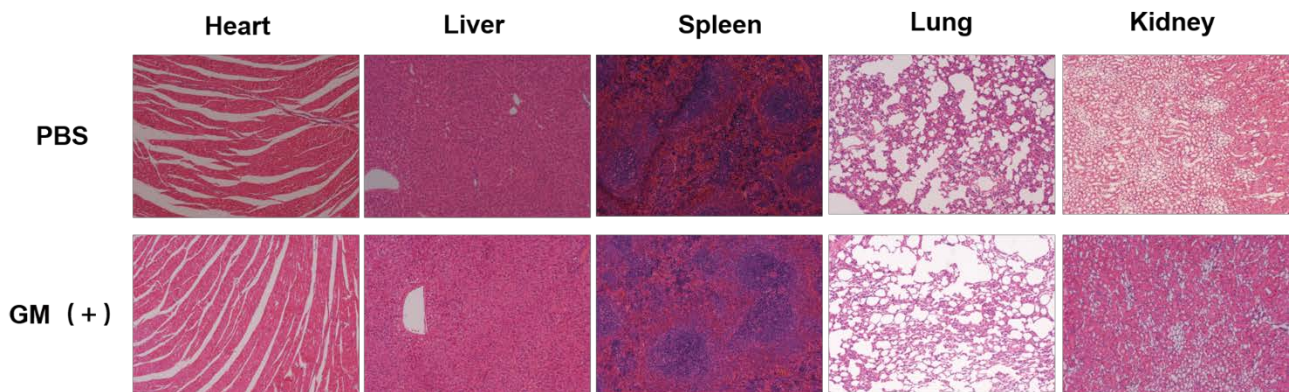


Fig S9 The H&E staining of major organs after 14d of PBS and GM treatment, scale bar = 100  $\mu$ m.

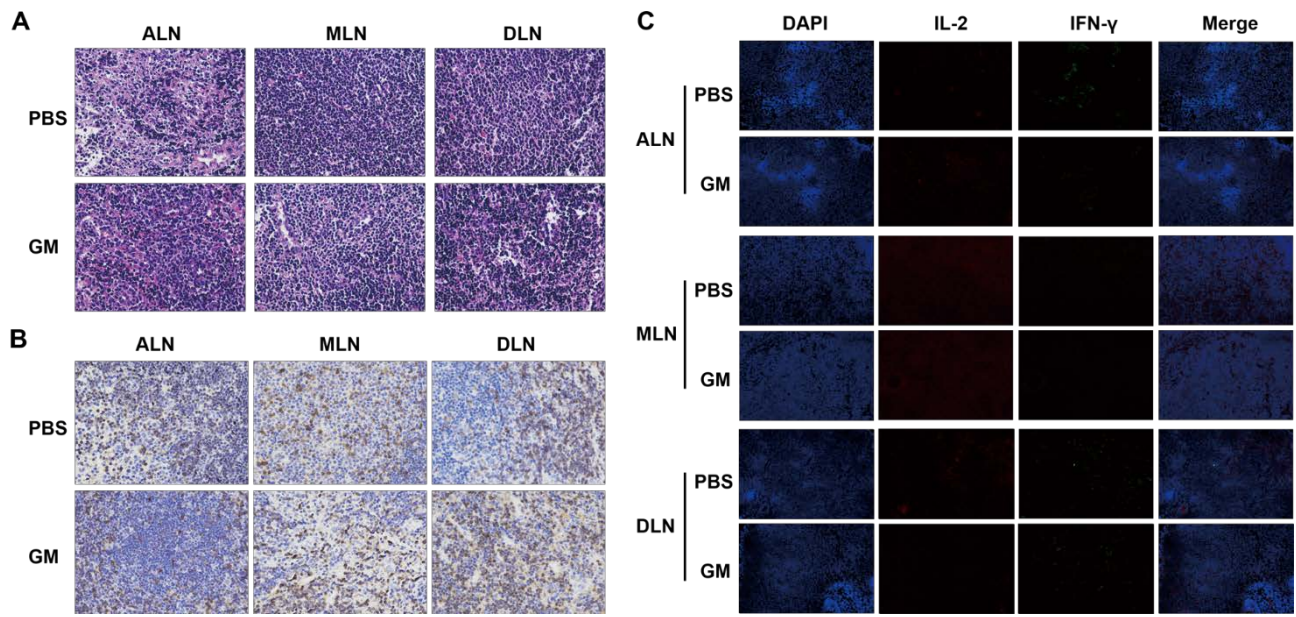


Fig S10 Effect of GM on LN cells after 5 days treatment with PBS and GM.. A. The H&E staining of LN after treatment PBS and GM, scale bar = 20  $\mu\text{m}$ . B. Immunohistochemistry staining with CD3+ T lymphocytes of LN, scale bar = 20  $\mu\text{m}$ . C. Immunofluorescence staining of IL-2 and IFN- $\gamma$  secretion in represented LN, scale bar = 50  $\mu\text{m}$ .

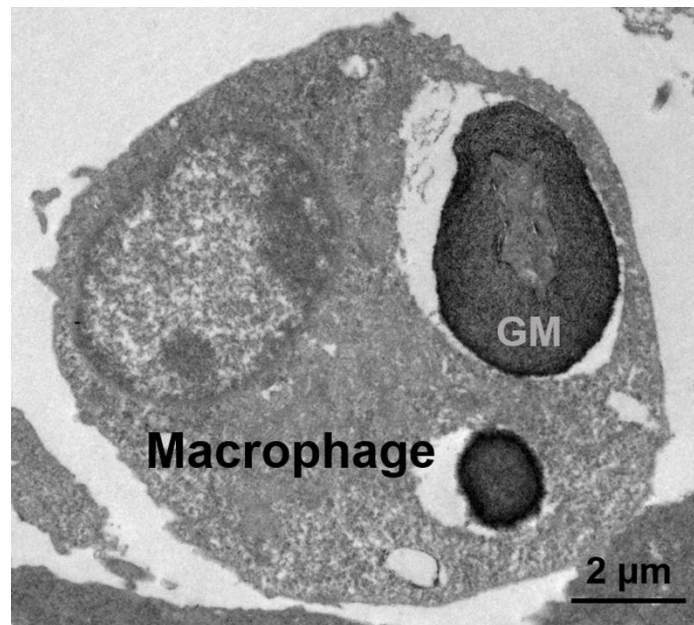


Figure S11 TEM of phagocytic GM in macrophage.