## **Supporting Information**

Heart valves cross-linked with erythrocyte membrane drug-loaded nanoparticles as a biomimetic strategy for anti-coagulation, antiinflammation, anti-calcification, and endothelialization

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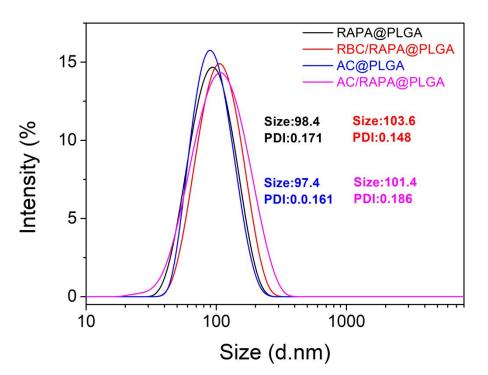
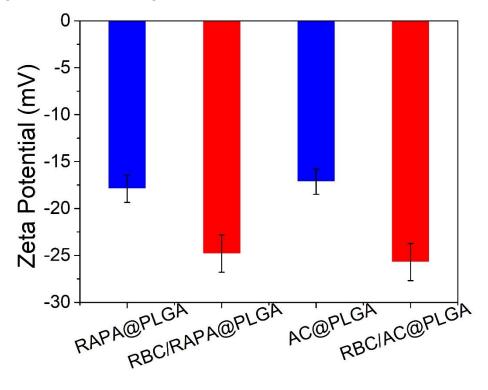


Figure S1. Particle size distribution of RAPA@PLGA, RBC/RAPA@PLGA, AC@PLGA and RBC/AC@PLGA in  $H_2O$  measured by DLS.



**Figure S2.** Zeta potential of RAPA@PLGA, RBC/RAPA@PLGA, AC@PLGA and RBC/AC@PLGA in H<sub>2</sub>O (n=3).

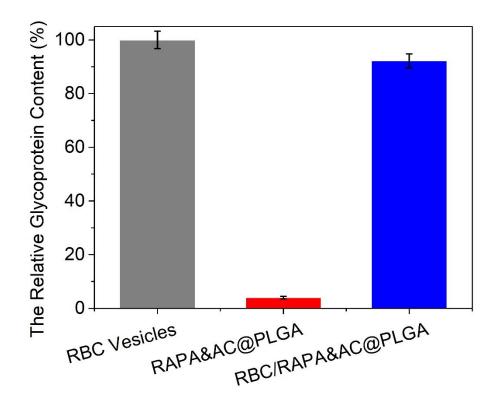
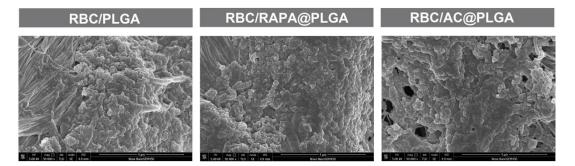
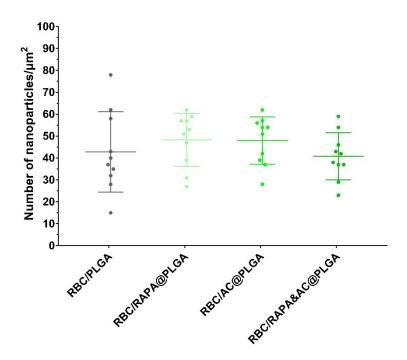


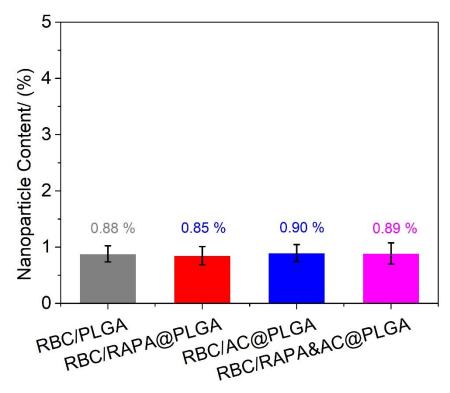
Figure S3. The relative glycoprotein content of the RBC vesicles, RAPA&AC@PLGA and RBC/RAPA&AC@PLGA (n = 5).



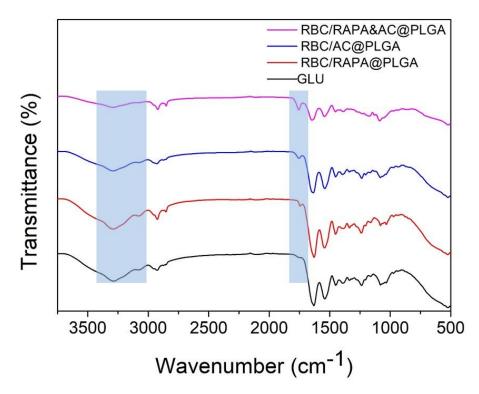
**Figure S4.** The SEM images of heart valves treated with RBC/PLGA, RBC/RAPA@PLGA and RBC/AC@PLGA (scale bar = 4  $\mu$ m).



**Figure S5.** Number of nanoparticles on the surface of differently treated heart valve samples.



**Figure S6.** Nanoparticle content of different heart valve samples after the cross-linked nanoparticles was calculated (n = 5).



**Figure S7.** ATR-FTIR spectra of GLU (black), RBC/RAPA@PLGA (red), RBC/AC@PLGA (blue), and RBC/RAPA&AC@PLGA (purple) were shown.

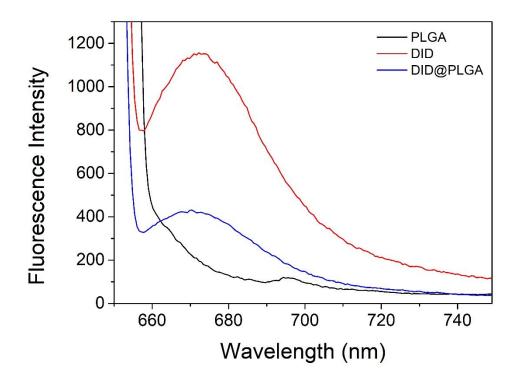


Figure S8. The fluorescence intensity of PLGA, DID, and DID@PLGA in H<sub>2</sub>O.

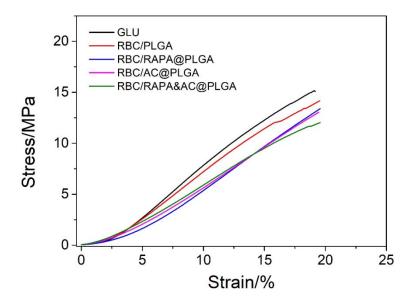
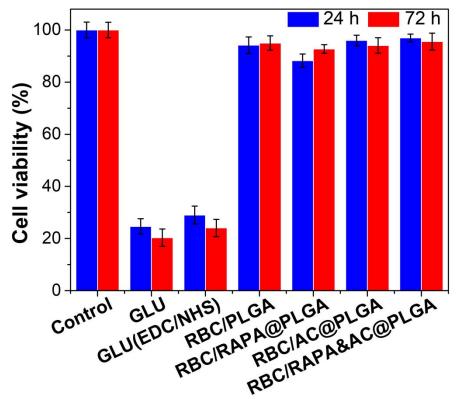
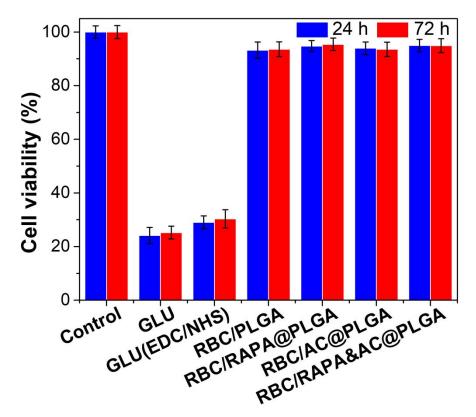


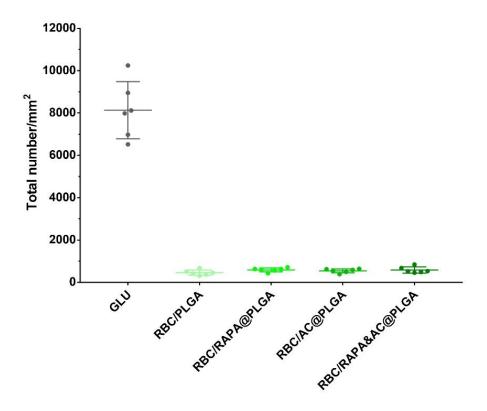
Figure S9. Representative stress-strain curves of heart valves before and after modification.



**Figure S10.** Cytotoxicity of different valve samples. Cell viability of L929 cells was determined by CCK-8 assay (n = 6) after culturing with the extracts of different valve samples for 24 h and 72 h. The GLU(EDC/NHS) group represents that the GLU-treated valves were treated by EDC/NHS only.



**Figure S11.** Cytotoxicity of different valve samples. Cell viability of HUVECs was determined by CCK-8 assay (n = 6) after culturing with the extracts of different valve samples for 24 h and 72 h. The GLU(EDC/NHS) group represents that the GLU-treated valves were treated by EDC/NHS only.



**Figure S12.** Total number of red blood cells and platelets adhered on the surface of differently treated heart valve samples.

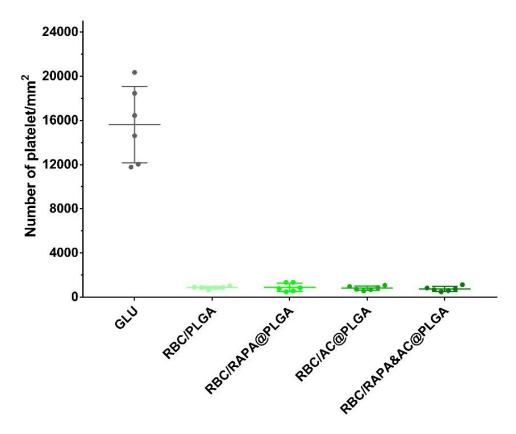
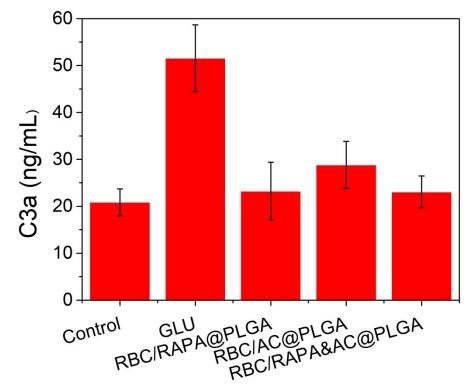


Figure S13. Number of platelets adhered on the surface of differently treated heart valve samples.



**Figure S14.** The concentrations of C3a in the plasma after treated with different heart valve samples (n = 5).

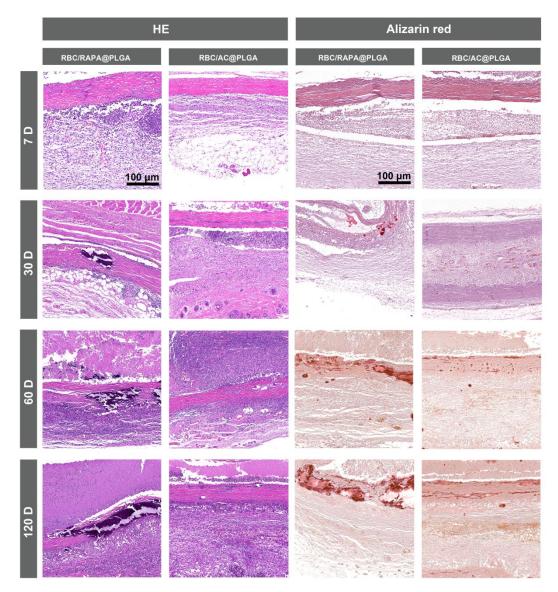
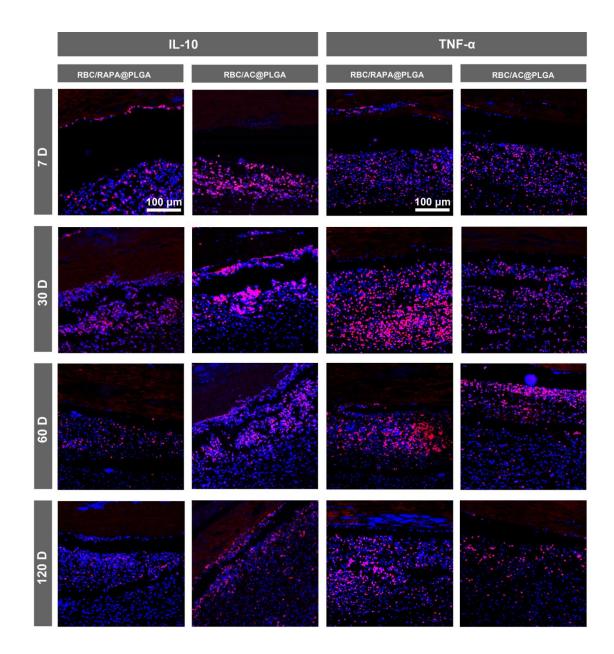


Figure S15. HE and alizarin red staining of different heart valve samples at 7, 30, 60, and 120 days postimplantation into male rats. The scale bars are  $100 \mu m$ .



**Figure S16.** IL-10 and TNF- $\alpha$  of different heart valve samples at 7, 30, 60, and 120 days postimplantation into male SD rats. The scale bars are 100  $\mu$ m.