Supporting Information

A novel long-acting azathioprine polyhydroxyalkanoate nanoparticle enhances treatment efficacy for systemic lupus erythematosus with reduced side effects

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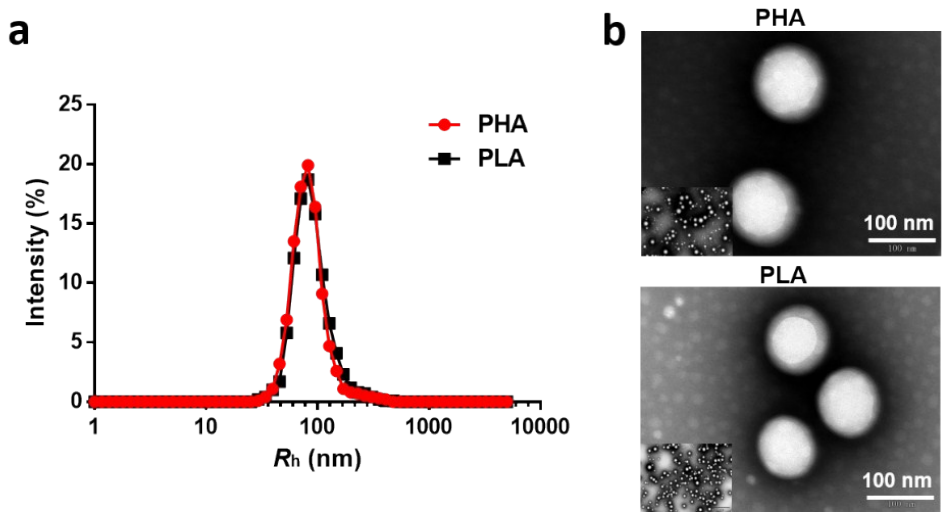

Figure S1. Characterization of PHA and PLA nanoparticles. (a) DLS analysis of PHA and PLA nanoparticles. (b) TEM images of PHA and PLA nanoparticles.

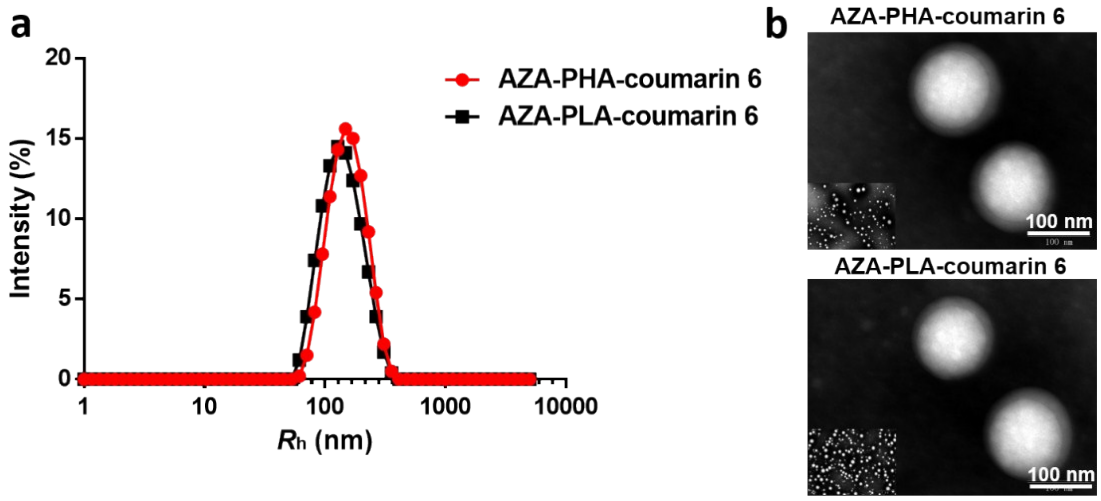

Figure S2. Characterization of AZA-PHA-coumarin 6 and AZA-PLA-coumarin 6 nanoparticles. (a) DLS analysis of AZA-PHA-coumarin 6 and AZA-PLA-coumarin 6 nanoparticles. (b) TEM images of AZA-PHA-coumarin 6 and AZA-PLA-coumarin 6 nanoparticles.

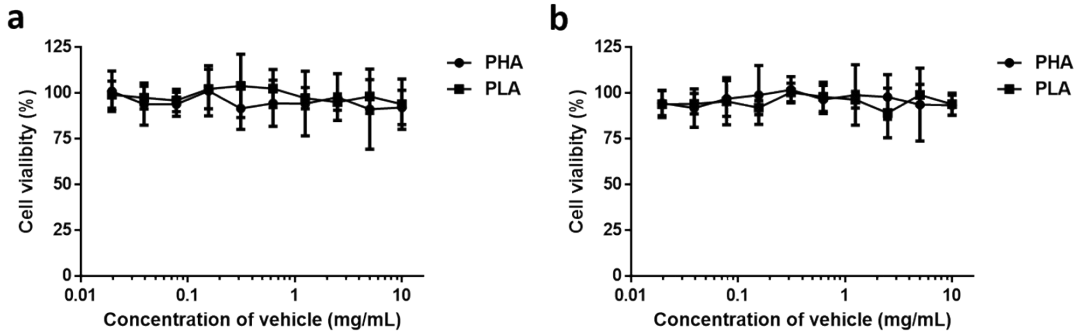

Figure S3. *In vitro* cytotoxicity of PHA and PLA nanoparticles. Data are shown as the mean ± standard deviation (n=3).

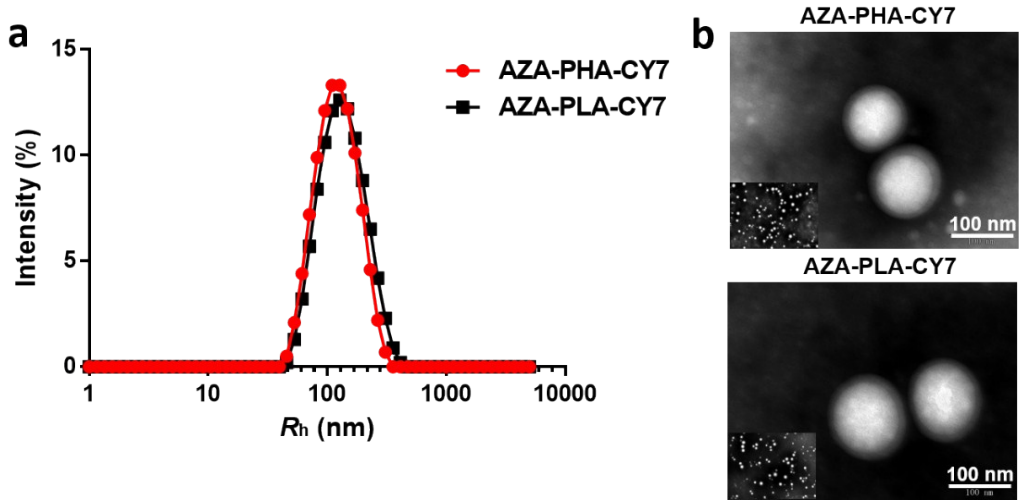

Figure S4. Characterization of AZA-PHA-CY7 and PLA-PHA-CY7 nanoparticles. (a) DLS analysis of PHA and PLA nanoparticles. (b) TEM images of PHA and PLA nanoparticles.

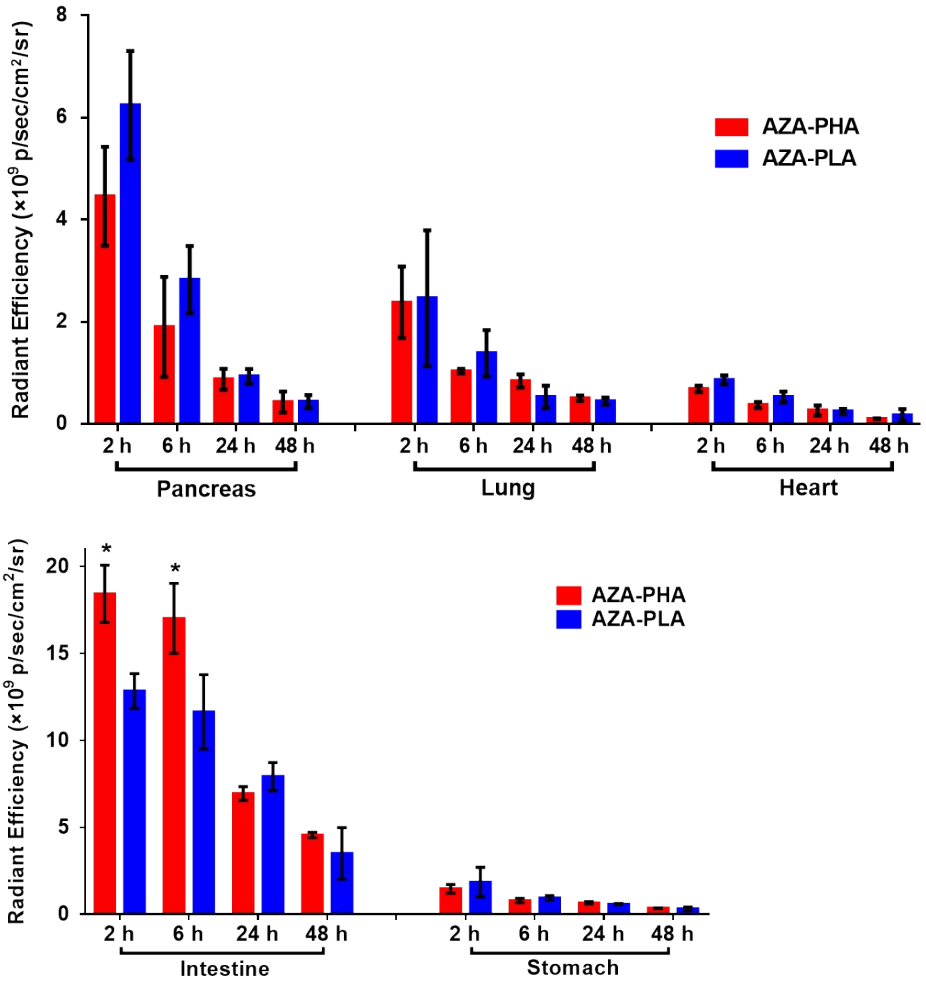

Figure S5. The radiant efficiency of nanoparticles in the pancreas, lung, heart, intestine and stomach 2, 6, 24 and 48 h after intravenous injection. Data are shown as mean ± standard deviation (n=3, $*P < 0.05$ for the AZA-PHA nanoparticles versus the AZA-PLA nanoparticles in tissues at the same time.)

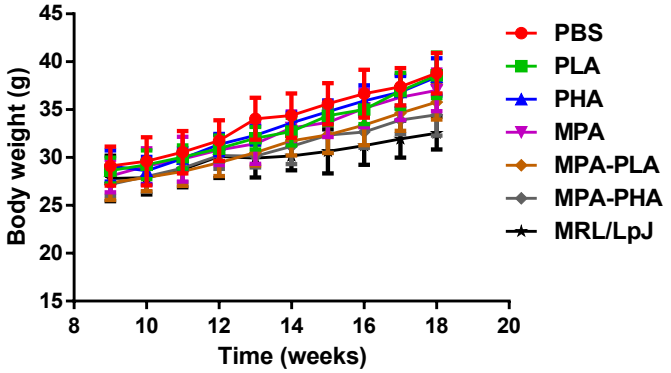

Figure S6. The change of mice body weight during experiment.

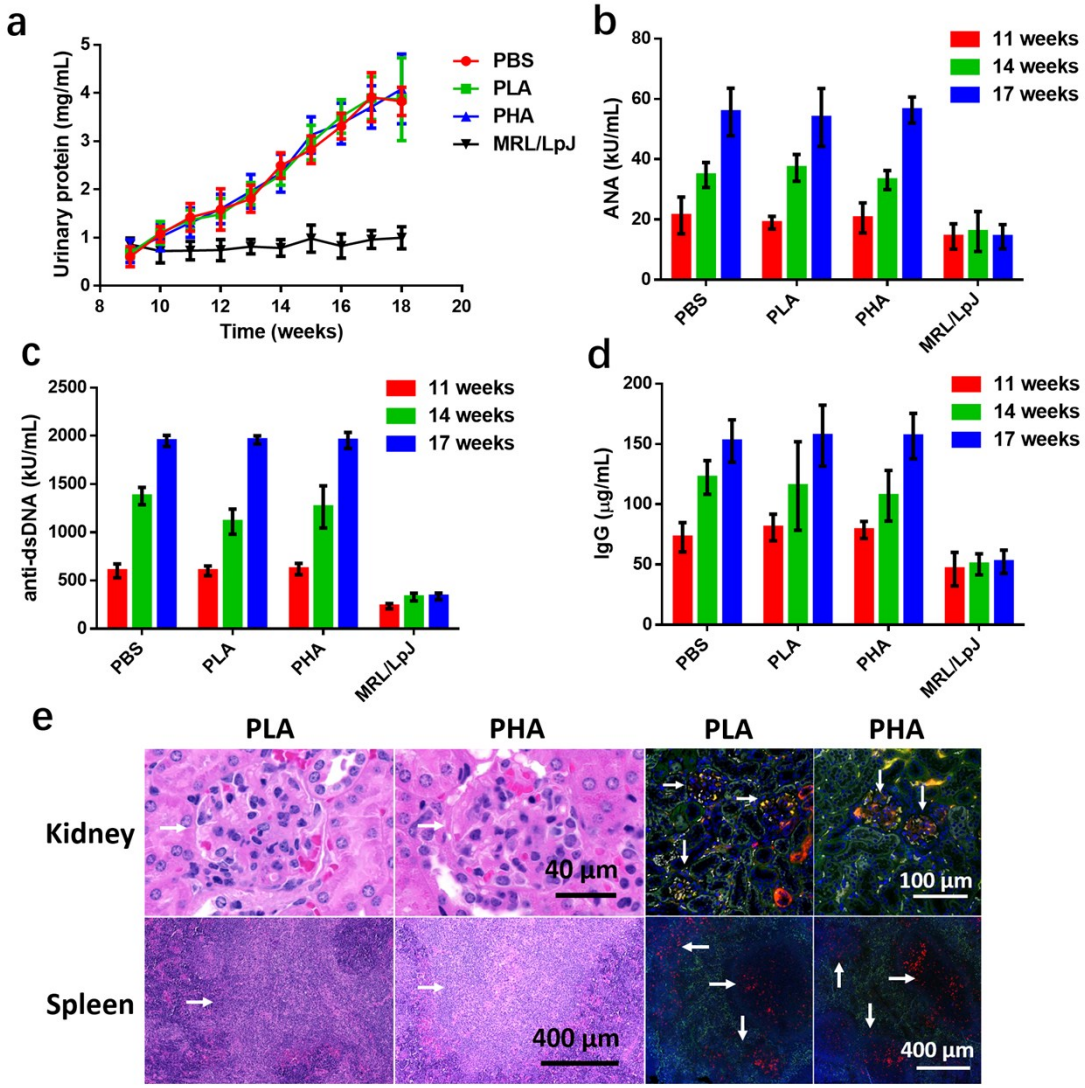

Figure S7. Therapeutic efficacy of PHA and PLA nanoparticles in MRL/lpr mice. (a) The concentration of urinary proteins. (b) The titre of ANA. (c) The titre of anti-dsDNA. (d) The concentration of IgG. (e) H&E and immunofluorescent staining of the kidney and spleen. Kidney: cell nuclei were stained with DAPI in blue; IgG was stained with anti-IgG Abs in green; IgM was stained with anti-IgM Abs in red; and C3 was stained with anti-C3 Abs in white. The arrows indicate glomeruli. Spleen: cell nuclei were stained with DAPI in blue; B220 stained with anti-B220 Abs in green represented B cells of all developmental stages, activated B cells or subsets of T and NK cells; and GL7 stained with anti-GL7 Abs in red represented pre-B and immature B cells, activated T and B cells. The overlap of B220 and GL7 indicates the splenic germinal center. The arrow points to glomeruli and splenic

germinal center in kidney and spleen slides, respectively. Data are shown as the mean ± standard deviation (n=4-6, no significance difference for PHA and PLA nanoparticles versus PBS).

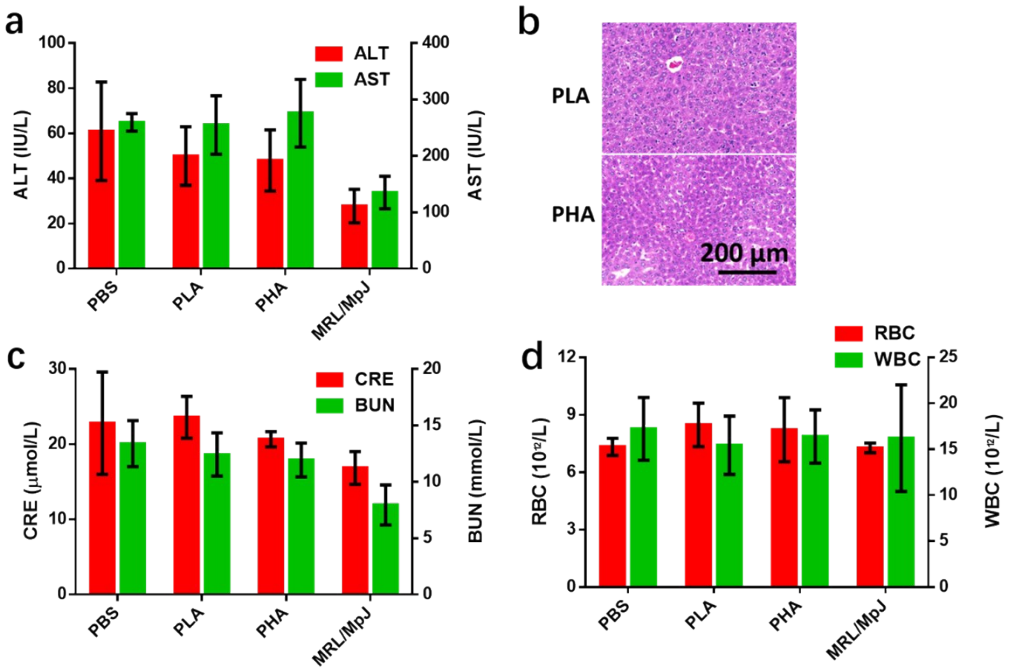

Figure S8. Systemic toxicity evaluation of PHA and PLA nanocarriers. (a) Clinical biochemical parameters of ALT and AST for liver function. (b) H&E staining of liver. (c) Clinical biochemical parameters of CRE and BUN for kidney function. (d) Hematological parameters of RBCs and WBCs. Data are shown as the mean ± standard deviation (n=4-6).