Supplementary Materials for

Poly(lactic acid)-hyperbranched polyglycerol nanoparticles enhance bioadhesive treatment of esophageal disease and reduce systemic drug exposure

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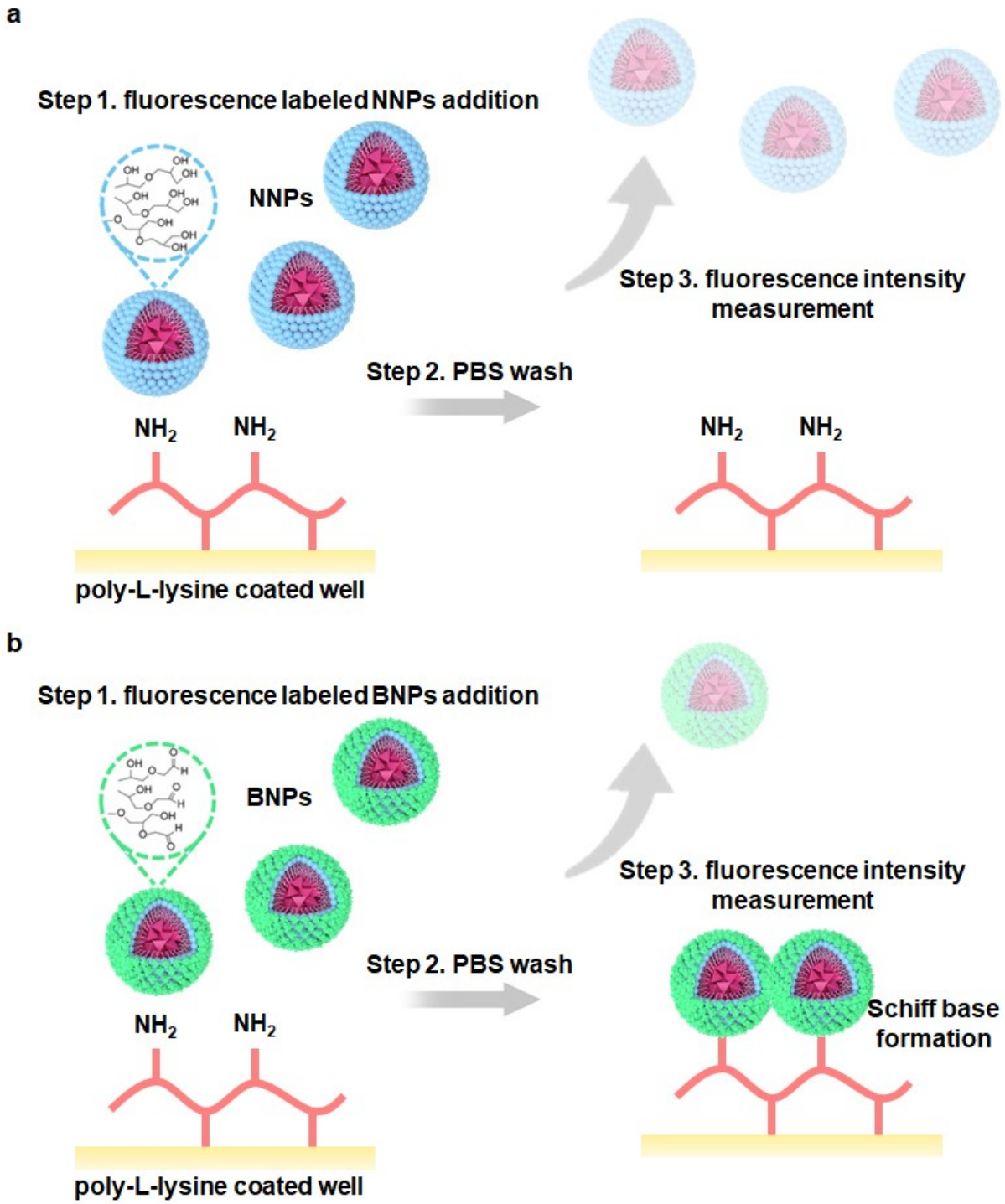


Figure S1. Schematic illustration of *in vitro* NPs adhesion ability assessment on poly-L-lysine coated plate. a) PLA-Cy5/NNPs or b) PLA-Cy5/BNPs were added into poly-L-lysine coated plate wells, respectively. After PBS washing, the remaining fluorescence intensity was measured in each well. The recovery rate was calculated as the remaining fluorescence intensity in wells/the fluorescence intensity of NPs in wells before washing. BNPs would retain in wells due to the Schiff base formation between BNPs and poly-L-lysines.

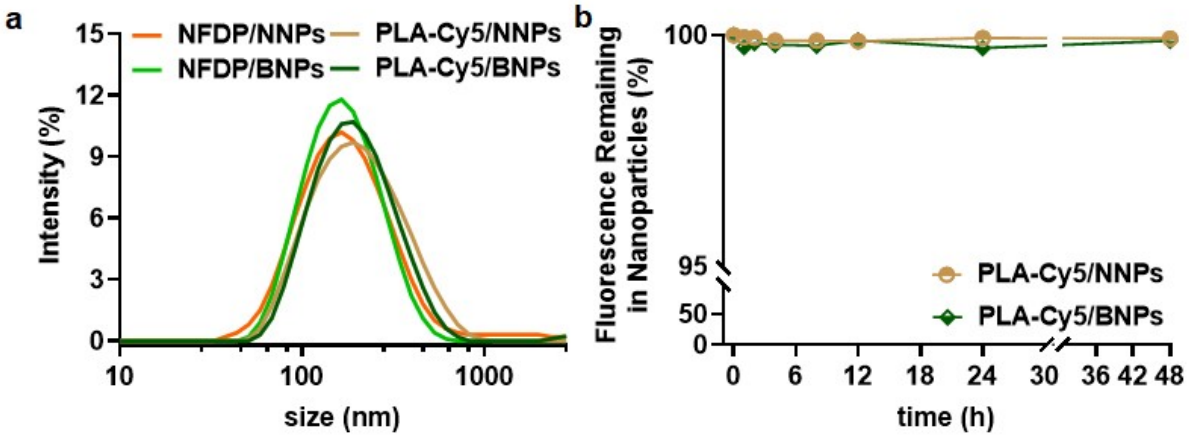


Figure S2. ***In vitro*** **characterization of NPs.** a) Hydrodynamic diameter distribution of NFDP/NNPs, NFDP/BNPs, PLA-Cy5/NNPs and PLA-Cy5/BNPs by dynamic light scattering (DLS). b) PLA-Cy5 retention within PLA-Cy5/NNPs and PLA-Cy5/BNPs incubated in PBS for 48 h at 37 °C. Data are shown as mean ± s.d. (n = 5).

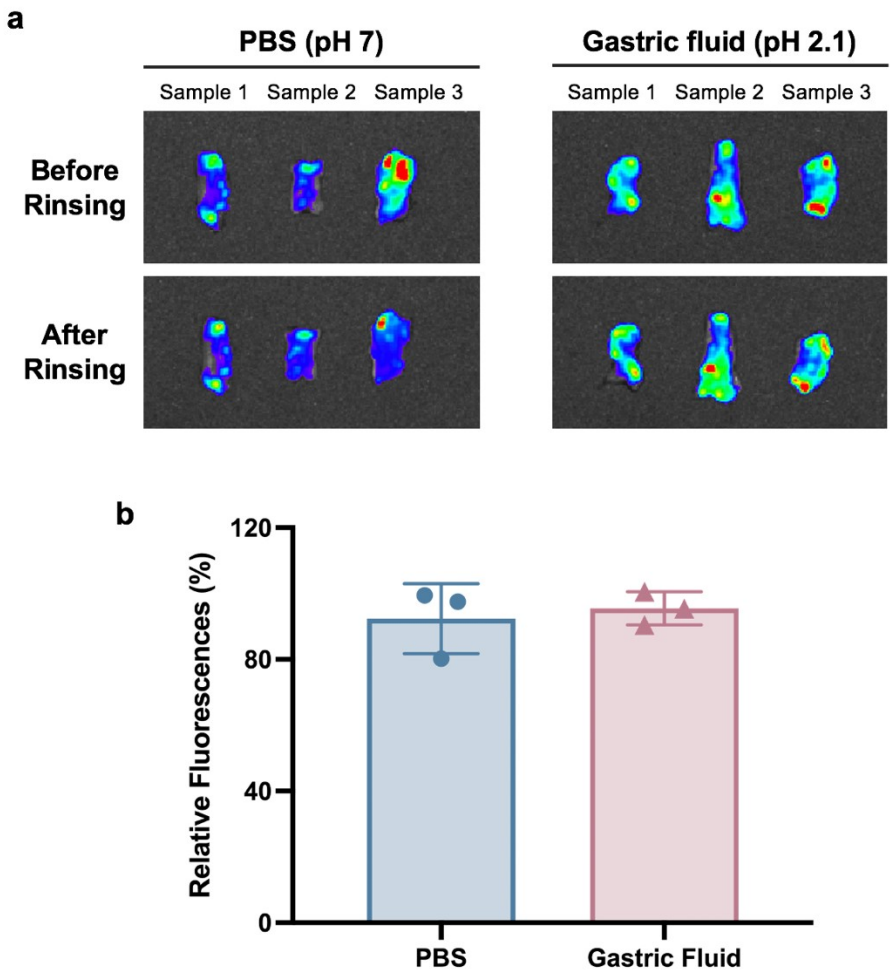


Figure S3. Effect of stimulated gastric fluid on the adhesion of BNPs to rat esophagus tissues. a) BNPs encapsulating PLA-Cy5 dye were added on the luminal surface of rat esophageal tissues for 15 s. *Ex vivo* tissue images were taken with Xenogen after 30 s with either PBS (pH = 7) or stimulated gastric fluid (pH = 2.1) rinsing. b) The fluorescence intensity of images after rinsing from **a)** was quantified and normalized by the fluorescence intensity of images before rinsing.

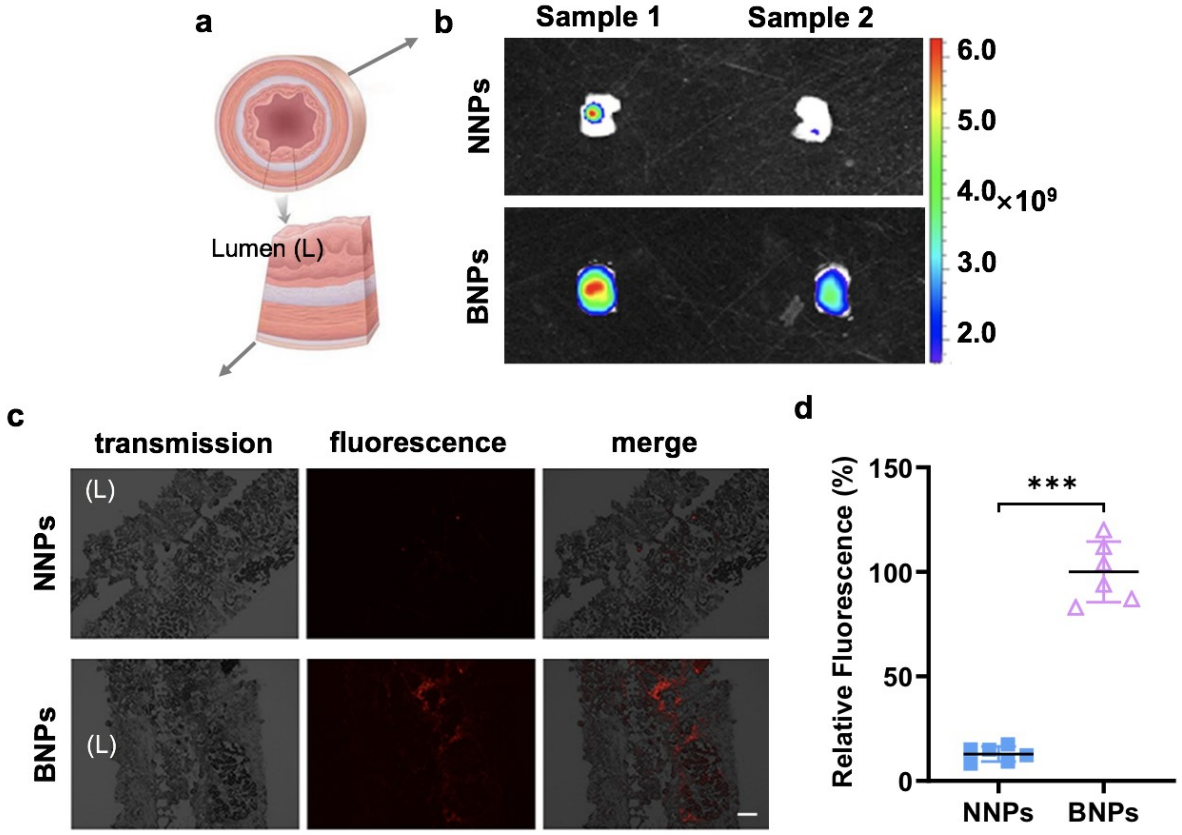
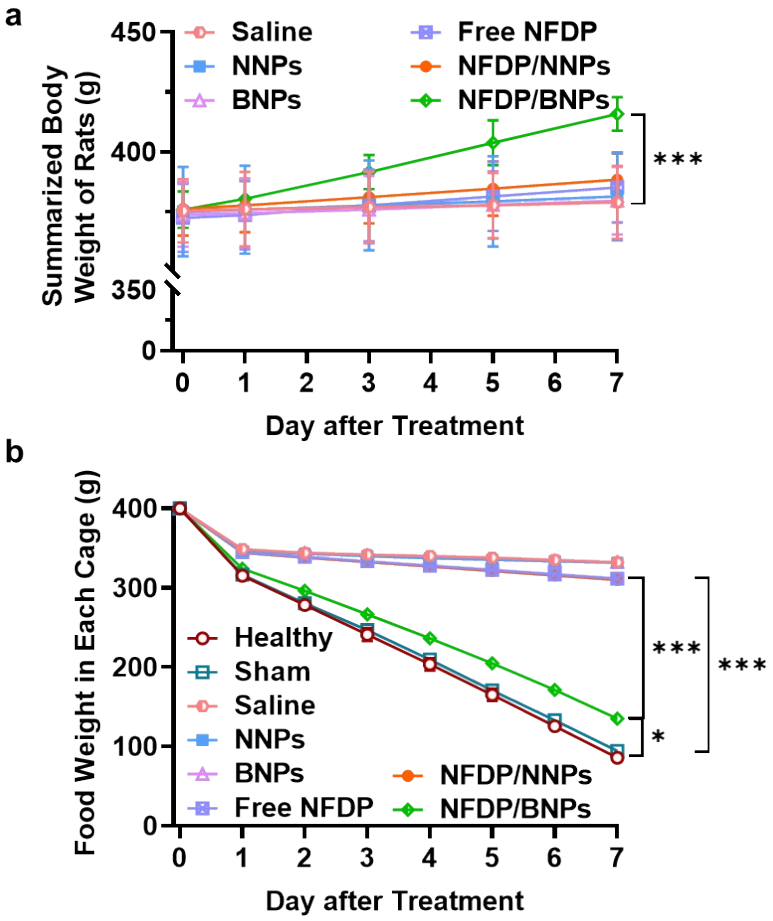


Figure S4. *Ex vivo* evaluation of NPs adhesion and diffusion on human esophagus tissues. a) A diagram of the esophageal tissues used and imaged in this study. b) NNPs and BNPs encapsulating PLA-Cy5 dye were added on the luminal surface of human esophageal tissues for 15 s. *Ex vivo* tissue images were taken with Xenogen after 30 s saline rinsing. c) NNPs and BNPs encapsulating PLA-Cy5 dye were added on the luminal surface of human esophageal tissues for 15 s following by 1 h incubation at 37 ℃. Frozen sections were collected and imaged with fluorescence microscope. Left column, transmission channel; middle column, Cy5 fluorescence channel, Cy5 signal in red; right column, merge images of left and middle columns. (L) indicated as lumen side of the esophagus tissues. Scale bars, 100 μm (applies to all images). d) The fluorescence of images from **d** was quantified and normalized to the average fluorescence of BNPs treated samples.



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58 **Figure S5. Body weight and food intake changes of different treatments in**
59 **pharmacodynamics study.** a) Summarized rat body weight results of different treatment groups
60 during the treatment. Statistical analysis was made between data from saline group and
61 NFDP/BNPs group at day 7 after treatment. Data are shown as mean ± s.d. (n = 5). b) Food weight
62 changes in each cage (group) during the treatment. Statistical analysis was made between data
63 from untreated group and NFDP/BNPs group, from untreated group and NFDP/NNPs group and
64 from NFDP/BNPs group and NFDP/NNPs group, respectively, at day 7 after treatment. Data are
65 shown as mean ± s.d. (n = 5). Asterisks indicate: $p < 0.05$ (*) and $p < 0.001$ (***).

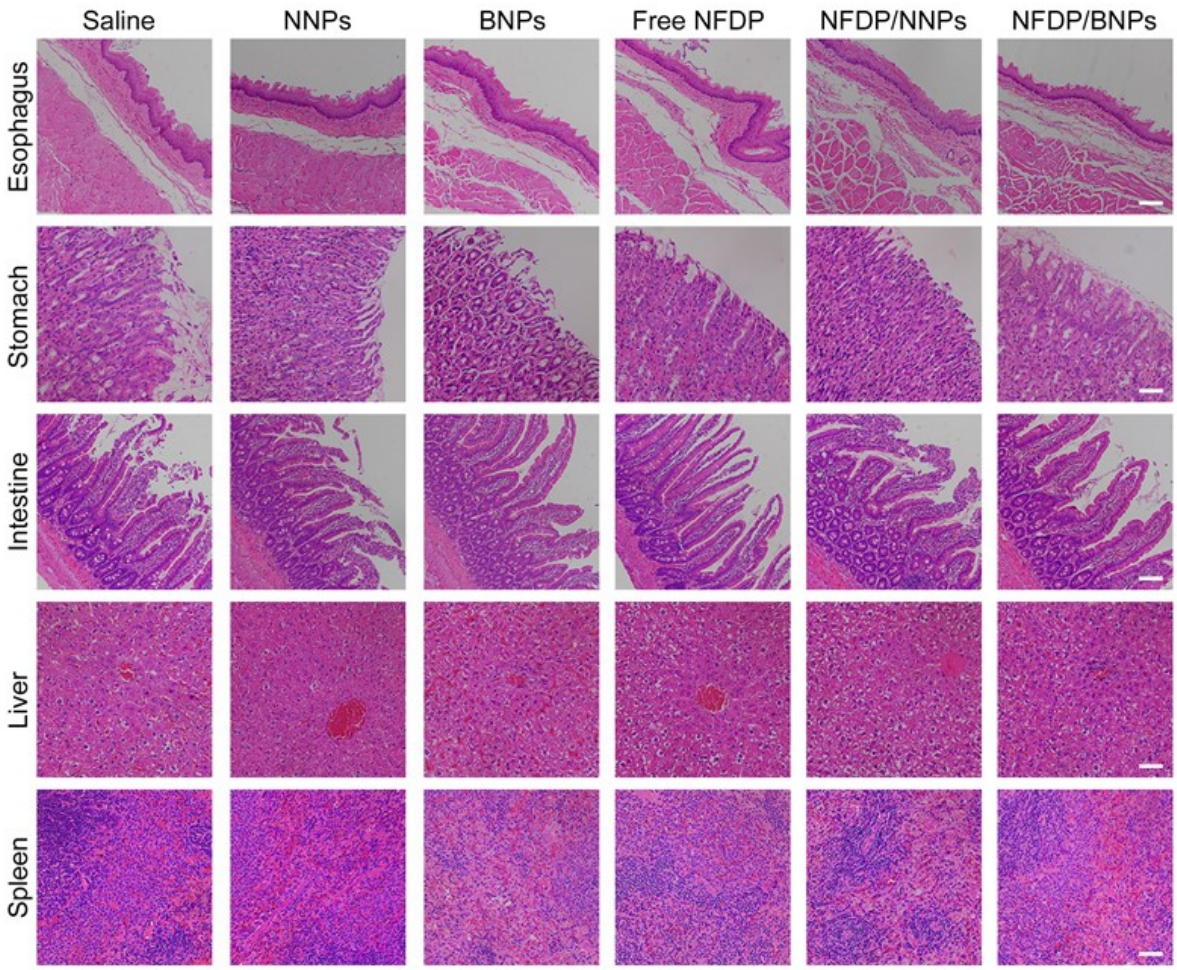

Figure S6. *In vivo* local and systemic toxicity evaluations of different treatments. H&E staining results of sections from tissues treated with saline as control, blank NNPs, blank BNPs, free NFDP, NFDP/NNPs and NFDP/BNPs. Images for esophagus and intestine were taken with the objective lens at 20x, scale bars: 200 μm; Images for stomach, liver and spleen were taken at 40x, scale bars: 100 μm. These images are representative of multiple sections from $n = 5$ for each group.