# Electronic Supporting Information

Constructing Passive Targeting and Long Retention Therapeutic Nanoplatform Based on Water-Soluble, Non-Toxicity and Highly Stable Core-Shell Poly(Amino Acid) Nanocomplexes Xin Wang,<sup>a,‡</sup> Bingqing Deng,<sup>b,‡</sup> Meng Yu,<sup>b</sup> Tao Zeng,<sup>a</sup> Yuyu Chen,<sup>b</sup> Jianqiang Hu<sup>b,\*</sup>, Qianqing Wu<sup>b</sup> and Aiqing Li<sup>a,\*</sup>

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Figure S1. Structure and labeling equation of the Cy7 dye.

Figure S2



Figure S2. Gel permeation chromatograph of PEG-PY.





Figure S3. <sup>1</sup>H NMR characterizations of PEG-PY, Gef and Gef-PY NCs.



**Figure S4.** Critical micelle concentration (CMC) of PYNPs measured by fluorescence techniques and using pyrene as the probe.



**Figure S5.** Digital photos of Gef-PY NCs solutions prepared by different feeding mass ratios of PEG-PY to Gef without further removement of unloaded drug.





Figure S6. Stability of Gef-PY NCs versus 50x dilution of water and lyophilization.

Figure S7



**Figure S7.** H&E stained section of major organs (heart, liver, spleen, lung and contralateral kidney) extracted from mice (200× magnification).





**Figure S8.** Weight ratio of (a) thymus and (b) spleen after 7 days injection of Saline, PYNPs and Gef-PY NCs (n=5).



**Figure S9.** Physiological manifestation (tail swelling and faeces forming condition) of mice after administration of (a, c) free Gef·HCl or (b, d) Gef-PY NCs.



Figure S10. Zeta potentials of PYNPs and Gef-PY NCs in different pH.



**Figure S11.** (a) Ex vivo fluorescence images and (b) fluorescence intensities of major organs collected from free Cy7 treated mice after intravenous injection for 1, 6, 12 and 24 h, 1-9: heart, liver, spleen, lung, kidney, thymus, intestine, muscle and brain.

Figure S12



**Figure S12.** (a) Ex vivo fluorescence images of major organs collected from Cy7-Gef-PY NCs treated mice after intravenous injection for 5, 7 and 14 days. (b) Fluorescence intensity of Cy7-Gef-PY NCs cumulated in major organs.





**Figure S13.** Increasing tendency of body weight after 7-day injection of saline, PYNPs, free Gef·HCl and Gef-PY NCs. Data were expressed as mean  $\pm$  SD, n=5.