

## Supporting Information

### **Intracellular Delivery and Biodistribution Study of CRISPR/Cas9 Ribonucleoprotein Loaded Bioreducible Lipidoid Nanoparticles**

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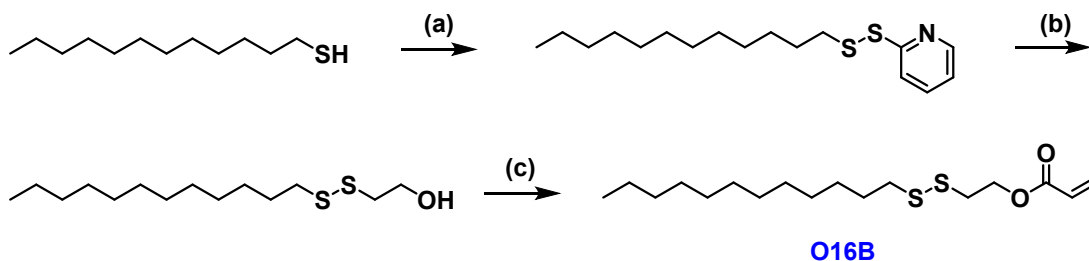
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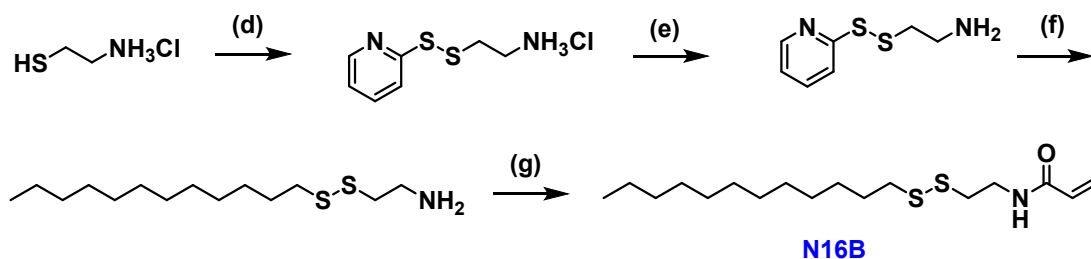
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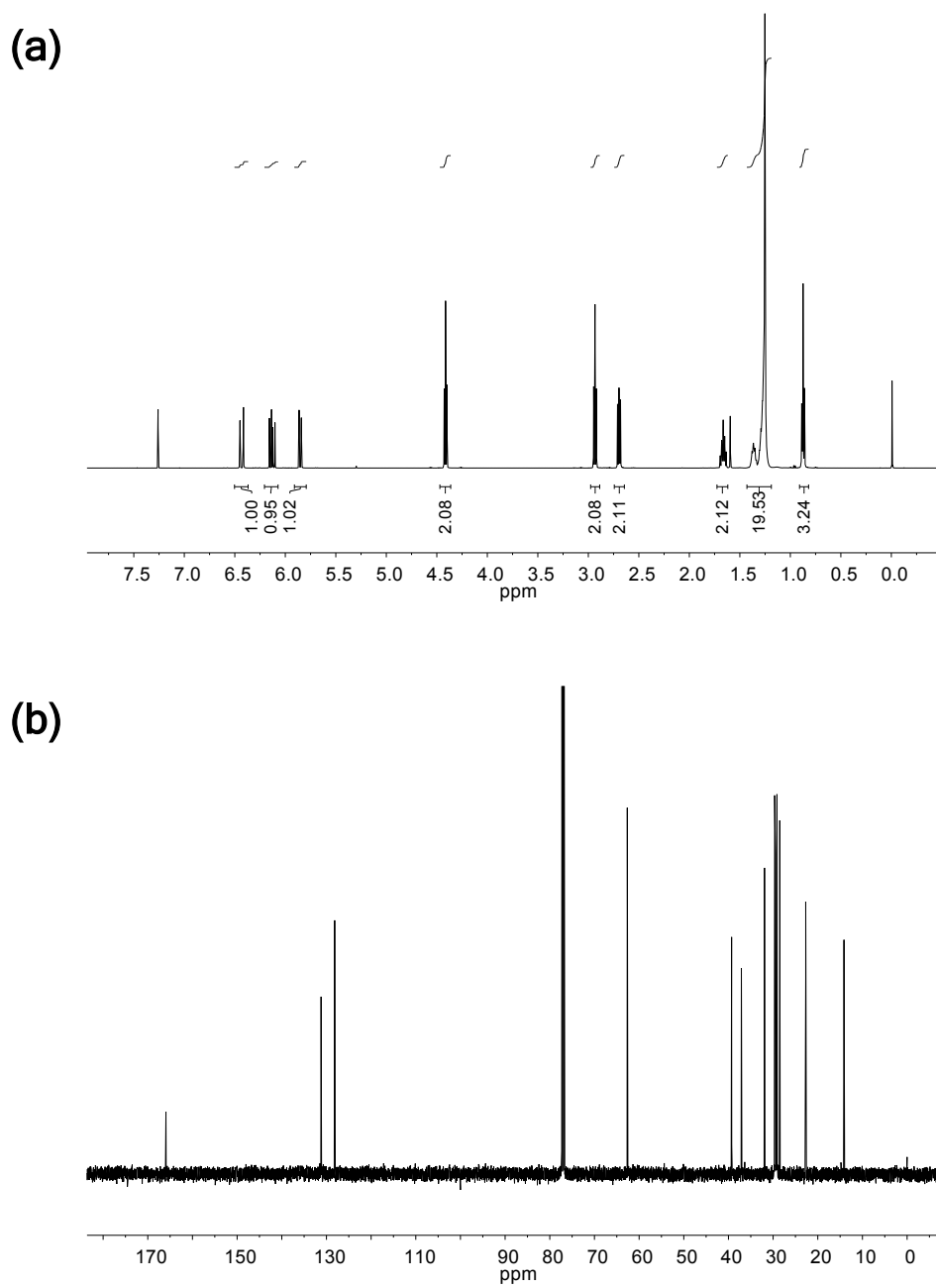
**i) Synthesis of O16B**



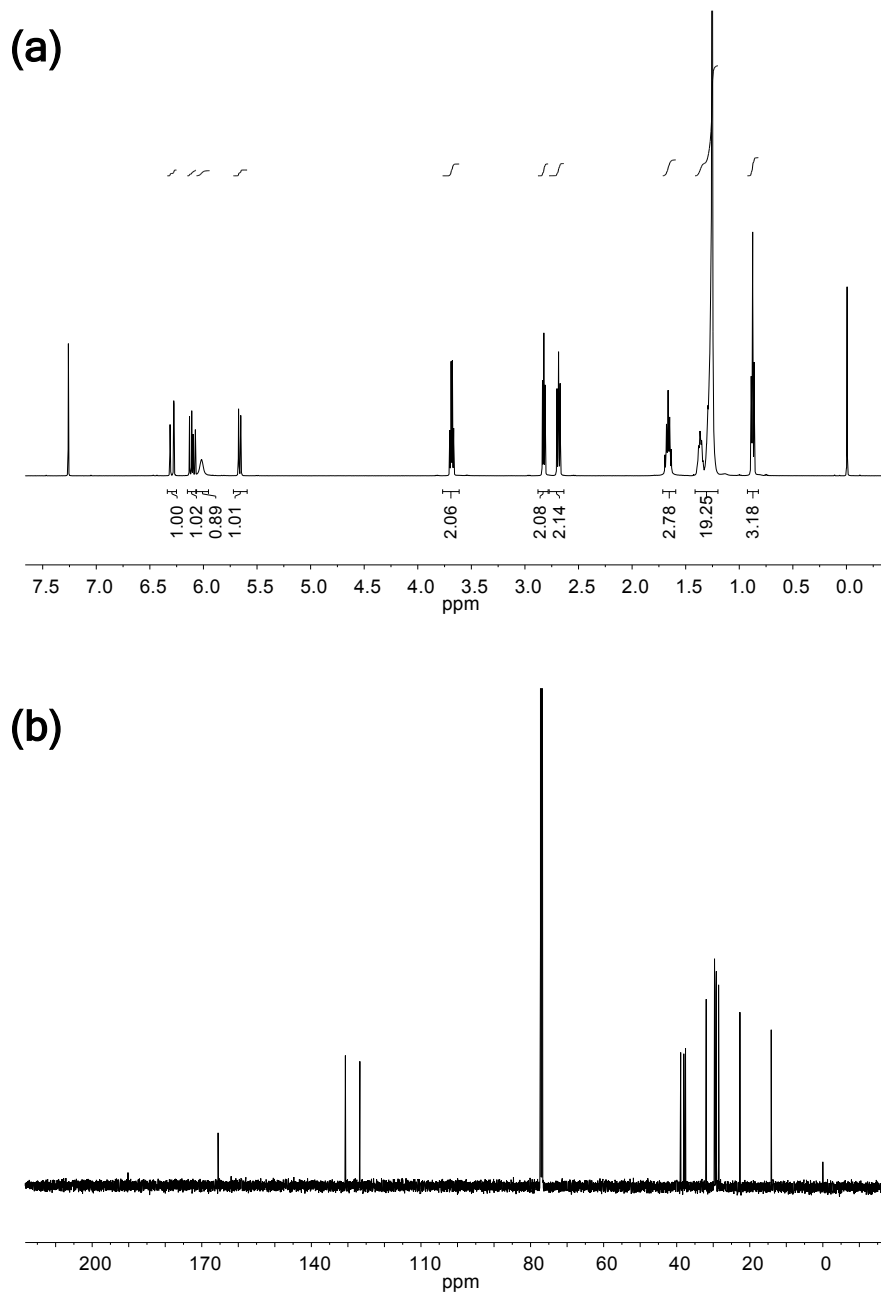
**ii) Synthesis of N16B**



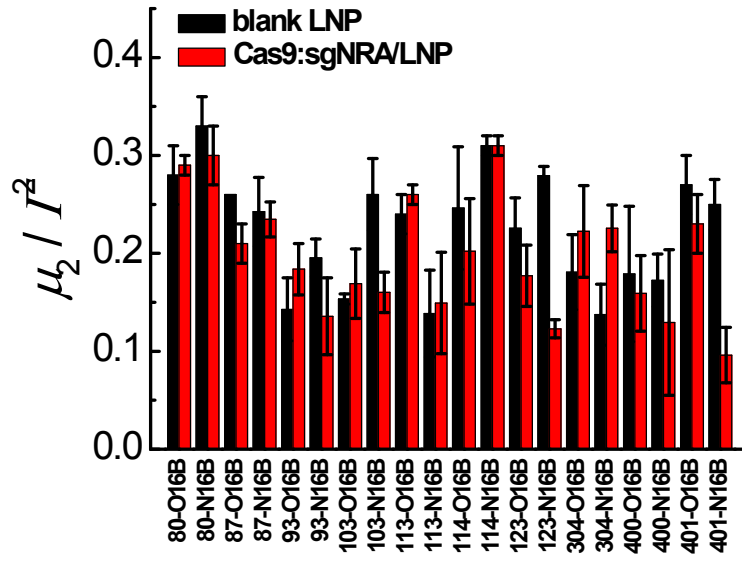
**Fig. S1** Synthetic routes employed for synthesis of O16B and N16B tails. (a) 2,2'-dithiopyridine, acetic acid, dichloromethane, 25 °C, 48 h. (b) 2-mercaptoethanol, acetic acid, dichloromethane, 25 °C, 26 h. (c) acryloyl chloride, triethylamine, dichloromethane, 0 °C, 24 h. (d) 2,2'-dithiopyridine, acetic acid, methanol, 25 °C, 48 h. (e) sodium hydroxide, water. (f) 1-dodecanethiol, acetic acid, dichloromethane, 25 °C, 26 h. (g) acryloyl chloride, triethylamine, dichloromethane, 0 °C, 24 h.



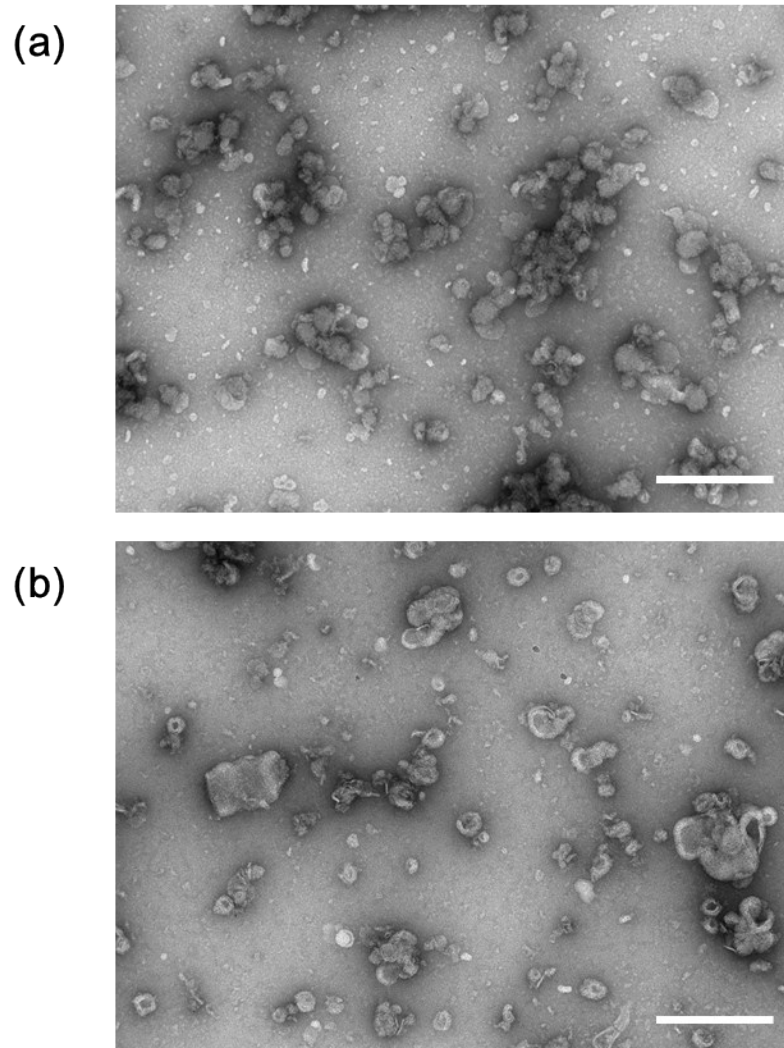
**Fig. S2** (a) $^1\text{H}$  and (b)  $^{13}\text{C}$  NMR spectra of O16B recorded in  $\text{CDCl}_3$ .



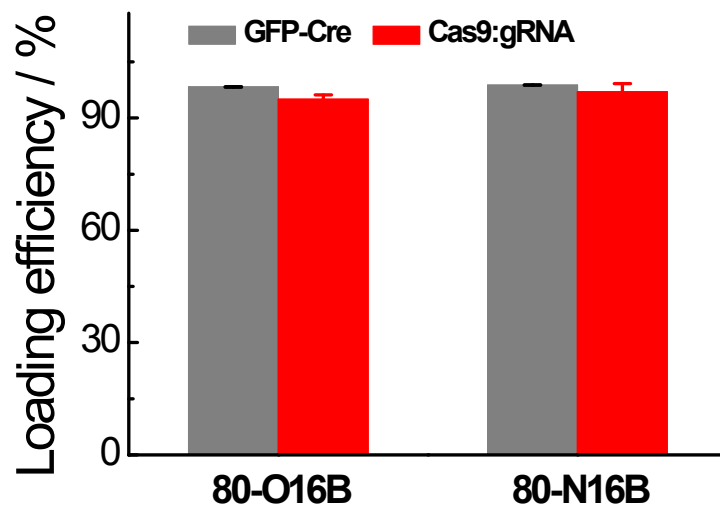
**Fig. S3** (a)  $^1\text{H}$  and (b)  $^{13}\text{C}$  NMR spectra of N16B recorded in  $\text{CDCl}_3$ .



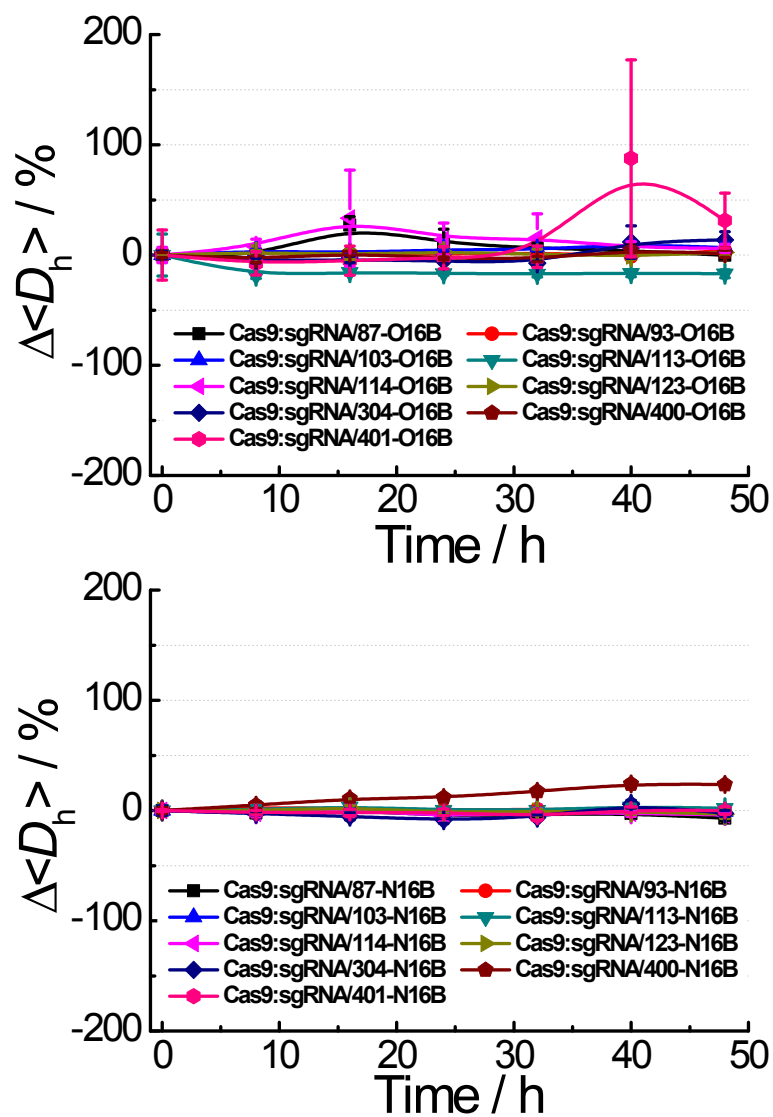
**Fig. S4** Polydispersity indexes of blank and Cas9:sgRNA loaded LNPs.



**Fig. S5** TEM images of (a) Cas9:sgRNA/80-O16B and (b) Cas9:sgRNA/80-N16B. Scale bar = 400 nm.

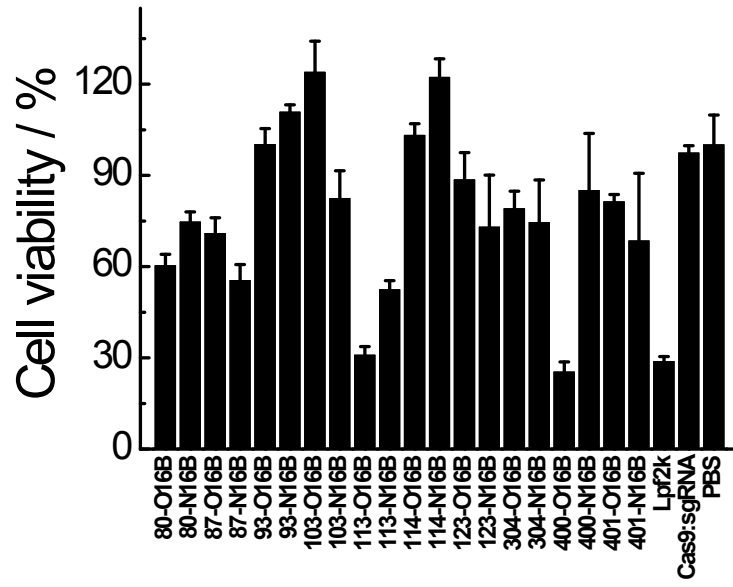


**Fig. S6** Protein loading efficiencies of 80-O16B and 80-N16B LNPs.

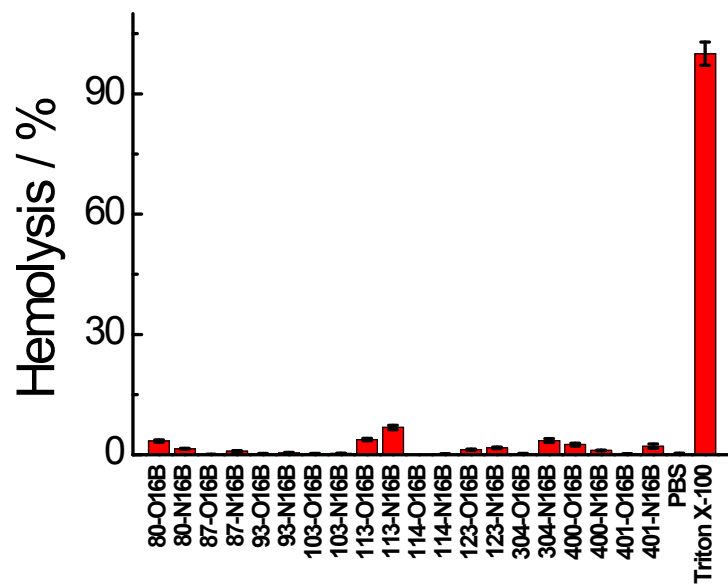


**Fig. S7** Relative size variations of Cas9:sgRNA loaded LNPs.

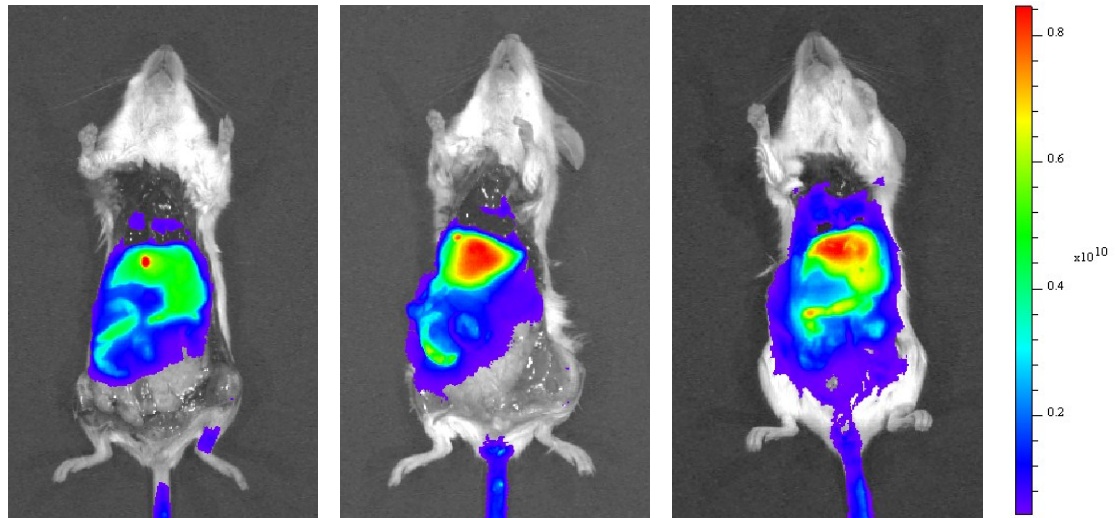




**Fig. S8** Cytotoxicity test of Cas9:sgRNA loaded LNPs against GFP-HEK cells.



**Fig. S9** Hemolysis test of LNPs using human red blood cells.



**Fig. S10** Fluorescence images of sacrificed Balb/c mice after 240 min of i.v. injection of Cas9:sgRNA/103-N16B nanoparticles.