

Supplementary Materials: Enzyme-Responsive Amphiphilic Peptide Nanoparticles for Biocompatible and Efficient Drug Delivery

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Table S1. Physical characterization of the RH-(GLFG)₃ nanoparticles. Values are reported as mean $\pm$ SEM (n=3).

Peptide	Hydrodynamic diameter (nm)	Polydispersity index (PDI)	ζ -Potential
RH-(GFLG) ₁	N/A	N/A	-
RH-(GFLG) ₂	N/A	N/A	-
RH-(GFLG) ₃	118.4 $\pm$ 7.7	0.245 $\pm$ 0.010	30.1 $\pm$ 0.4

Table S2. Physical characterization of the ¹RH-¹(GLFG)₃ (LL), ¹RH-^D(GLFG)₃ (LD), ^DRH-¹(GLFG)₃ (DL), and ^DRH-^D(GLFG)₃ (DD). Values are reported as mean $\pm$ SEM (n=3).

Peptide	Hydrodynamic diameter (nm)	Polydispersity index (PDI)	ζ -Potential
¹ RH- ¹ (GLFG) ₃ (LL)	118.4 $\pm$ 7.7	0.245 $\pm$ 0.010	30.1 $\pm$ 0.4
¹ RH- ^D (GLFG) ₃ (LD)	80.4 $\pm$ 1.5	0.531 $\pm$ 0.127	40.2 $\pm$ 0.8
^D RH- ¹ (GLFG) ₃ (DL)	112.7 $\pm$ 7.9	0.325 $\pm$ 0.010	33.0 $\pm$ 1.5
^D RH- ^D (GLFG) ₃ (DD)	162.0 $\pm$ 7.9	0.303 $\pm$ 0.033	29.7 $\pm$ 1.3

Table S3. Physical characterization of the ¹RH-¹(GLFG)₃ (LL), ¹RH-^D(GLFG)₃ (LD), ^DRH-¹(GLFG)₃ (DL), and ^DRH-^D(GLFG)₃ (DD). nanoparticles with respect to the concentration of doxorubicin. Values are reported as mean $\pm$ SEM (n=3).

Formulation condition (molar ratio)	Hydrodynamic size (nm)	ζ -Potential (mV)	Loading efficiency (%)	Encapsulation efficiency (%)
LL/Dox (1:0.1)	470.2 $\pm$ 102.0	31.5 $\pm$ 5.6	0.82 $\pm$ 0.02	8.22 $\pm$ 0.26
LL/Dox (1:0.5)	335.0 $\pm$ 133.4	30.7 $\pm$ 2.9	2.90 $\pm$ 0.07	5.79 $\pm$ 0.15
LL/Dox (1:1)	189.6 $\pm$ 6.6	35.9 $\pm$ 1.6	5.79 $\pm$ 0.15	5.79 $\pm$ 0.11
LL/Dox (1:2)	168.2 $\pm$ 2.3	36.5 $\pm$ 4.8	12.46 $\pm$ 0.011	6.23 $\pm$ 0.06
LL/Dox (1:3)	170.8 $\pm$ 3.6	35.4 $\pm$ 3.2	12.90 $\pm$ 0.41	4.03 $\pm$ 0.14
LD/Dox (1:2)	185.6 $\pm$ 2.4	33.7 $\pm$ 2.1	11.78 $\pm$ 0.63	5.33 $\pm$ 0.09
DL/Dox (1:2)	179.3 $\pm$ 3.9	34.7 $\pm$ 3.1	12.16 $\pm$ 0.55	5.96 $\pm$ 0.20
DD/Dox (1:2)	180.6 $\pm$ 6.3	32.7 $\pm$ 3.7	9.61 $\pm$ 0.15	4.70 $\pm$ 0.07

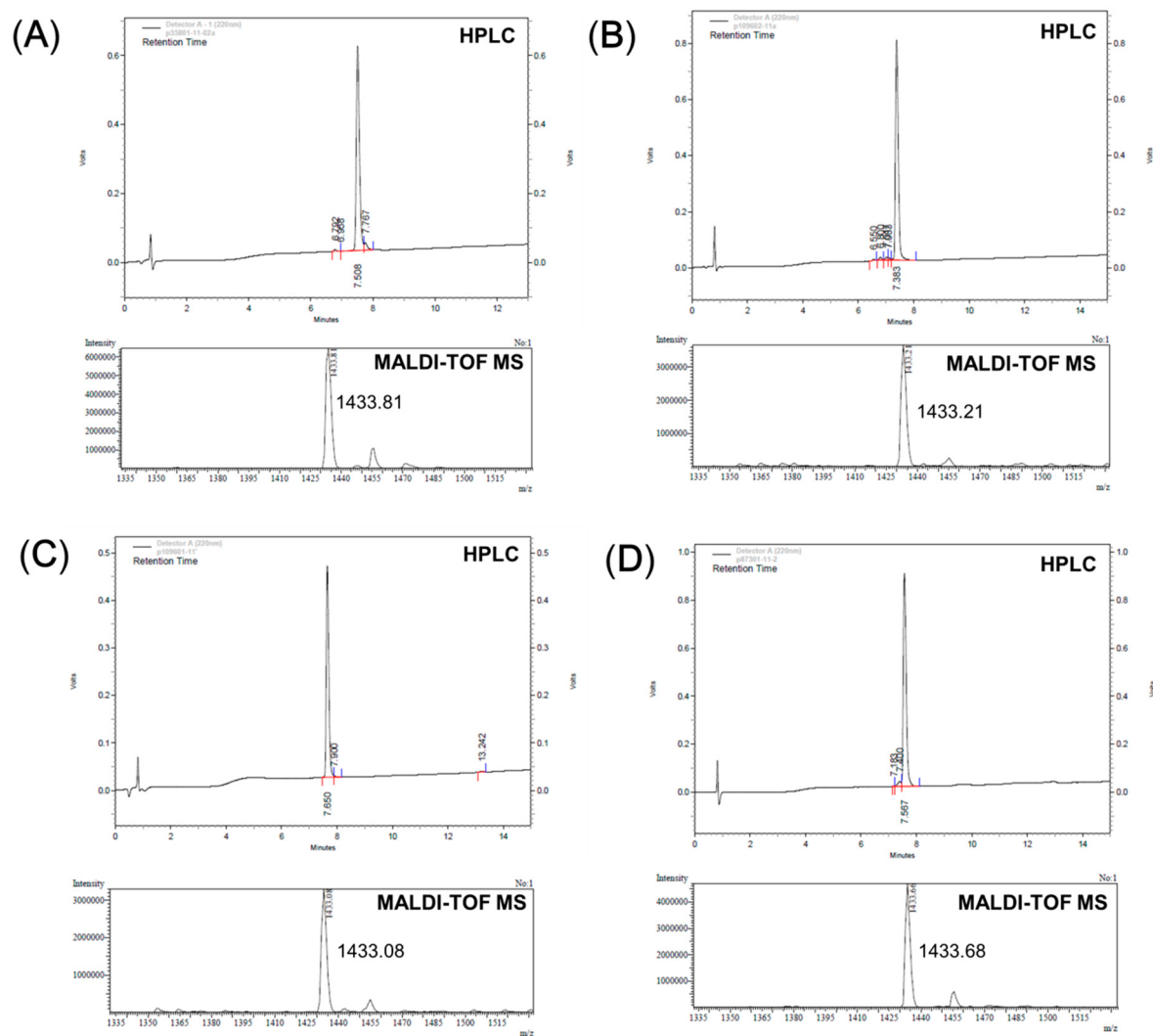


Figure S1. Results of high performance liquid chromatograph and mass spectrum of matrix assisted laser mass spectroscopy of (A) $^1\text{RH-}^1(\text{GLFG})_3$ (LL), (B) $^1\text{RH-}^D(\text{GLFG})_3$ (LD), (C) $^D\text{RH-}^1(\text{GLFG})_3$ (DL), and (D) $^D\text{RH-}^D(\text{GLFG})_3$ (DD) peptide monomers.

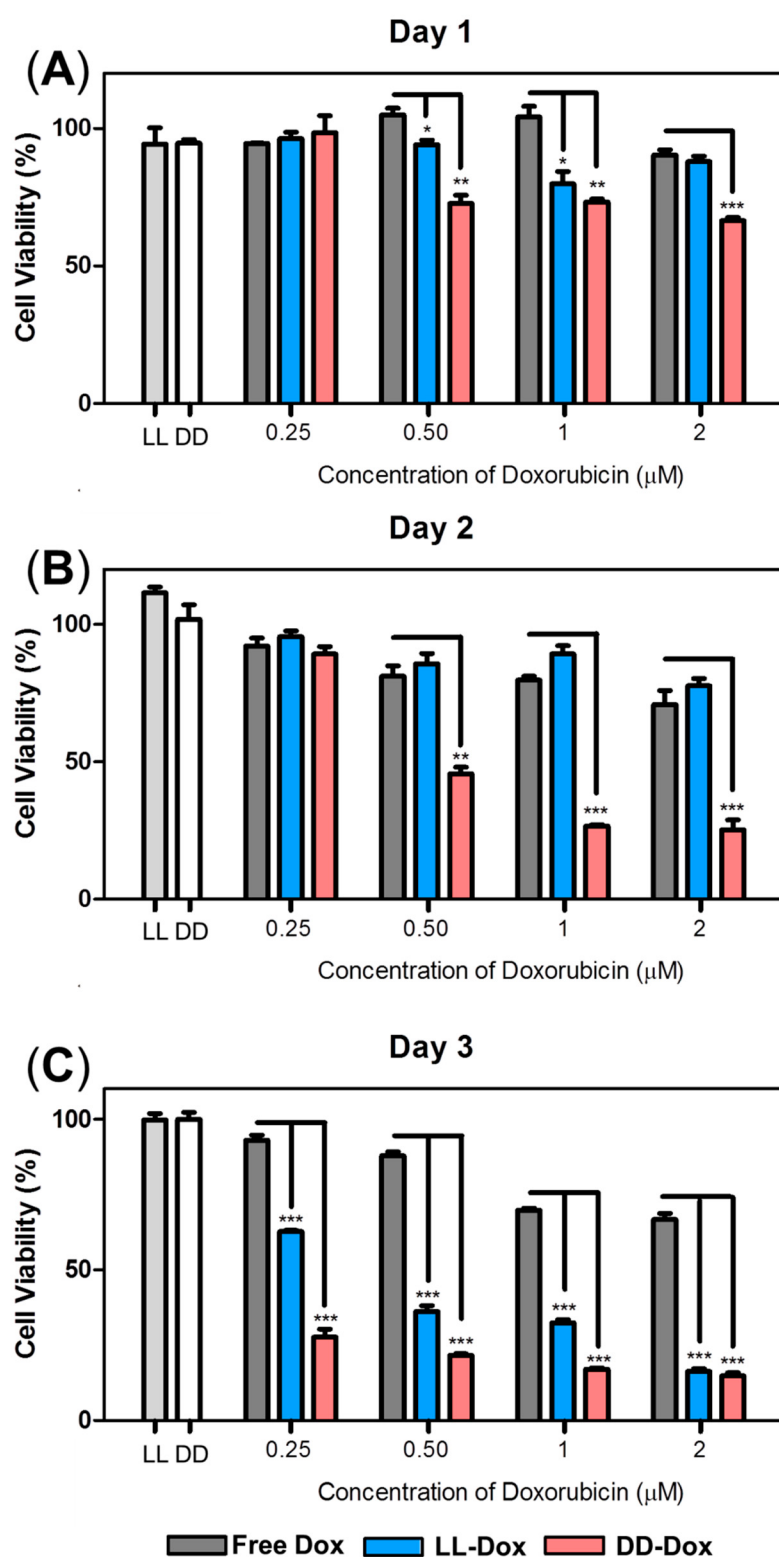


Figure S2. Anti-cancer activity of RH-(GLFG)₃ in HeLa cells. Viability of (A) 24-h incubation, (B) 48h-incubation, and (C) 72h-incubation. Values are reported as mean ± SEM (n=3). Statistical analysis by one-way Anova, **p* < 0.05, ***p* < 0.01, and ****p* < 0.001 versus free-Dox.