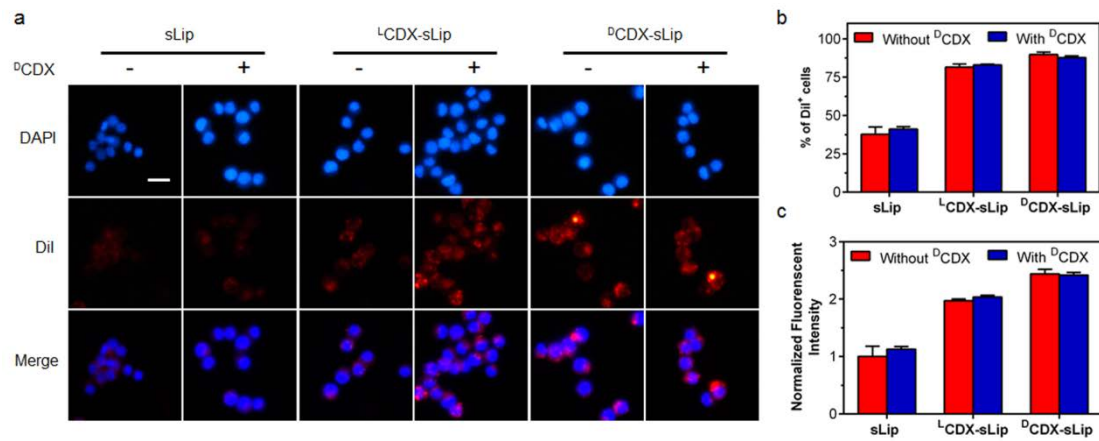


**Supplementary Information**

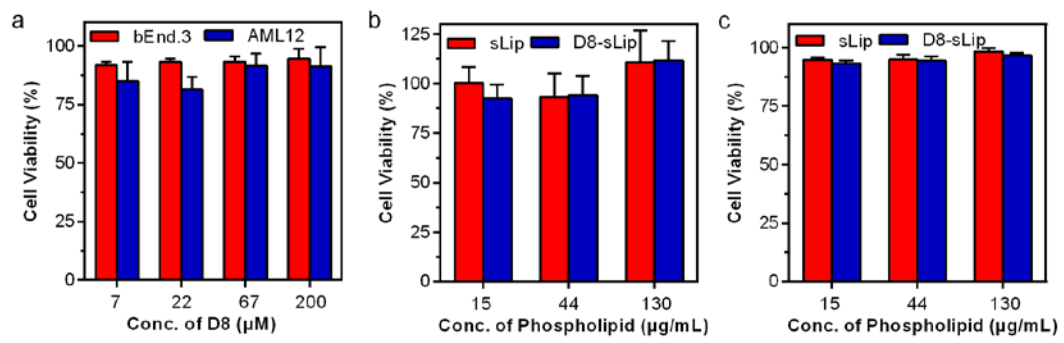
**Enhanced Immunocompatibility of Ligand-targeted Liposomes by Attenuating Natural  
IgM Absorption**

Guan and Shen et al

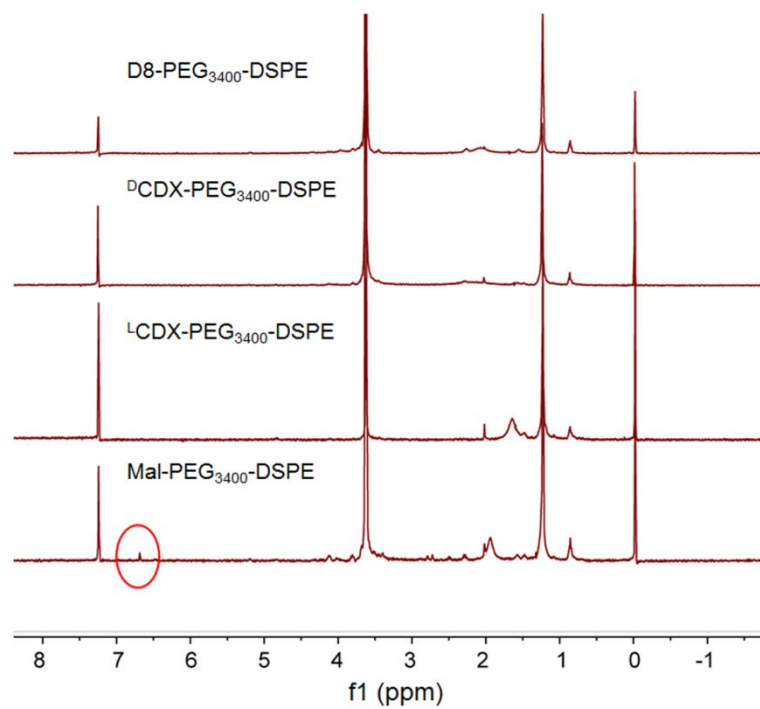
## Supplementary Figures



Supplementary Figure 1. The uptake of sLip, <sup>1</sup>CDX-sLip and <sup>D</sup>CDX-sLip by RAW264.7 cells. (a) Microscopic observation and (b, c) quantitative analysis of phagocytosis of sLip, <sup>1</sup>CDX-sLip and <sup>D</sup>CDX-sLip with or without 2 h pre-incubation with 200  $\mu$ M free <sup>D</sup>CDX peptide. Scale bar = 20  $\mu$ m. n = 3, Data are means  $\pm$  s.d.



Supplementary Figure 2. Cytotoxicity of free D8 peptide and D8-sLip. (a) Cytotoxicity of free D8 peptide against bEnd.3 and AML12 cells. sLip and D8-sLip against (b) AML12 and (c) bEnd.3 cells after 48 h incubation at 37 °C. Data are means  $\pm$  s.d. (n = 3).



Supplementary Figure 3. <sup>1</sup>H-NMR spectra of mal-PEG<sub>3400</sub>-DSPE and peptide-PEG<sub>3400</sub>-DSPE. The characteristic peak of maleimide at 6.8 ppm was circled.

## Supplementary Tables

Supplementary Table 1. Area under the curve ( $AUC_{0-24}$ ) of liposomes (50 mg HSPC per kg of mouse) with or without pre-dose of blank liposomes (5 mg HSPC per kg of mouse, no DiI loading) in BALB/c mice. n=3, data are means  $\pm$  s.d.

	$AUC_{0-24}$ ( $\mu\text{g}\cdot\text{h mL}^{-1}$ )	
	Without pre-dose	With pre-dose
sLip	584.2 $\pm$ 6.8	350.3 $\pm$ 10.7
<sup>L</sup> CDX-sLip	164.8 $\pm$ 10.1	8.7 $\pm$ 4.7
<sup>D</sup> CDX-sLip	18.3 $\pm$ 2.4	7.3 $\pm$ 0.6
D8-sLip	286.8 $\pm$ 21.5	112.7 $\pm$ 13.9

Supplementary Table 2. Characterization of sLip, <sup>L</sup>CDX-sLip and <sup>D</sup>CDX-sLip with or without pre-incubation with serum at 37°C for 1 h, n = 3, data are means ± s.d.

	Without serum			With serum		
	Size (nm)	PDI	Zeta (mV)	Size (nm)	PDI	Zeta (mV)
sLip	138.9±0.72	0.059±0.02	-48.33±1.97	120.8±0.98	0.286±0.01	-19.23±1.57
<sup>L</sup> CDX-sLip	138.8±0.14	0.086±0.02	-30.87±0.95	123.4±2.82	0.246±0.02	-14.63±1.28
<sup>D</sup> CDX-sLip	136.4±2.48	0.057±0.01	-31.45±0.46	118.8±1.56	0.301±0.02	-15.46±2.02

Supplementary Table 3. Peptide sequences.

Peptide	Sequence	Length (AA)
<sup>L</sup> CDX	FKESWREARGTRIERG	16
<sup>D</sup> CDX	G <sup>D</sup> R <sup>D</sup> E <sup>D</sup> I <sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> E <sup>D</sup> R <sup>D</sup> W <sup>D</sup> S <sup>D</sup> E <sup>D</sup> K <sup>D</sup> F	16
<sup>D</sup> CDX-1	G <sup>D</sup> R <sup>D</sup> A <sup>D</sup> I <sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> E <sup>D</sup> R <sup>D</sup> W <sup>D</sup> S <sup>D</sup> A <sup>D</sup> K <sup>D</sup> F	16
<sup>D</sup> CDX-2	G <sup>D</sup> A <sup>D</sup> E <sup>D</sup> I <sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> E <sup>D</sup> R <sup>D</sup> W <sup>D</sup> S <sup>D</sup> E <sup>D</sup> A <sup>D</sup> F	16
<sup>D</sup> CDX-S8	<sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> E <sup>D</sup> R <sup>D</sup> W	8
ANG	TFYGGSRGKRNNFKTEEY	19
D8	<sup>D</sup> RTG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> RE <sup>D</sup> W	8

Supplementary Table 4. Characterization of different liposomes shown in the table with or without pre-incubation of serum at 37°C for 1 h. Size and zeta potential were all measured by Malvern laser particle size analyzer. n = 3, data are means  $\pm$  s.d.

Liposomes	Without serum			With serum		
	Size (nm)	PDI	Zeta-potential (mV)	Size (nm)	PDI	Zeta-potential (mV)
D8-sLip	135.7 $\pm$ 1.79	0.017 $\pm$ 0.02	-38.5 $\pm$ 1.73	128.6 $\pm$ 1.28	0.302 $\pm$ 0.01	-17.2 $\pm$ 1.02
DOTAP-sLip	157.8 $\pm$ 0.57	0.104 $\pm$ 0.02	59.5 $\pm$ 0.95	122.5 $\pm$ 0.56	0.247 $\pm$ 0.02	-16.9 $\pm$ 0.86
<sup>D</sup> CDX-1-sLip	141.6 $\pm$ 0.46	0.116 $\pm$ 0.04	17.5 $\pm$ 2.96	125.8 $\pm$ 0.58	0.267 $\pm$ 0.01	-20.4 $\pm$ 1.31
<sup>D</sup> CDX-2-sLip	136.9 $\pm$ 1.34	0.163 $\pm$ 0.02	-38.9 $\pm$ 0.89	99.74 $\pm$ 0.86	0.222 $\pm$ 0.03	-19.4 $\pm$ 0.97
Angiopep-2-sLip	128.1 $\pm$ 1.90	0.091 $\pm$ 0.02	-32.6 $\pm$ 1.69	246.9 $\pm$ 1.97	0.683 $\pm$ 0.02	-17.1 $\pm$ 0.58
<sup>D</sup> CDX-S8-sLip	136.5 $\pm$ 2.19	0.064 $\pm$ 0.01	-37.9 $\pm$ 0.20	124.6 $\pm$ 1.86	0.158 $\pm$ 0.03	-16.1 $\pm$ 0.75



Supplementary Table 5. Predicted free energies of binding of the peptides with  $\alpha 7$  nAChR

Peptide sequence	Predicted $\Delta G$ [kcal mol <sup>-1</sup> ]
G <sup>D</sup> R <sup>D</sup> E <sup>D</sup> I <sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> E <sup>D</sup> R <sup>D</sup> W <sup>D</sup> S <sup>D</sup> E <sup>D</sup> K <sup>D</sup> F	-10.11
<sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> E <sup>D</sup> R <sup>D</sup> W	-10.47
<sup>D</sup> R <sup>D</sup> TG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> RE <sup>D</sup> W	-11.06
<sup>D</sup> RTG <sup>D</sup> R <sup>D</sup> A <sup>D</sup> RE <sup>D</sup> W	-11.48