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Supporting Information

The effect of ionizable lipids on the cellular uptake of lipid bilayer coated mesoporous silica nanoparticles in liver

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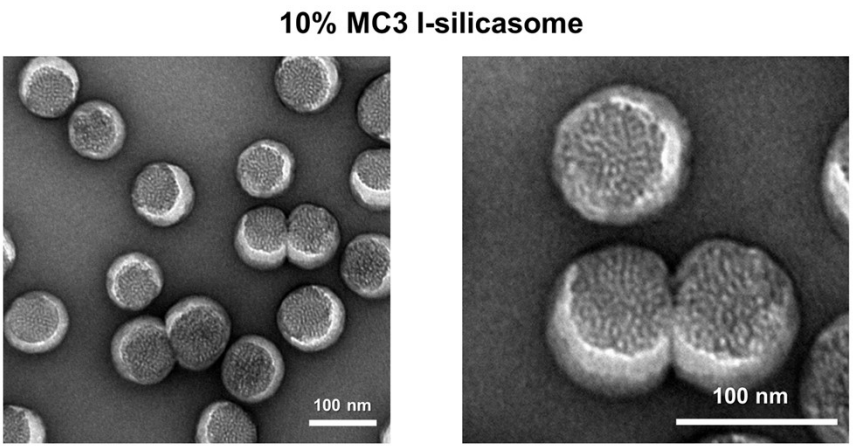
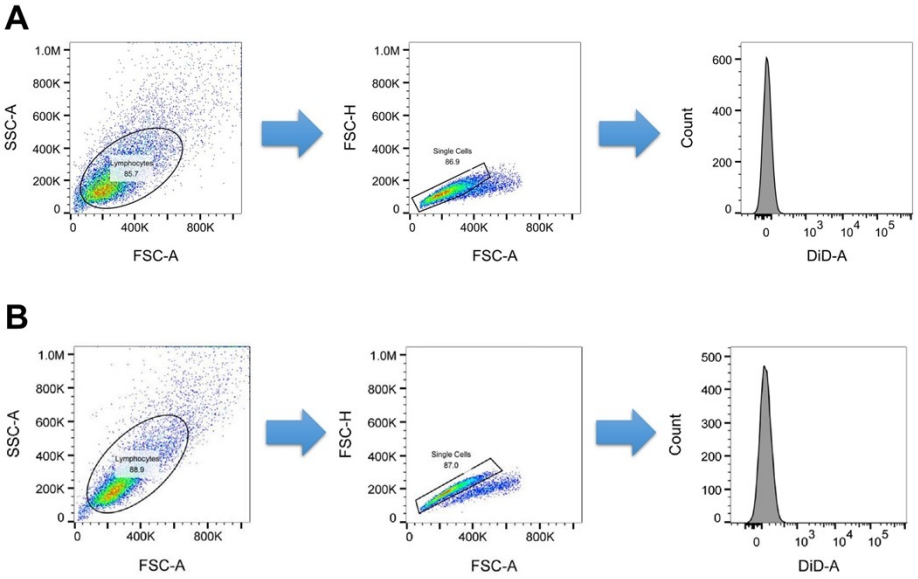
A

	Lipid Composition					PBS (Size)	
	MC3	SM-102	DSPC	Chol	DMG-PEG_{2000}	Size (nm)	PDI
a	5	/	55	37	3	118.8	0.078
b	10	/	50	37	3	129.9	0.102
C	15	/	45	37	3	158.4	0.114
d	/	10	50	37	3	171.7	0.094
e	/	15	45	37	3	180.1	0.140

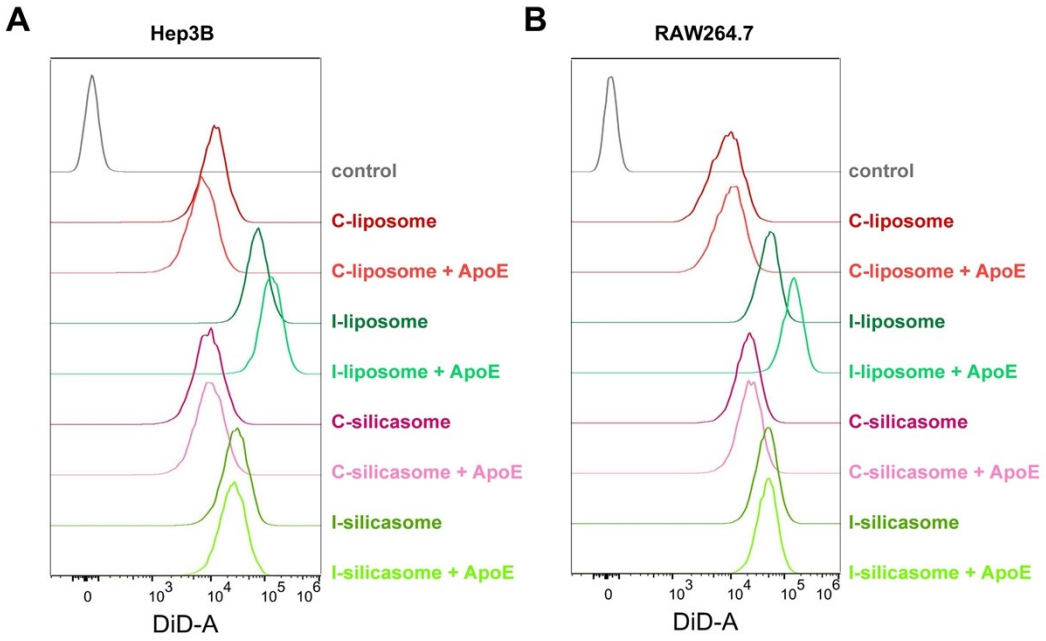
B



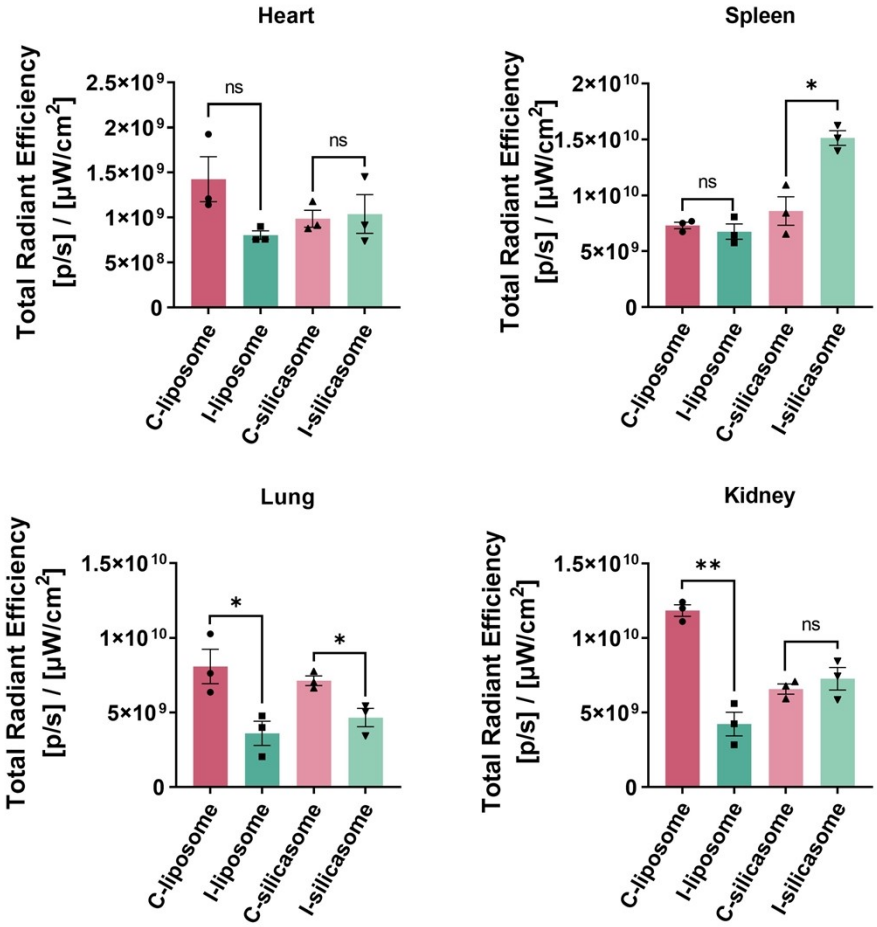
Supplementary Figure 1. Design and characterization of ionizable silicasomes. (A) I-silicaomes with different size were synthesized by optimizing the MSNP coated with lipid membranes. Data are presented as mean values, n = 3. (B) Representative TEM images of I-silicasomes containing 10% MC3 (negative staining). Scale bar: 100 nm.



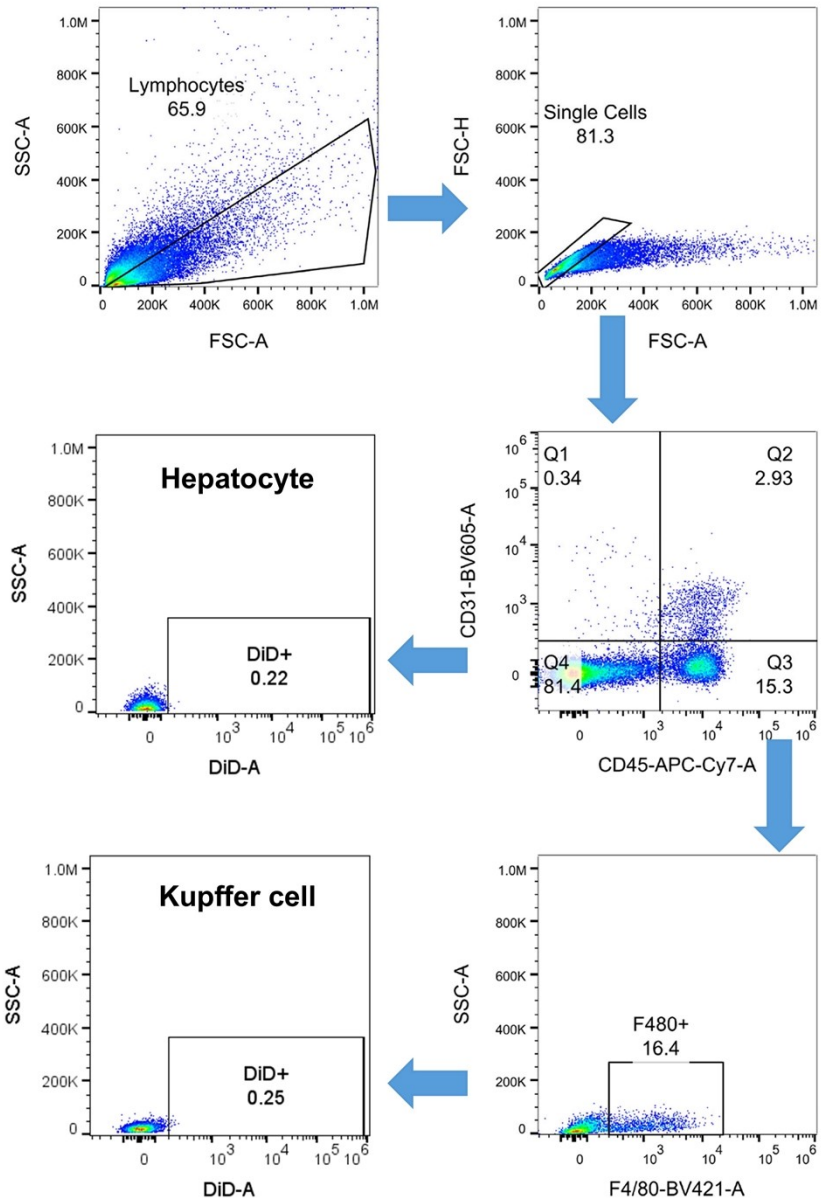
Supplementary Figure 2. Gating strategy of (A) DiD^+ Hep3B cells, (B) DiD^+ RAW264.7 cells. Experiment was performed in Thermo Fisher Attune NxT.



Supplementary Figure 3. ApoE impact cellular uptake of lipids coated nanoparticles. Cellular uptake of nanoparticles in (B) Hep3B cells and (D) RAW264.7 cells. Histogram plots of flow cytometry analysis showing nanoparticle internalization in (A) Hep3B hepatocytes and (B) RAW264.7 cells after treatment with or without ApoE-bound formulations.



Supplementary Figure 4. Quantitative analysis of DiD signal at the position of heart, spleen, lung and kidney in main Figure 5B. Data are presented as mean ± SEM, n = 3. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$ and ns, no significant difference.



Supplementary Figure 5. Gating scheme for flow cytometric analysis of DiD^+ cells from liver cells.