Supplementary Information

Table S1. The mean and standard error values of the surface fluorescence intensity of R18 in tissue and organs at different time points after single I.V. administration of the DSPE-pHLIP or Pyr-pHLIP (5 mol%), Span20 (43 mol%), cholesterol (50 mol%) and R18 (2 mol%) niosomes. The autofluorescence signal, which was in the range of 200-250 was subtracted.

	Time	DSPE-pHLIP n=3	Pyr-pHLIP n=3
Tumor	4 h	447 ± 84	498 ± 232
	24 h	1870 ± 153	2409 ± 334
	48 h	1401 ± 209	1562 ± 194
Muscle	4 h	76 ± 34	94 ± 44
	24 h	337 ± 40	297 ± 7
	48 h	410 ± 80	223 ± 35
Kidney	4 h	134 ± 34	207 ± 55
	24 h	370 ± 60	255 ± 22
	48 h	384 ± 54	225 ± 20
Liver	4 h	446 ± 133	417 ± 154
	24 h	1020 ± 225	893 ± 195
	48 h	1343 ± 388	482 ± 52

Table S2. The mean and standard error values of the surface fluorescence intensity of R18 in tissue and organs at 24 hours after single I.V. administration of different formulations of niosomes: DSPE-PEG, DSPE-pHLIP or Pyr-pHLIP (5 mol%), Span20 (43 mol%), cholesterol (50 mol%) and R18 (2 mol%) niosomes.

	DSPE-PEG n=4	DSPE-pHLIP n=3	Pyr-pHLIP n=3
Tumor	889 ± 191	1870 ± 153	2409 ± 334
Muscle	173 ± 38	337 ± 40	297 ± 7
Kidney	187 ± 43	370 ± 60	255 ± 22
Liver	343 ± 97	1020 ± 225	893 ± 195

Figures

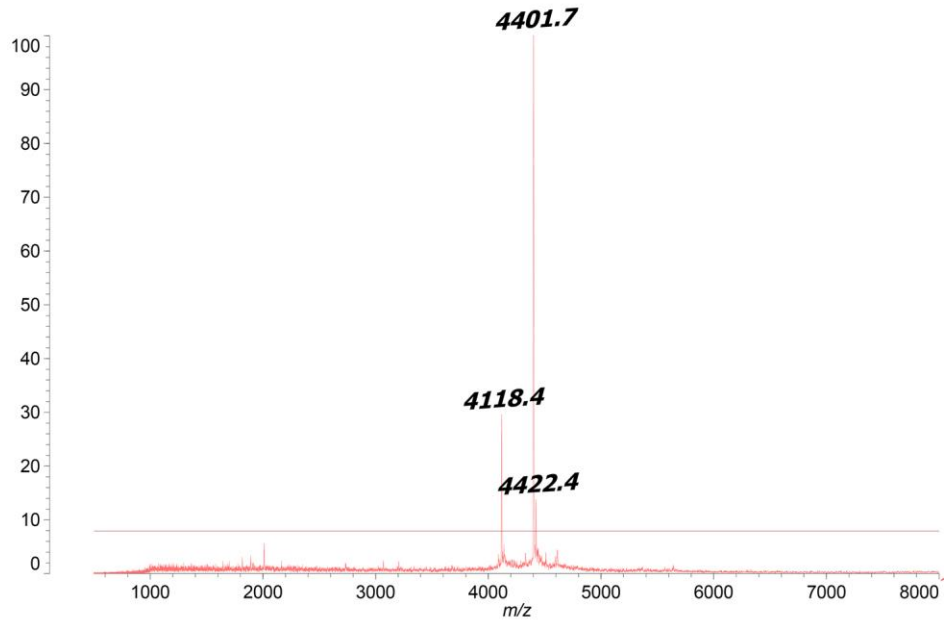

Figure S1. The SELDI-TOF mass spectrum of Pyr-pHLIP.

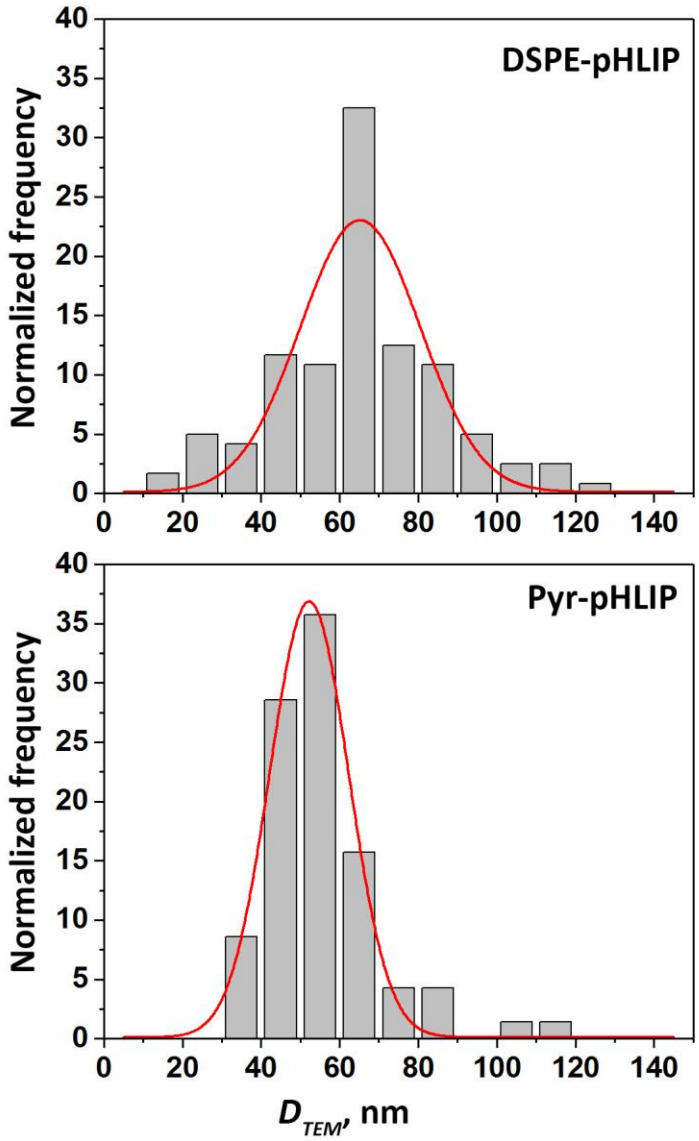

Figure S2. The size histograms of the DSPE-pHLIP and Pyr-pHLIP containing niosomes obtained after analyzing multiple cryo-TEM images. The red lines demonstrate fittings by Gauss functions.

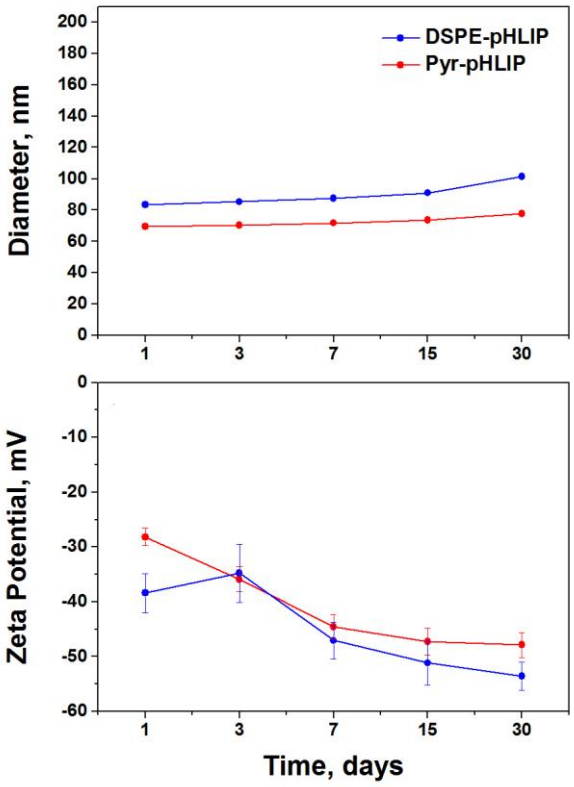

Figure S3. The results of stability study of DSPE-pHLIP and Pyr-pHLIP (5 mol%), Span20 (43 mol%), cholesterol (50 mol%) and R18 (2 mol%) niosomes in HEPES buffer in a course of 30 days (niosomes were kept refrigerated at 4°C). The changes of mean hydrodynamic diameter and Zeta potential are presented.

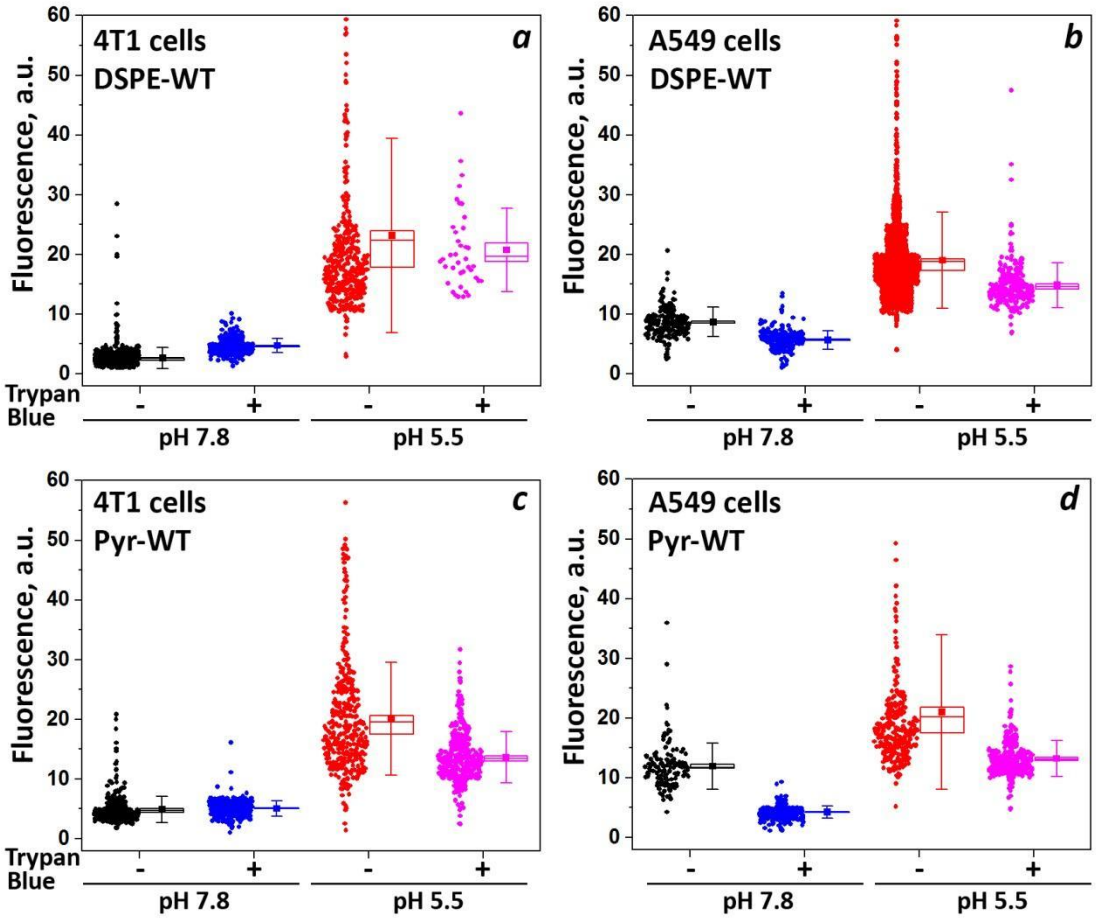

Figure S4. Fluorescent uptake of DSPE-pHLIP or Pyr-pHLIP (5 mol%), Span20 (43 mol%) and cholesterol (50 mol%) niosomes containing 2 mol% of fluorescent R18 by 4T1 mammary and A549 lung cancer cells at pH 7.8 and pH 5.5 before and after treatment with Trypan blue. The cellular uptake of fluorescent niosomes was assessed by counting of fluorescent cells using cellometer at 525 nm excitation and 595 nm emission channels.

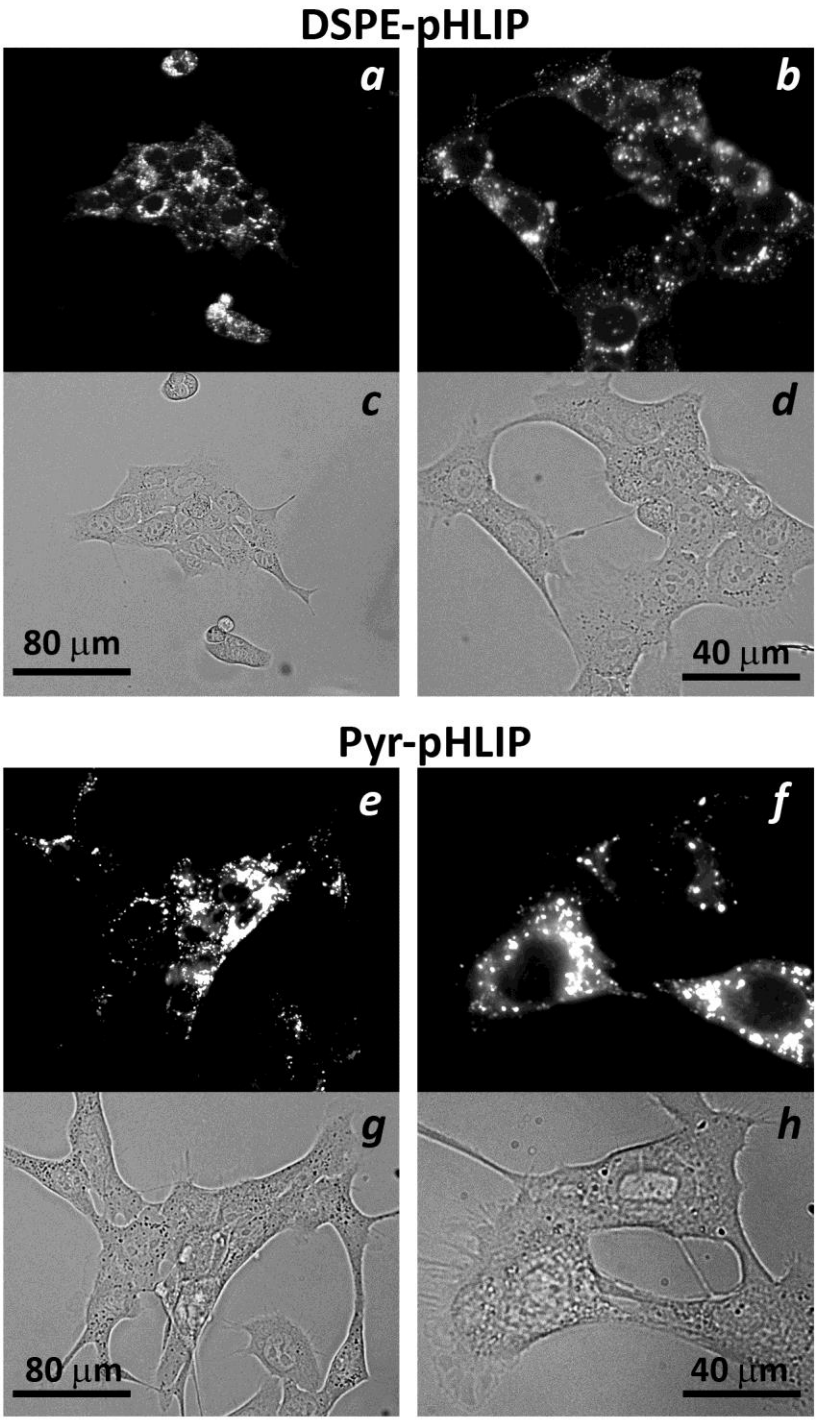

Figure S5. Uptake and cellular distribution of ***a-d***) DSPE-pHLIP (5 mol%) and ***e-h***) Pyr-pHLIP (5 mol%) coated Span20 (43 mol%) and cholesterol (50 mol%) niosomes containing 2 mol% of fluorescent R18 by 4T1 lung cancer cells. Cells were treated with fluorescence niosomes at pH 6.4 for 1 hour, followed by washing, seeding cells in glass bottom collagen coated cell dishes and imaging at next day. Fluorescence (***a, b, e, f***) and phase contrast (***c, d, g, h***) images were obtained using 20x (***a, c, e, g***) and 40x (***b, d, f, h***) magnification objective lenses