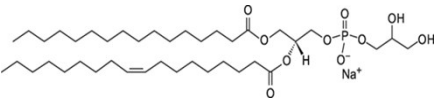
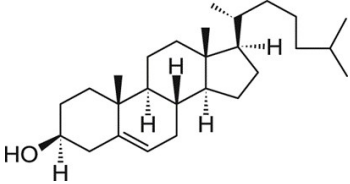
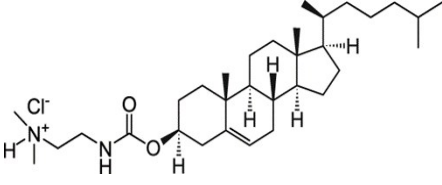


SUPPLEMENTARY INFORMATION

Supplementary Table 1. Summary of abbreviations, full names and structures of lipids used in nanoparticle formulations.

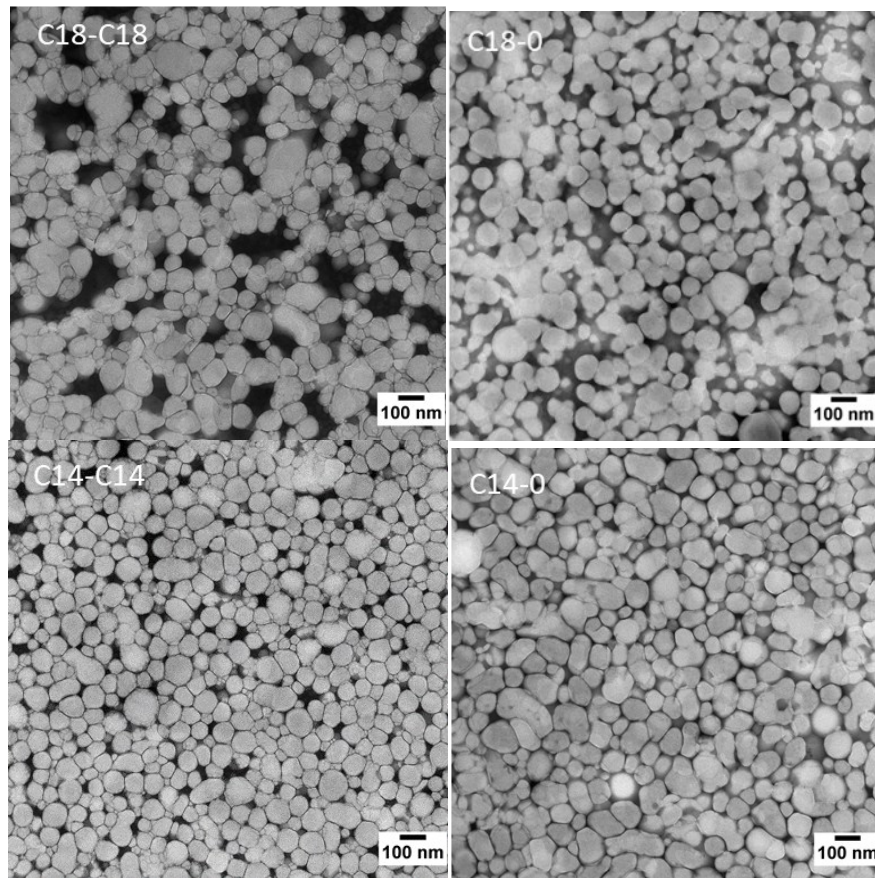
Abbreviation	Full name	Net Charge at pH 7.4	Structure
DL-048	1-((9Z,28Z)-heptatriaconta-9,28-dien-19-yl)-4-methylpiperazine	Neutral	
DC-036	2-(dimethylamino)-N-((6Z,9Z,28Z,31Z)-heptatriaconta-6,9,28,31-tetraen-19-yl) acetamide	Neutral	
Dlin-MC3-DMA (MC3)	6Z,9Z,28Z,31Z)-heptatriaconta-6,9,28,31-tetraen-19-yl-4-(dimethylamino) butanoate	Neutral	
DSPE-PEG2k (C18)	1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (ammonium salt)	Neutral	
DMPE-PEG2k (C14)	1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (ammonium salt)	Neutral	
C20 PEG	1,2-Diarachidoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (ammonium salt)	Neutral	
C12 PEG	1,2-Dilauroyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (ammonium salt)	Neutral	
DSPC	1,2-distearoyl-sn-glycero-3-phosphocholine	Neutral	

POPG	1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-(1'-rac-glycerol) (sodium salt)	Negative	
CHOL	Cholesterol	Neutral	
DC-CHOL	DC-Cholesterol	Positive	

Supplementary Table 2. LNPs short-term and long-term stability by size, PDI and zeta potential.

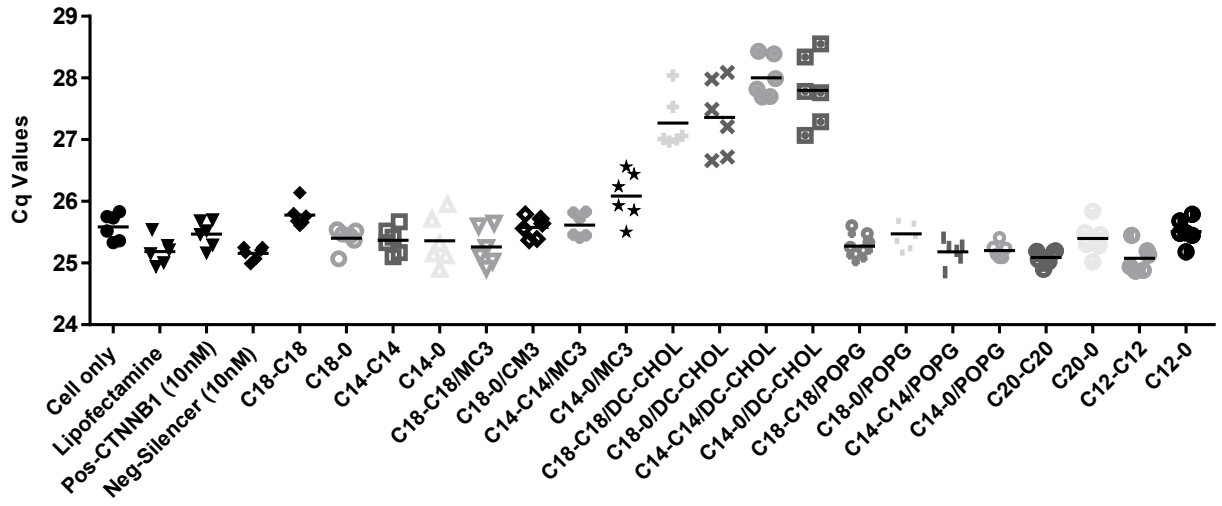
Formulation	Original			3 months		11 months		
Characterization	Size (Z-ave) (d.nm)	PDI	ZP (mV)	Size (Z-ave) (d.nm)	PDI	Size (Z-ave) (d.nm)	PDI	ZP (mV)
C18-C18	85.15	0.084	-6.45	84.91	0.058	81.41	0.085	-5.36
C18-0	90.21	0.091	-3.95	88.09	0.069	87.46	0.072	-6.59
C14-C14	87.54	0.061	-4.47	85.57	0.084	85.22	0.09	-7.49
C14-0	92.14	0.065	-3.76	90.49	0.066	91.33	0.079	-4.82
C18-C18/MC3	84.97	0.072	-4.22	82.63	0.068	83.55	0.081	-6.78
C18-0/CM3	89.02	0.039	-3.59	85.7	0.039	87.48	0.037	-7.39
C14-C14/MC3	86.45	0.057	-4.03	84.32	0.045	84.85	0.044	-6.69
C14-0/MC3	91.94	0.04	-3.23	90.37	0.031	90.06	0.079	-8.47
C18-C18/DC-CHOL	66.46	0.089	3.27	65.18	0.09	66.05	0.074	3.45
C18-0/DC-CHOL	77.78	0.075	4.67	75.91	0.082	73.54	0.086	2.49
C14-C14/DC-CHOL	72.07	0.087	3.28	68.57	0.065	68.95	0.068	3.54
C14-0/DC-CHOL	79.76	0.085	5.44	76.04	0.066	76.33	0.073	6.39
C18-C18/POPG	80.28	0.121	-10.4	77.31	0.138	78.45	0.121	-7.97
C18-0/POPG	93.97	0.087	-9.55	90.9	0.117	92.45	0.097	-9.69
C14-C14/POPG	95.55	0.134	-8.65	93.79	0.12	96.78	0.089	-8.55
C14-0/POPG	100.4	0.101	-11	98.97	0.088	98.17	0.095	-9.65
C20-C20	85.19	0.089	-5.67	83.81	0.096	82.44	0.073	-5.82
C20-0	91.34	0.051	-7.62	88.43	0.063	88.67	0.067	-7.67
C12-C12	96.98	0.084	-5.06	98.71	0.072	97.82	0.049	-6.9
C12-0	109.7	0.087	-6.66	111.7	0.095	110.2	0.077	-7.46

Supplementary Figure 1. Transmission electron microscopy (TEM) images of the original set of LNPs (C18-C18, C18-0, C14-C14, C14-0).

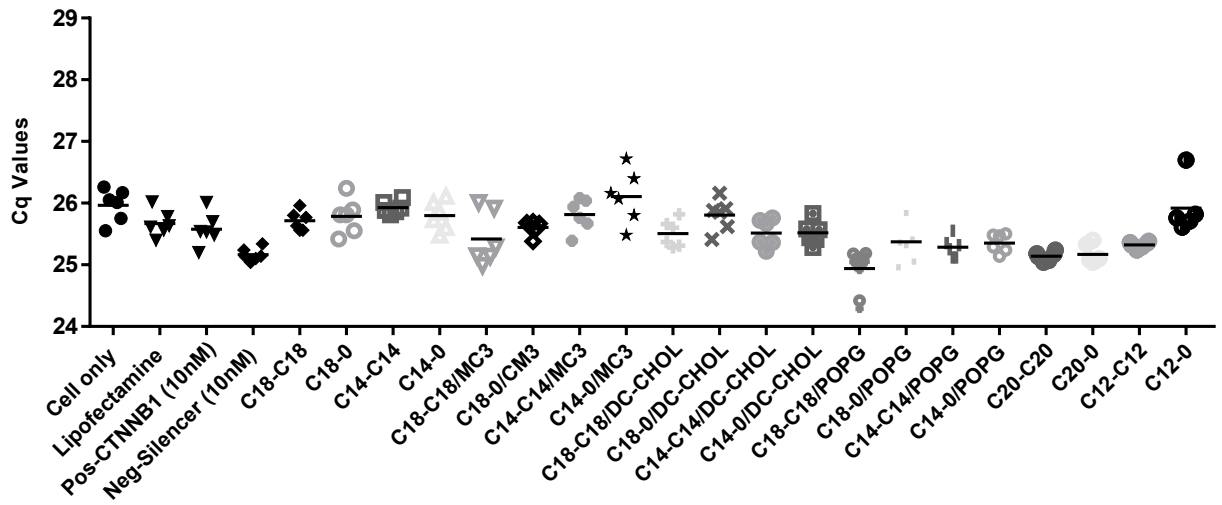


Supplementary Figure 2. Housekeeping gene Cq values after transfection

(a) Serum-free



(b) 5% Nude mice serum



Supplementary Figure 3. LNPs impact on cell viability with and without serum

