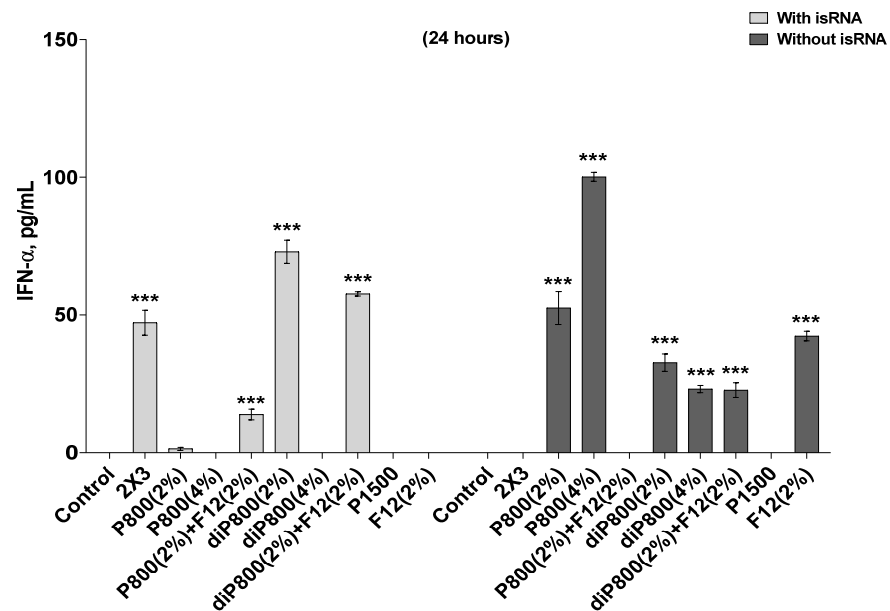
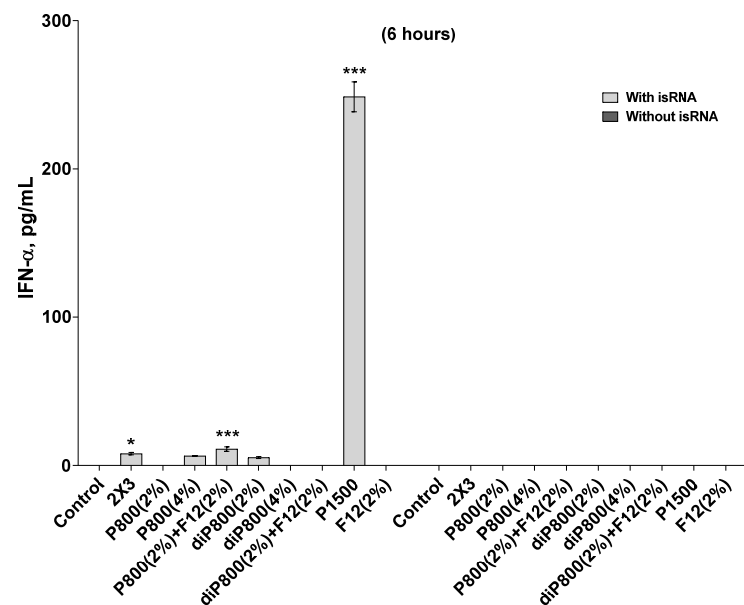


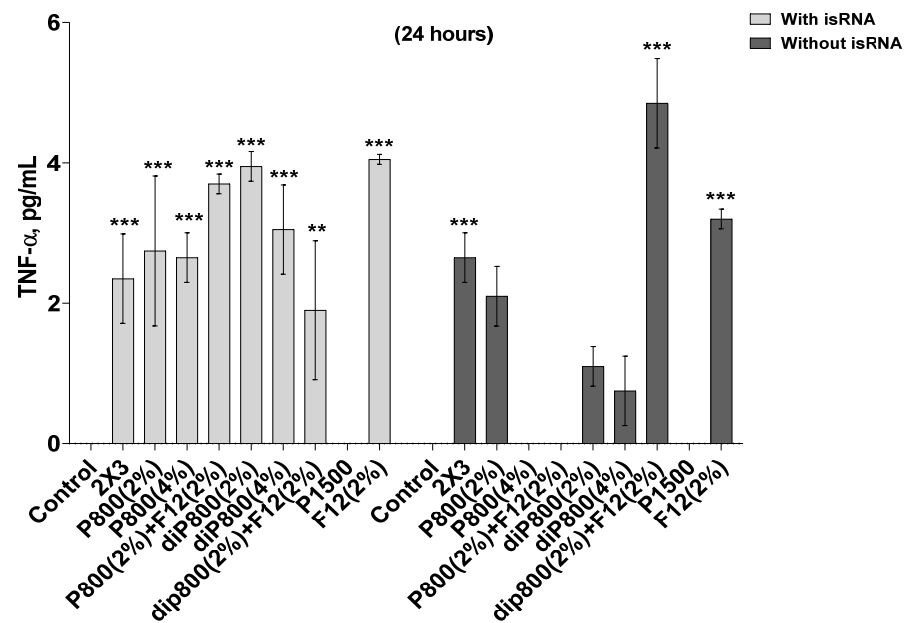
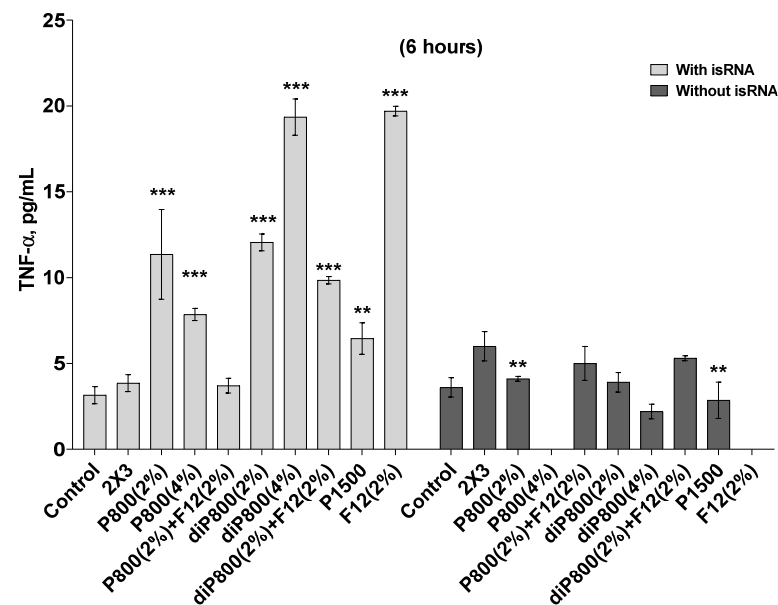
**Table S1:** Cytokines profiling measured using LEGEND plex™ Mouse Inflammation Panel (13-plex) kit after injections with isRNA + liposomes of different structures. The data represent mean ± standard deviation (SD) calculated from measurements from at least three mice. Statistically significant differences between experimental groups and the Control group are indicated by asterisk (\*\*\* = P value ≤0.0001, \*\* = P value <0.001, \* = P value <0.05); ordinary Two-way ANOVA, Dunnett's multiple comparisons test.

	CTRL	2X3	F12	P800	P800(4%)	P800+F12	diP800	diP800(4%)	diP800+F12	P1500	diP1500	P2000	diP2000
<b>IL-23</b>	0	29.11±10.15	0	0	0	0	0	4.85±11.88 ***	13.39±2.078	0	0	0	38.2±15.39
<b>IL-1α</b>	58.33±15.75	151.44±14.92	31.26±2.15	90.87±7.94	47.05±21.28	33.38±1.36	254.06±7.08	331.306±314.91	58.85±2.80	74.35±15.89	58.31±33.98	25.85±10.98	59.04±2.056
<b>IFN-γ</b>	0	180.18±63.75 *	451.09±138.24 ***	832.43±340.51 ***	608.68±67.84 ***	279.41±10.82 **	286.02±7.615 ***	567.56±31.56 ***	273.59±59.38 ***	753.63±71.64 ***	105.73±26.17	191.45±8.02 *	0
<b>TNF-α</b>	0	124.31±25.19	79.48±34.03	140.36±49.10	150.53±32.78	0	285.8±14.31	160.67±8.200 **	66.09±19.29 ***	188.05±16.97	0	79.75±0	106.45±56.60 ***
<b>MCP-1</b>	0	483.68±146.37 ***	887.88±243.91 ***	1488.43±131.06 ***	919.51±183.54 ***	70.41±5.51	903.56±169.44 ***	1220.31±241.35 ***	672.23±62.69 ***	2101.24±857.31 ***	773.48±214.73 ***	1239.09±370.26 ***	586.81±120.2
<b>IL-12p70</b>	0	15.04±6.47	19.95±6.46	15.26±3.45	29.69±5.47	0	9.85±1.55	26.41±5.59	13.85±1.070	37.57±16.18	0	167.8±0	0
<b>IL-1β</b>	0	0	0	0	0	0	110.28±56.08	0	23.68±12.00	0	0	0	0
<b>IL-10</b>	0	103.1±10.61	0	0	0	0	248.29±147.71 **	0	52.47±42.10	0	0	196.27±25.44 **	0
<b>IL-6</b>	3.98±1.46	120.31±56.47	85.11±41.76	181.53±48.86 *	100.72±51.04	87.77±5.05	228.63±2.08	127.65±38.89	103.11±6.48	277.3±64.89 ***	180.88±100.71 *	193.58±82.48	171.87±65.99
<b>IL-27</b>	0	236.5±61.99	0	22.38±0	0	0	95.44±17.82	0	65.77±55.68	139.66±107.37 *	0	0	0
<b>IL-17A</b>	0	3.05±1.20	0.57±0	0	0	0	14.81±9.20	0	4.17±3.89	0	0	0	0
<b>IFN-β</b>	0	28.26±13.56	97.97±36.84	118.44±21.99	142.57±24.90	0	31.88±9.52	140.85±2.075	46.13±34.58	330.35±55.69 ***	122.97±32.03	274.98±38.28	49.62±30.55
<b>GM-CSF</b>	3.31±5.17	7.45±1.71	0	0	0	0	23.69±1.56	0	0	0	0	63.79±0.1	7.32±1.55

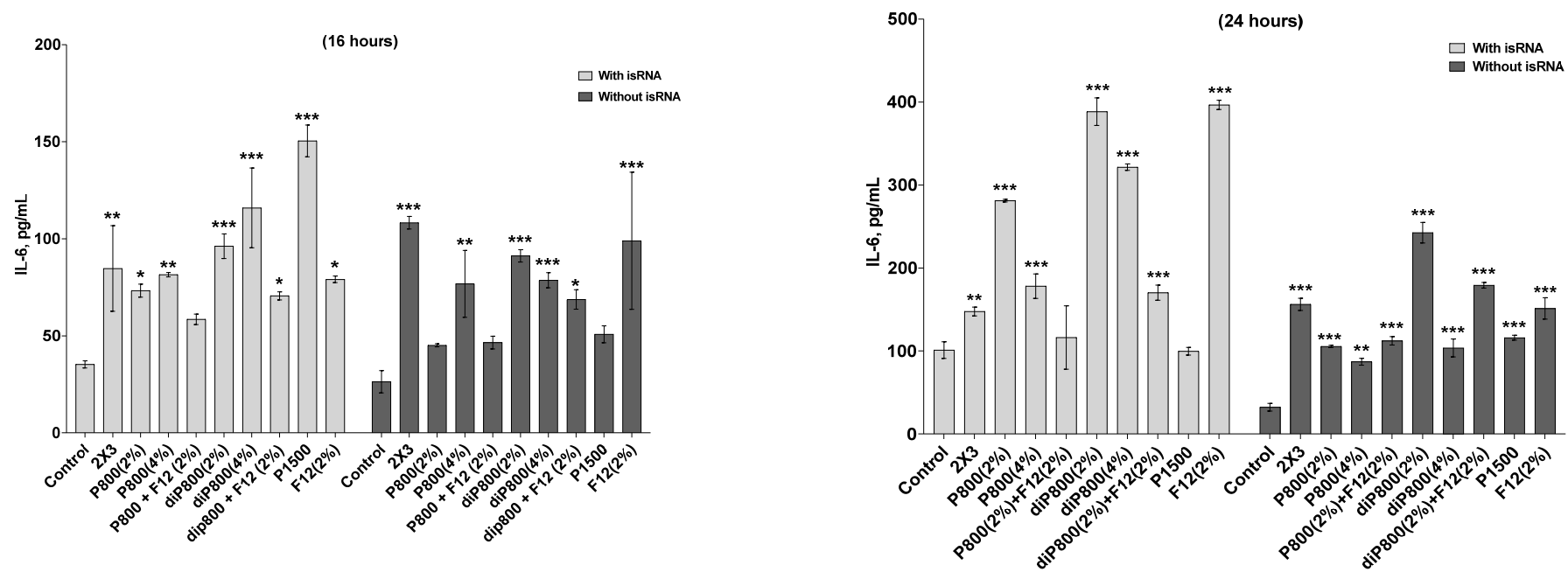
**A**



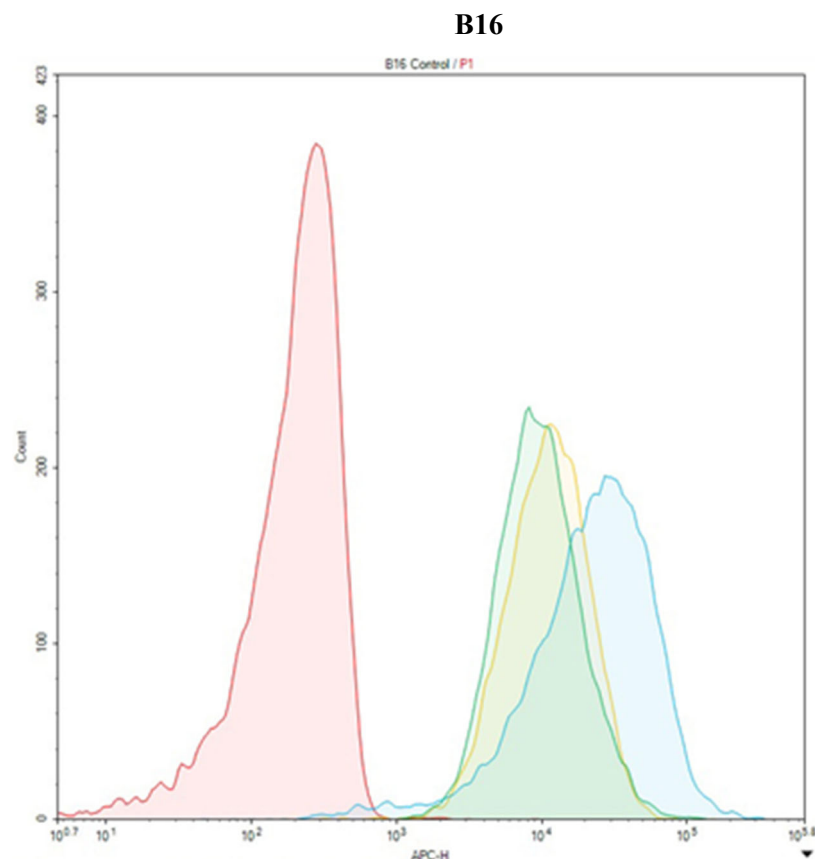
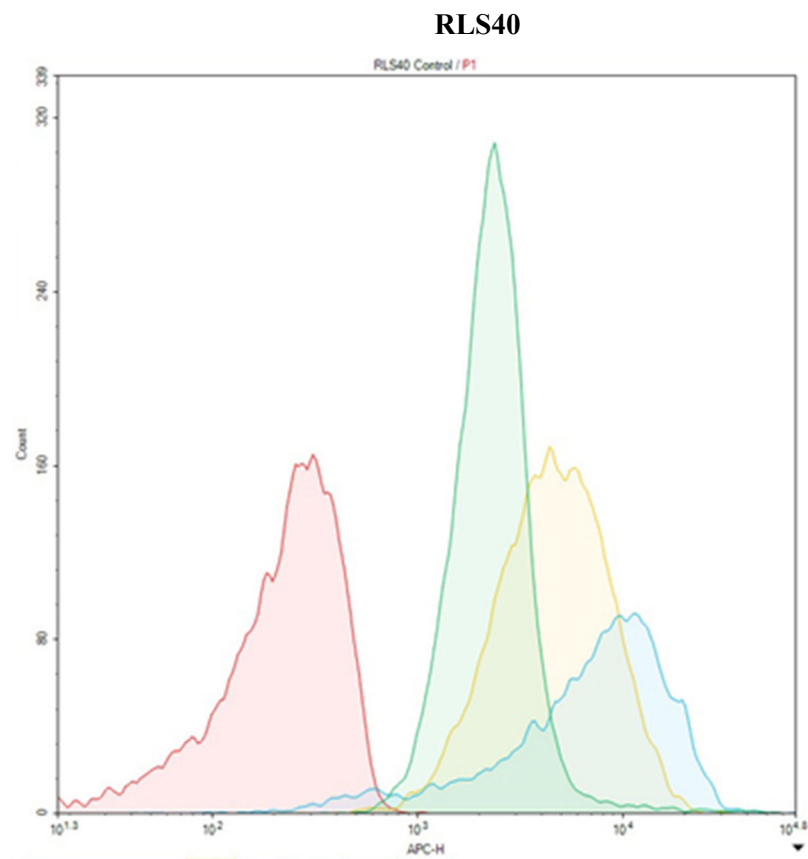
**B**



C



**Supplementary Figure S1.** Cytokines levels in human PBMCs primary cell culture after the transfection of isRNA/liposomes. The levels of IFN- $\alpha$  (A) and TNF- $\alpha$  (B) 6 and 24 h after transfection, the levels IL-6 (C) 16 and 24 h after transfection were measured by ELISA. The data represent mean  $\pm$  standard deviation (SD). Statistically significant differences between samples treated with isRNA/liposomes and the samples treated with only liposomes are indicated by asterisk (\* = P value <0.05, \*\* = P value <0.01, \*\*\* = P value <0.001); ordinary two-way ANOVA, Dunnett's multiple comparisons test.



**Supplementary Figure S2.** Representative flow histograms of Cy5.5-isRNA and its complexes with liposomes accumulation in B16 and RLS40 cells. The accumulation was measured 4 h after transfection of Cy5.5-isRNA mediated by liposomes. Red – untreated cells cell, Green – cells incubated with -siRNA, Yellow – cells incubated with Cy5.5-isRNA/P2000 complexes, Blue – cells incubated with Cy5.5-isRNA/2X3-DOPE complexes.