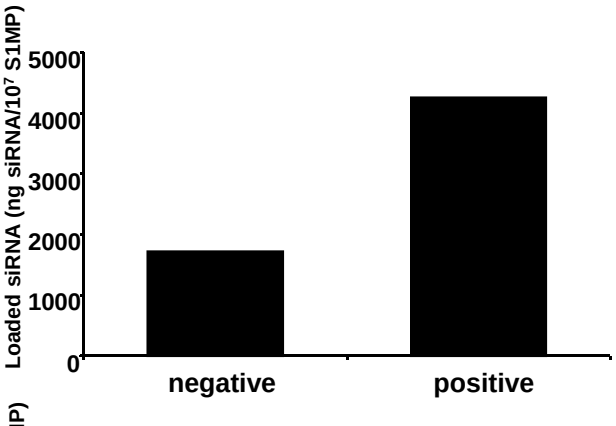
Supplementary Figure 1

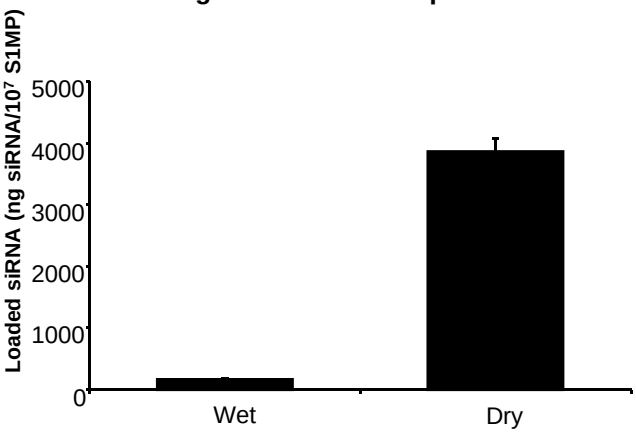
a

delivery system	net charge (mV)
DOPC-siRNA	- 2.8
S1MP positive	+ 8.0
S1MP negative	-30.5

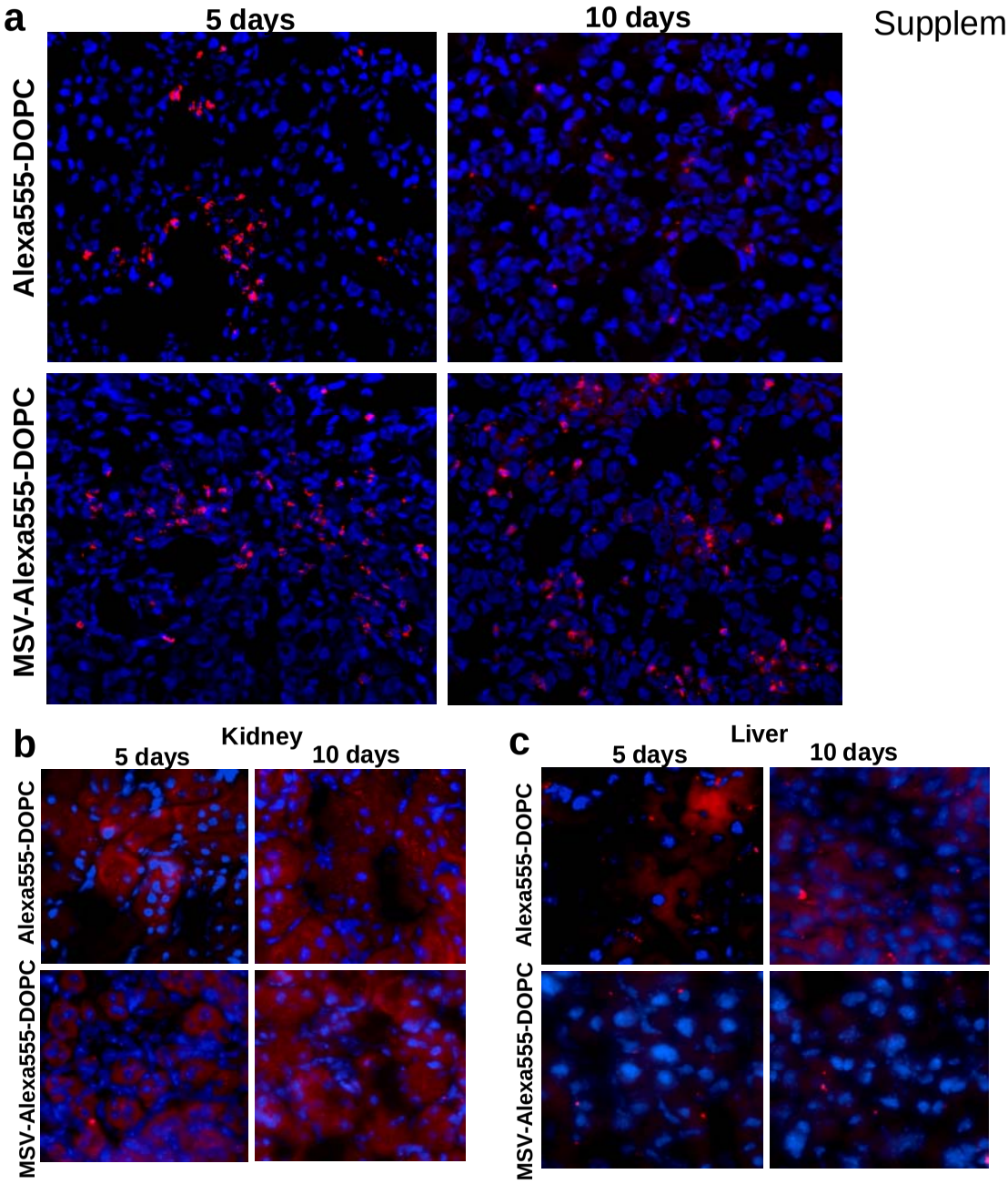
b



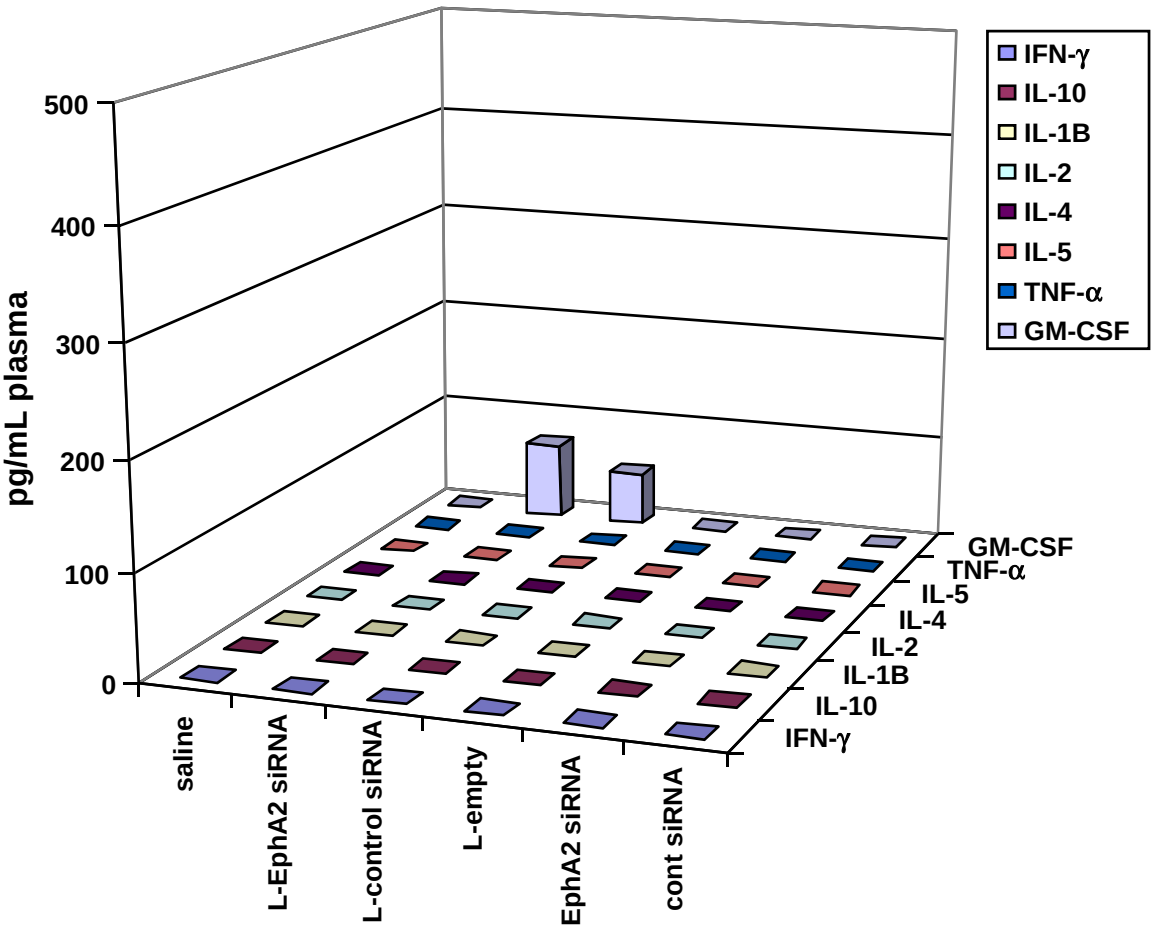
c



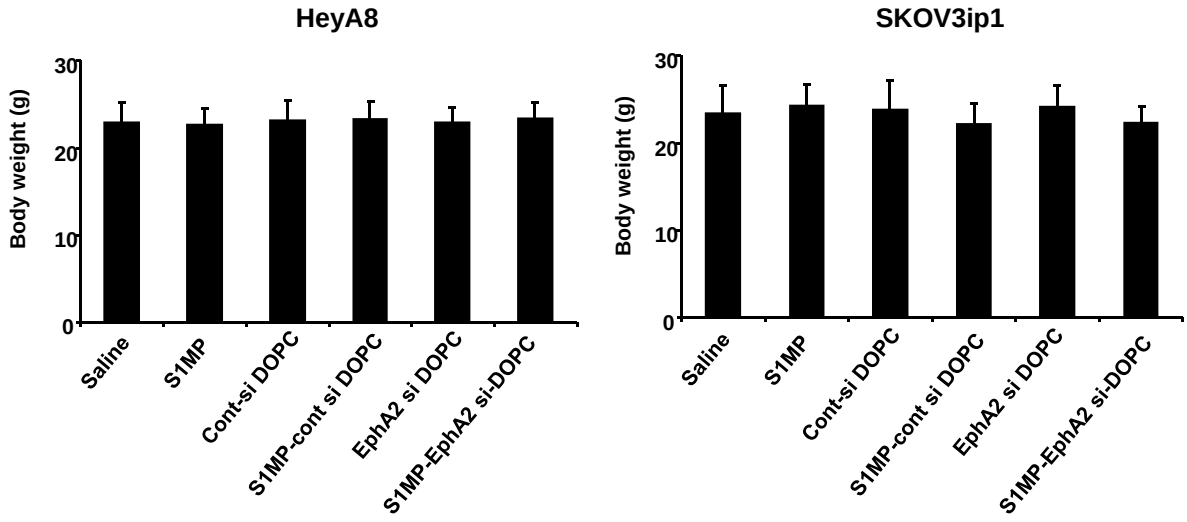
Supplementary Figure 2



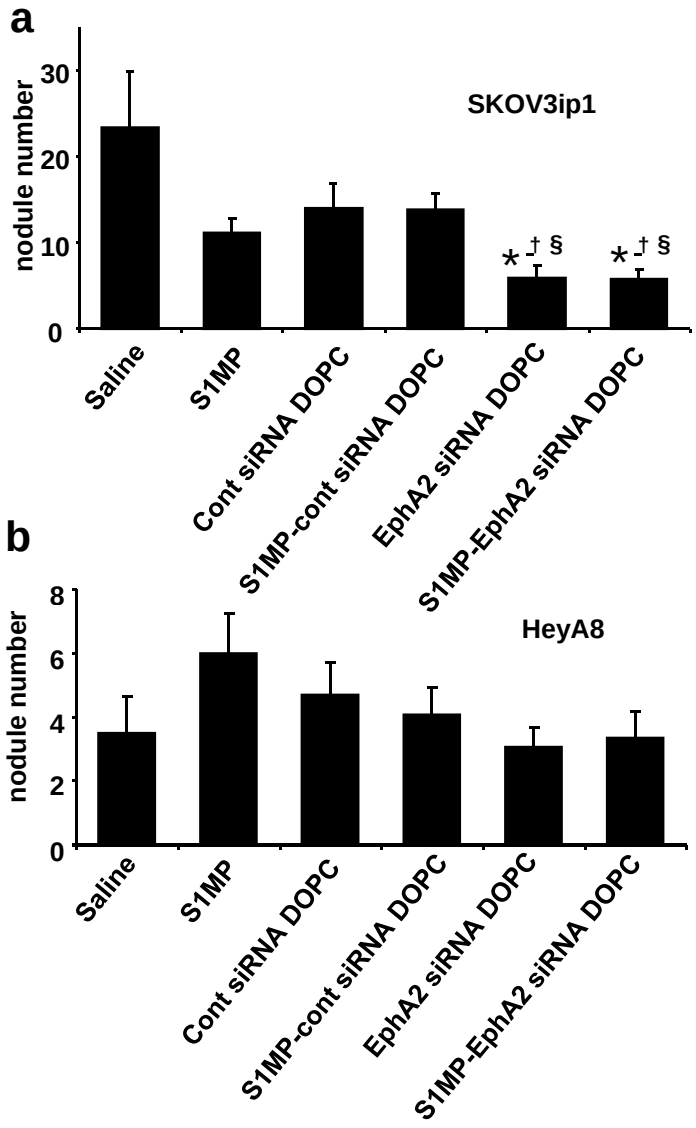
Supplementary Figure 3



Supplementary Figure 4

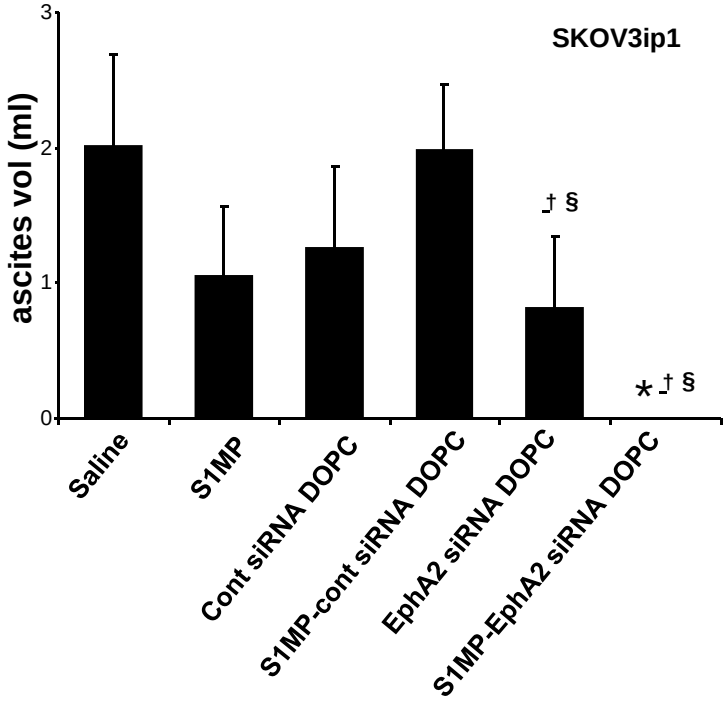


Supplementary Figure 5



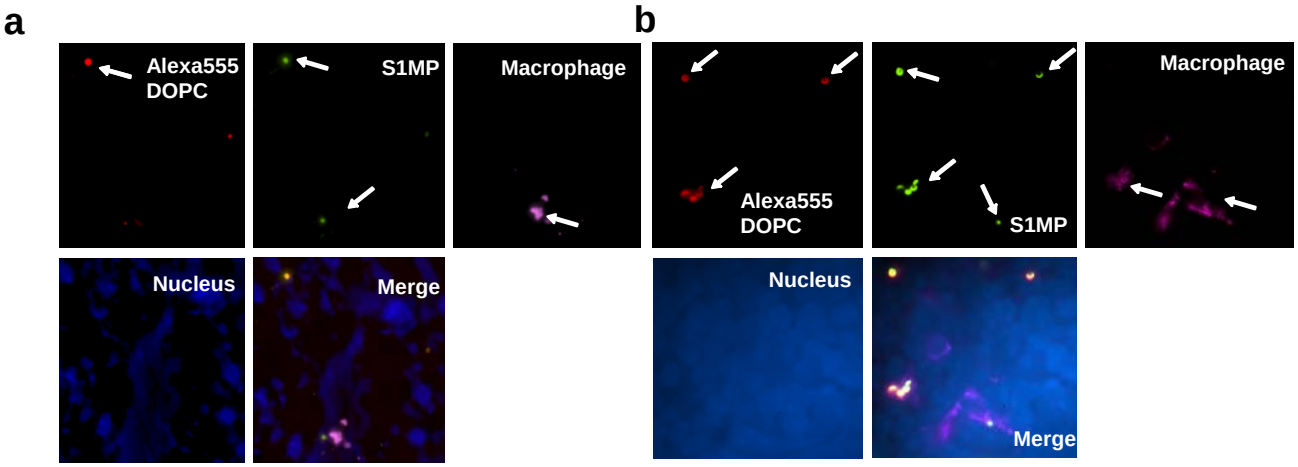
*** p<0.05 compared to S1MP**
§ p<0.05 compared to saline
† p<0.05 compared to S1MP-cont siRNA-DOPC

Supplementary Figure 6

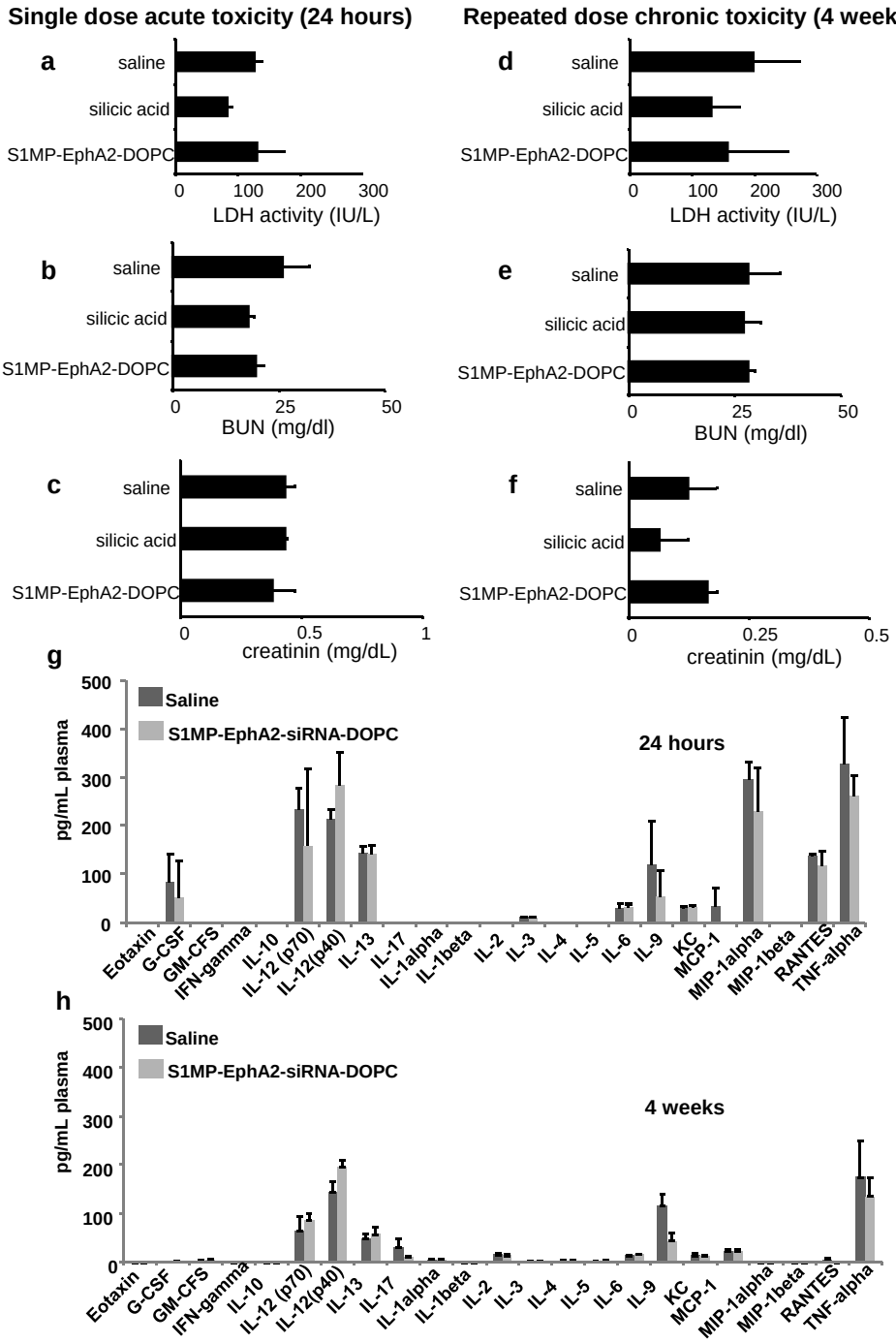


*** p<0.05 compared to S1MP**
§ p<0.05 compared to saline
† p<0.05 compared to S1MP-cont siRNA-DOPC

Supplementary Figure 7



Supplementary Figure 8



Supplemental figure legends

Supplementary Figure 1. Effect of physico-chemical properties of S1MP on liposome loading. (a) Net charge of delivery vectors. (b) The effect of surafce charge of the S1MP on liposomal siRNA loading. (c) Enhanced loading of liposomal siRNA to the dried positively charged S1MP.

Supplementary Figure 2. Effect of multistage delivery on siRNA tumor uptake and tissue distribution. Mice with the HeyA8 orthotopic tumors (15 days after intraperitoneal inoculation of tumor cells) were injected with the S1MP loaded with single dose (5 μg siRNA) of Alexa555-siRNA DOPC (MSV-Alexa555-siRNA DOPC) or Alexa555-siRNA DOPC alone (3 mice/time point). Tumors were harvested at 5 and 10 days and examined for abundance of fluorescence in the tumor (a), kidney (b), and liver (c). Eight micron frozen section of tumor was fixed and the nucleus was counterstained with Hoechst 33342 to examine for presence of fluorescence. The amounts of Alexa555 siRNA (red fluorescence) was counted microscopically from randomly selected at least 5 fields from the serial step sections of tumor (5 steps/tumor).

Supplementary Figure 3. Immunostimulatory effects of EphA2-siRNA-DOPC and EphA2. The mice (n=3-5) were intravenously injected with a single dose of EphA2-siRNA-DOPC and peripheral blood was collected from retro-orbital sinus at 5 hours post injection. Plasma cytokine levels were measured and compared to saline injected mice. All functions were expressed as mean values ± SD.

Supplementary Figure 4. Effect of delivery carriers on mouse body weight. The mouse body weight was recorded for each of the groups from experiments presented in **Figure 3** (in the main paper) at the time of necropsy. There was no difference in average mouse weights among the treatment groups.

Supplementary Figure 5. Effect of sustained EphA2 siRNA delivery on number of tumor nodules *in vivo* orthotopic models of ovarian cancer. The tumor nodule number was recorded for each of the groups from experiments presented in **Figure 3** (in the main paper) at the time of necropsy. Overall ANOVA, $p<0.05$ for both cell line.

Supplementary Figure 6. Effect of sustained EphA2 siRNA delivery on ascites formation *in vivo* orthotopic models of ovarian cancer. The ascited volume in the peritoneal cavity was measured for each of the groups from experiments presented in **Figure 3** (in the main paper) at the time of necropsy. Overall ANOVA, $p<0.05$.

Supplementary Figure 7. Localization of S1MP. Immunofluorescence analysis of the liver (a) and spleen (b) sections from mice injected with FITC labeled S1MP loaded with Alexa 555 siRNA-DOPC at 20 days post injection. The sections were stained with anti-f4/80 to detect macrophages (pink). Alexa555 siRNA DOPC (red) and FITC conjugated S1MP (green) were seen in both organs. Nuclei were counter stained with Hoescht (blue). (final magnification= x 600).

Supplementary Figure 8. Safety of S1MP-EphA2-siRNA-DOP. (a-c) The mice (n=3-5) were intravenously injected with a single dose of EphA2-siRNA-DOPC loaded S1MP once and peripheral blood was collected from retro-orbital sinus at 24 hours post injection. (d-f) The mice were intravenously injected with multiple doses of EphA2-siRNA-DOPC loaded S1MP (4 injections once a week for 4 weeks). Equivalent amounts of silicic acid (degradation product of porous silicon particles) were also injected as negative control. Clinical chemistry parameters were measured. LDH (a and d), BUN (b and e), and creatinine (c and f). (g-h) The mice (n=5-6) were intravenously injected with S1MP-EphA2-siRNA-DOPC and peripheral blood was collected from retro-orbital sinus at either 24 hours or 4 weeks post injection. Plasma cytokine levels were measured and compared to saline injected mice. All functions were expressed as mean values ± SD.