SUPPLEMENTAL MATERIALS

Figure legends for Supplemental Figures:

Fig. 1. *MSNP size distribution in aqueous solutions.* Dynamic light scattering (DLS) for MSNP exhibiting different surface modifications was performed in water, DMEM plus 10% FCS, BEGM or BEGM plus 2 mg/ml BSA. The presence of serum and BSA in the cell culture media improves MSNP dispersity.

Fig. 2. *Assessment of cell viability and mitochondrial membrane potential (MMP) in RAW 264.7 and BEAS-2B cells.* (A) Cell viability, following treatment with MSNP displaying different surface modifications, wise determined by the MTS assay as described in Fig. 2. Cells were exposed to MSNP at doses of 12.5-50 μg/ml for 16 hrs. All the MTS values were normalized as outlined in Fig. 2 in the manuscript. The IC_{50} values for image NP-PEI-25 KD in RAW 264.7 and BEAS-2B cells are 40.6 μg/ml and 9.7 μg/ml, respectively. (B) Cell death and mitochondrial depolarization after treatment with MSNP-phosphonate and MSNP-PEI backspace-25kD was determined using PI and JC-1, respectively.

Fig. 3. *Effect on cell viability after conversion of primary amines to COOH.* Succinic anhydride was used to convert the primary NH_2- to COOH- groups on MSNP-PEI-25 KD. (A) Cell viability comparing non-modified with succinic anhydride treated particles in RAW 264.7 cells using MTS assay. (B) The conversion was confirmed using

fluorescamine, which yields green fluorescence when complexed to the primary NH_2 groups. The decline in fluorescence intensity was followed in a fluorometer.

Fig. 4. *Determination of the stability of PEI coating on the MSNP surface.* Rhodamine-B labeled PEI was used to coat the surface of FITC-labeled MSNP and the dual-labeled particles were added to RAW 264.7 cells prior to the performance of confocal microscopy. The composite yellow color confirms that the polymer and the particle co-localize at the same intracellular site at 3 and 6 hrs.

Fig. 5. *Cellular uptake of FITC-labeled MSNP in RAW 264.7 cells.* MSNP were FITC labeled as described in Materials and Methods. (A) A representative histogram showing the shift in fluorescence intensity in RAW 264.7 cells treated with 25 µg/ml FITC-MSNP exhibiting different surface modifications for 3 hrs (left panel). The fold-increase in MFI was calculated and used to generate the graph. RITC-labeled MSNP was used as a control as discussed in Fig. 2 in the manuscript (right panel). (B) Confocal microscopy to study the cellular uptake of FITC-MSNP in RAW 264.7 cells. Cells were exposed to 25 µg/ml FITC-labeled particles for 3 hr. After the cell membrane was stained with 5 µg/ml red fluorescent wheat germ agglutinin (WGA), cells were visualized in a Confocal 1P/FCS Inverted microscope. Data are representative of 3 separate experiments. *$p<0.01$ compared with control.

Fig. 6. *Cell viability detection by the MTS assay in RAW 264.7 and BEAS-2B cells.* After incubation with particles coated with different length PEI polymers at doses from 6.25-

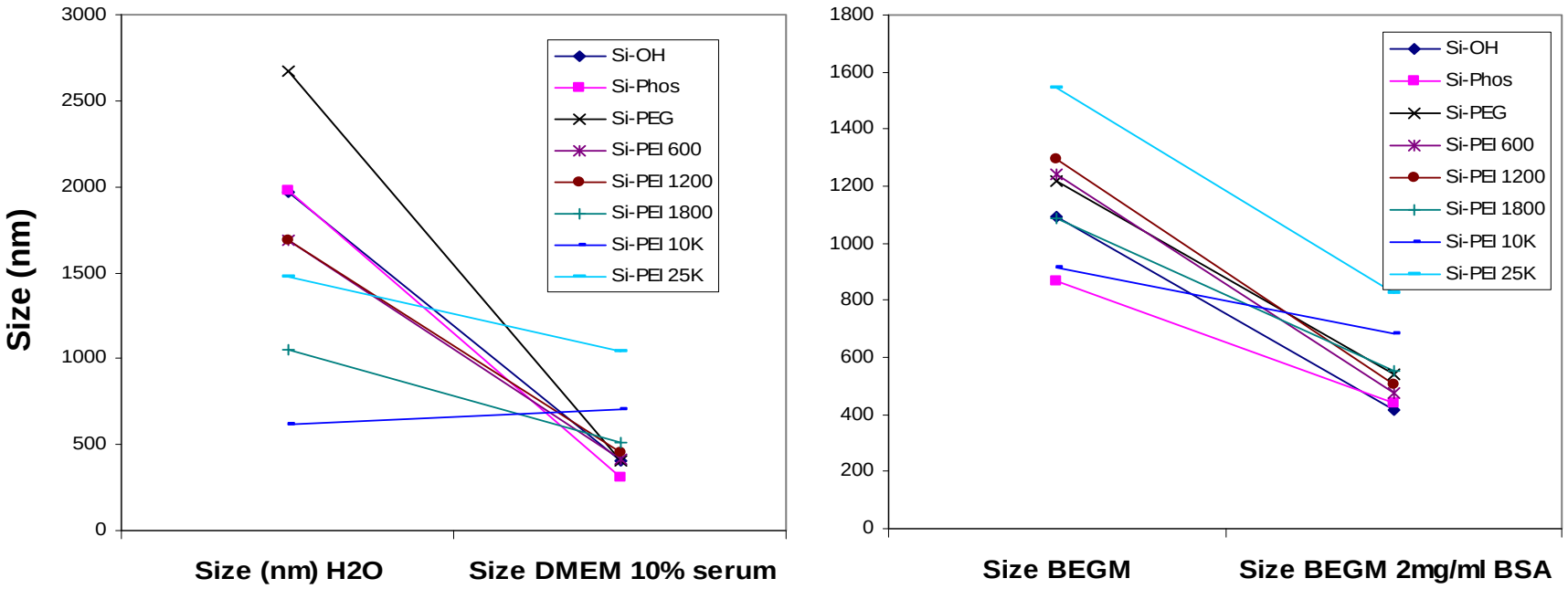
100 μg/ml for 16 hrs, the MTS assay and data calculation were performed as described in Fig. 1.

Fig. 7. *Detection of GFP knockdown by siRNA using western blotting in HEPA-1 cells.* (A) HEPA-1 cells with stable GFP expression was used for siRNA knockdown as described in Fig. 6. The procedure, including use of particles coated with different polymer lengths and the control agent, Lipofectamine 2000, was carried out as described in Fig. 6. However, instead of using confocal microscopy, cells were lyzed and the lysates used to conduct anti-GFP immunoblotting. The blotting membrane was also overlaid with an antibody recognizing β-actin to correct for protein loading. (B) The MFI of siRNA was calculated to show relative quantity of siRNA uptake into cells transfected by PEI-MSNP in HEPA-1 cells (arbitrary units).

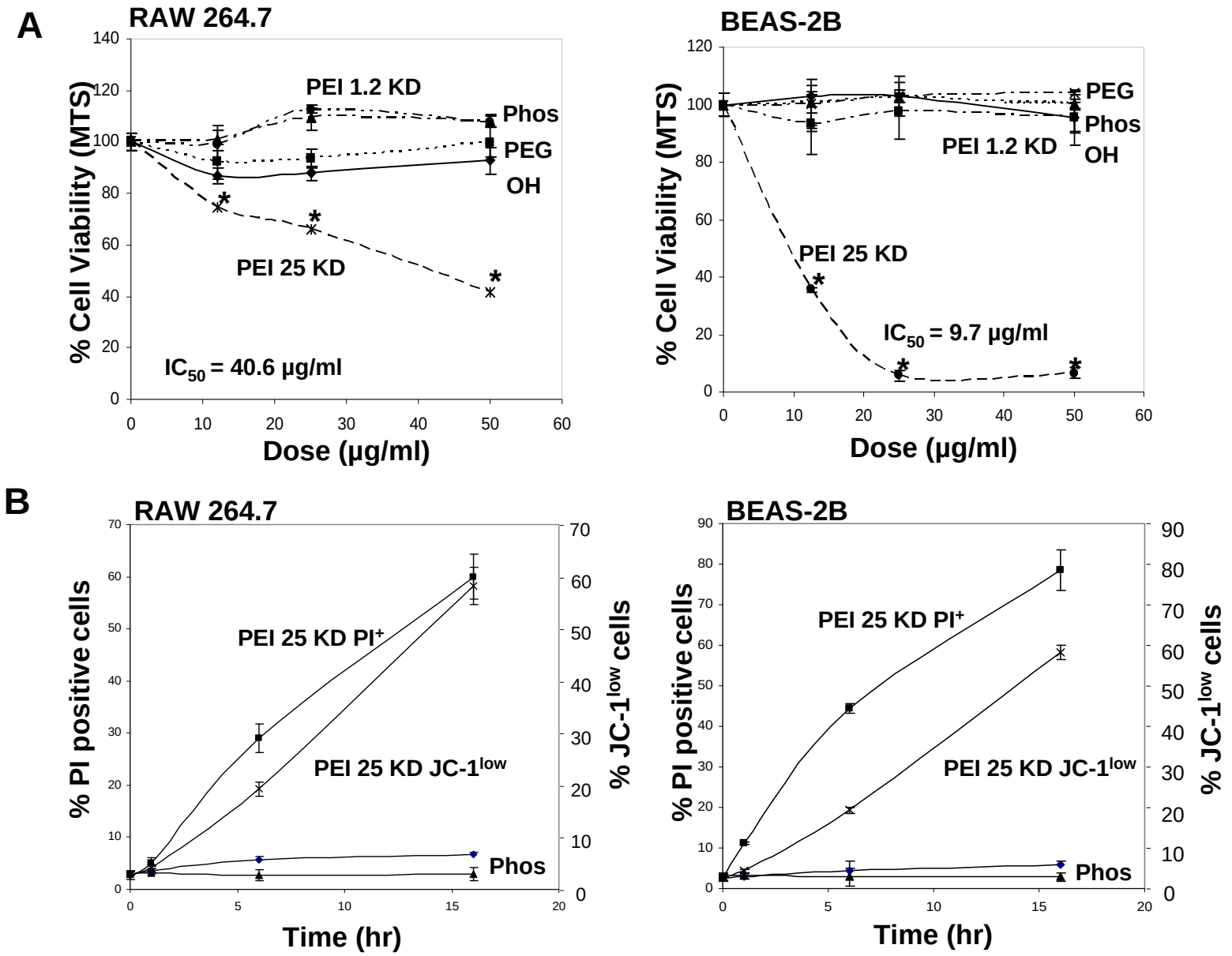
Fig. 8. *Quantification of paclitaxel (Pac) loading capacity in MSNP*. MSNP with different surface modifications were loaded with paclitaxel. Methanol was used for complete release of the drug from washed particles and the amount of paclitaxel in the supernatant was determined by UV absorbance at 230 nm.

Fig. 9. *Animal weight and histology of major organs.* (A) Animal weight was monitored after MSNP-phosphonate and MSNP-PEI 25 KD particle injections. (B) Histology of liver, kidney, spleen was performed by UCLA Division of Laboratory Animal Medicine (DLAM) diagnostic laboratory services. The sections were stained with hematoxylin-eosin and examined by light microscopy.

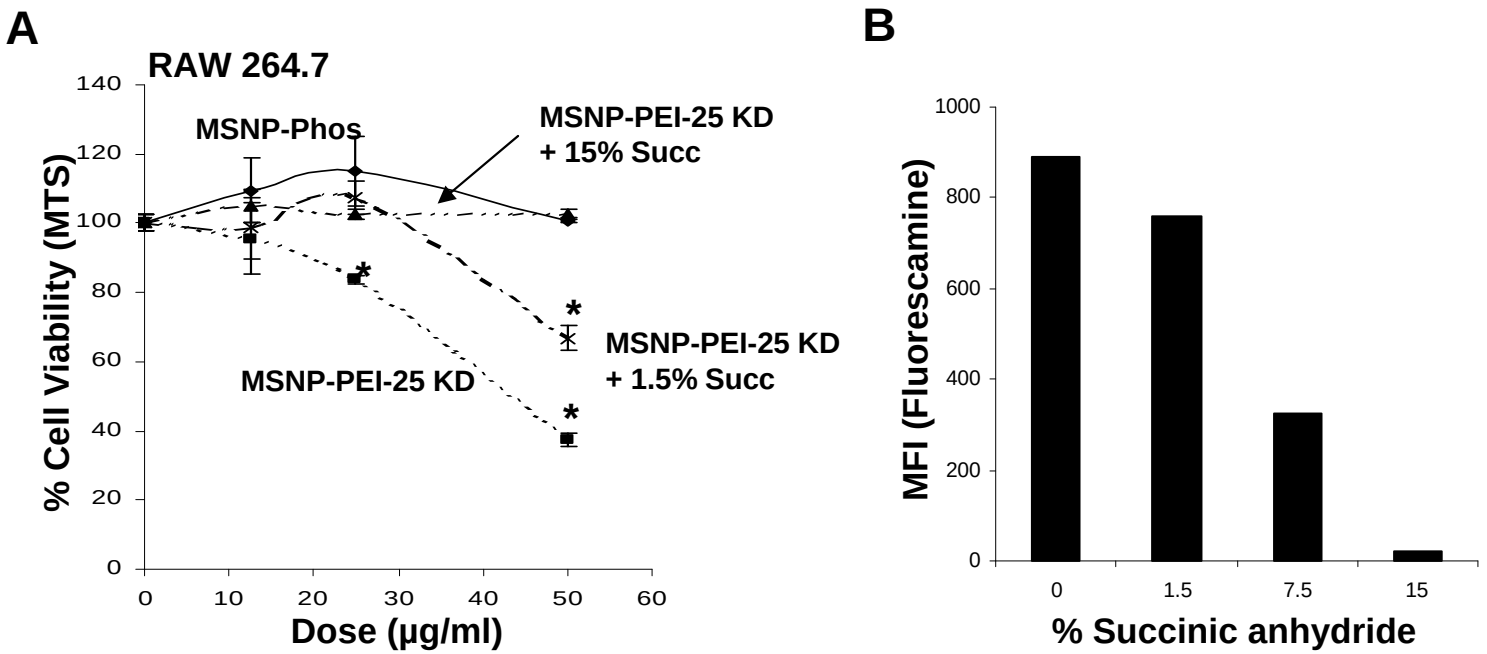
SFig. 1


Size (nm)
3000
2500
2000
1500
1000
500
0
Size (nm) H2O
Size DMEM 10% serum
Si-OH
Si-Phos
Si-PEG
Si-PEI 600
Si-PEI 1200
Si-PEI 1800
Si-PEI 10K
Si-PEI 25K
1800
1600
1400
1200
1000
800
600
400
200
0
Size BEGM
Size BEGM 2mg/ml BSA
Si-OH
Si-Phos
Si-PEG
Si-PEI 600
Si-PEI 1200
Si-PEI 1800
Si-PEI 10K
Si-PEI 25K

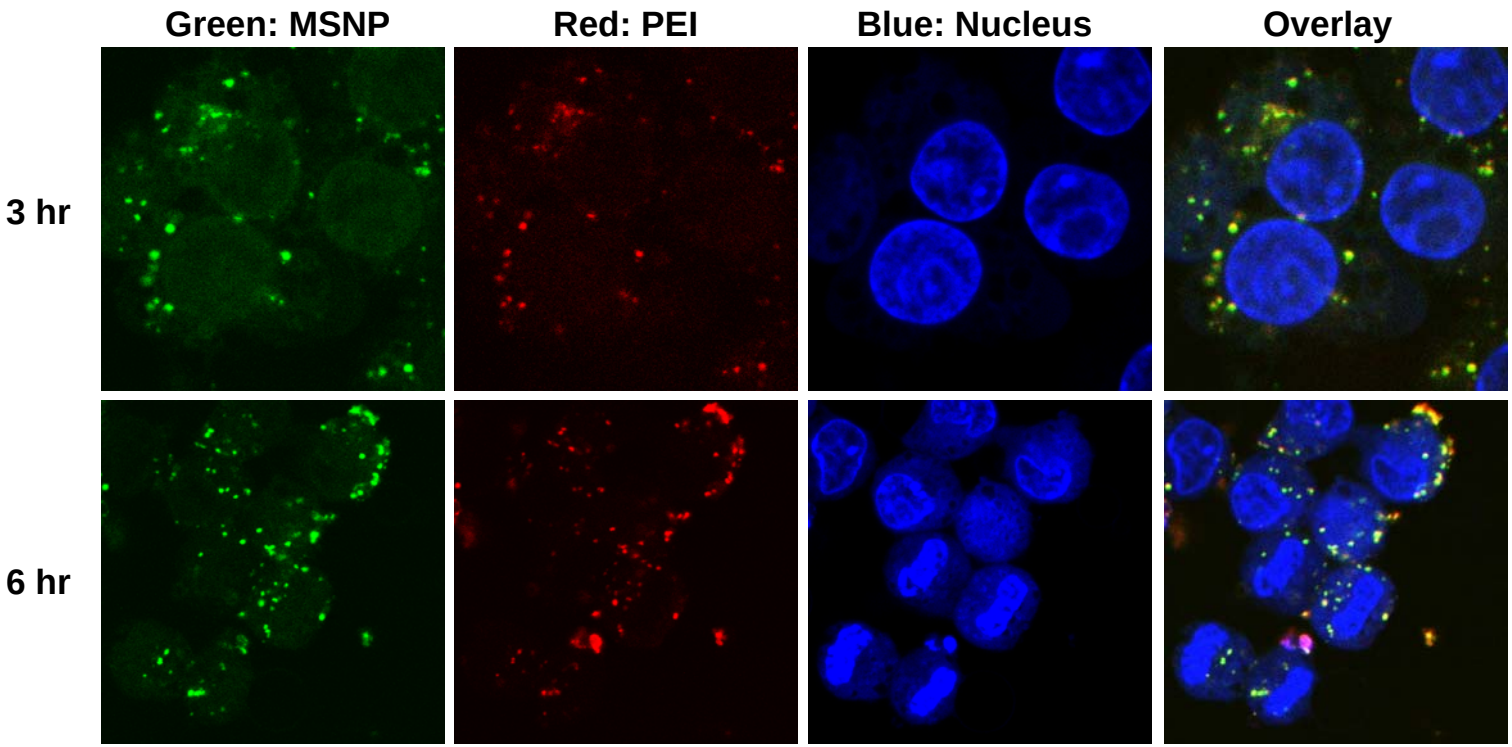
SFig. 2


A
RAW 264.7
% Cell Viability (MTS)
Dose (µg/ml)
PEI 1.2 KD
Phos
PEG
OH
PEI 25 KD
IC50 = 40.6 µg/ml
BEAS-2B
% Cell Viability (MTS)
Dose (µg/ml)
PEG
Phos
OH
PEI 1.2 KD
PEI 25 KD
IC50 = 9.7 µg/ml
B
RAW 264.7
% PI positive cells
% JC-1low cells
Time (hr)
PEI 25 KD PI+
PEI 25 KD JC-1low
Phos
BEAS-2B
% PI positive cells
% JC-1low cells
Time (hr)
PEI 25 KD PI+
PEI 25 KD JC-1low
Phos

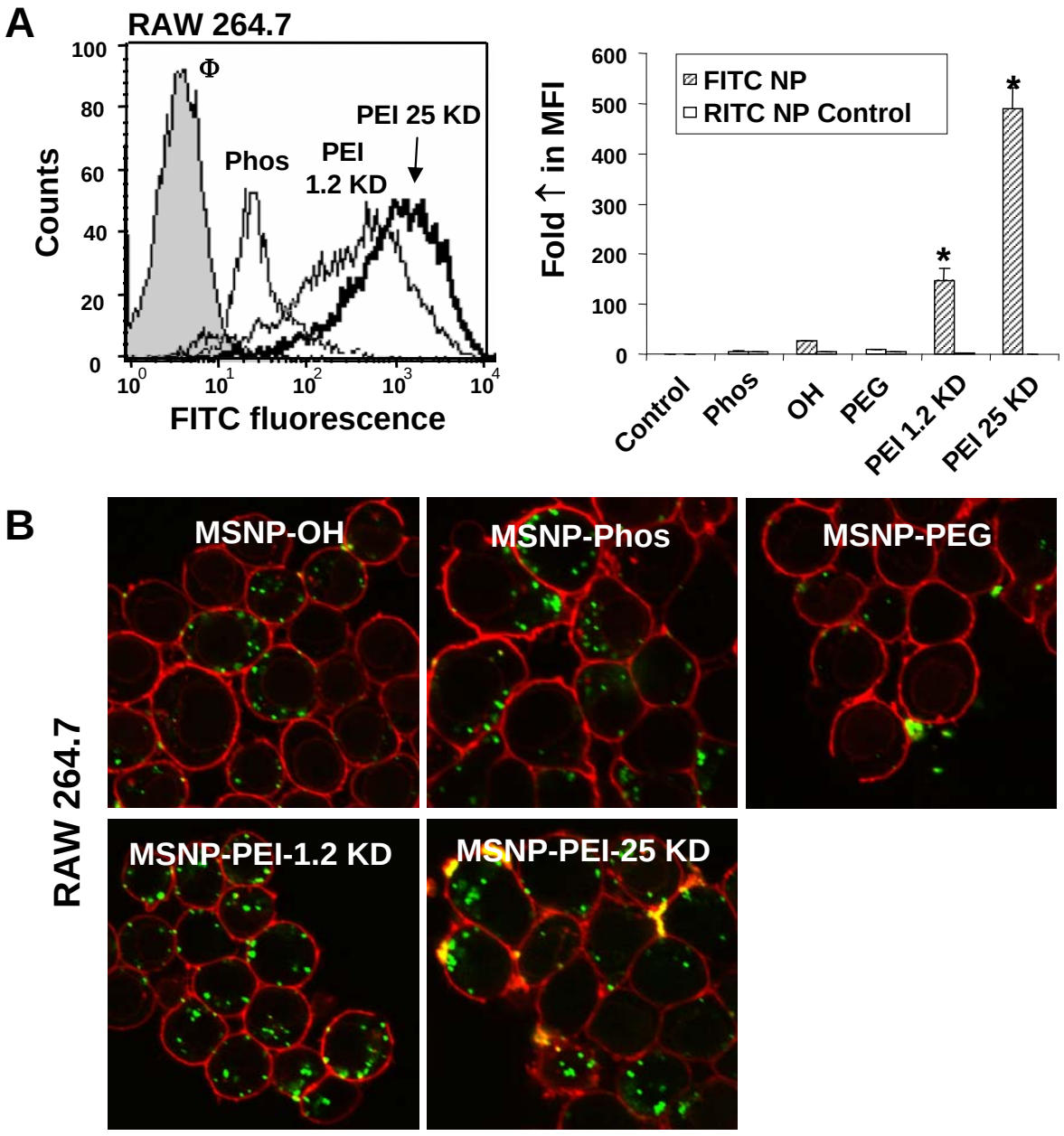
SFig. 3


A
RAW 264.7
MSNP-Phos
MSNP-PEI-25 KD
+ 15% Succ
MSNP-PEI-25 KD
+ 1.5% Succ
MSNP-PEI-25 KD
% Cell Viability (MTS)
Dose (µg/ml)
0
20
40
60
80
100
120
140
0
10
20
30
40
50
60
B
MFI (Fluorescamine)
% Succinic anhydride
0
200
400
600
800
1000
0
1.5
7.5
15

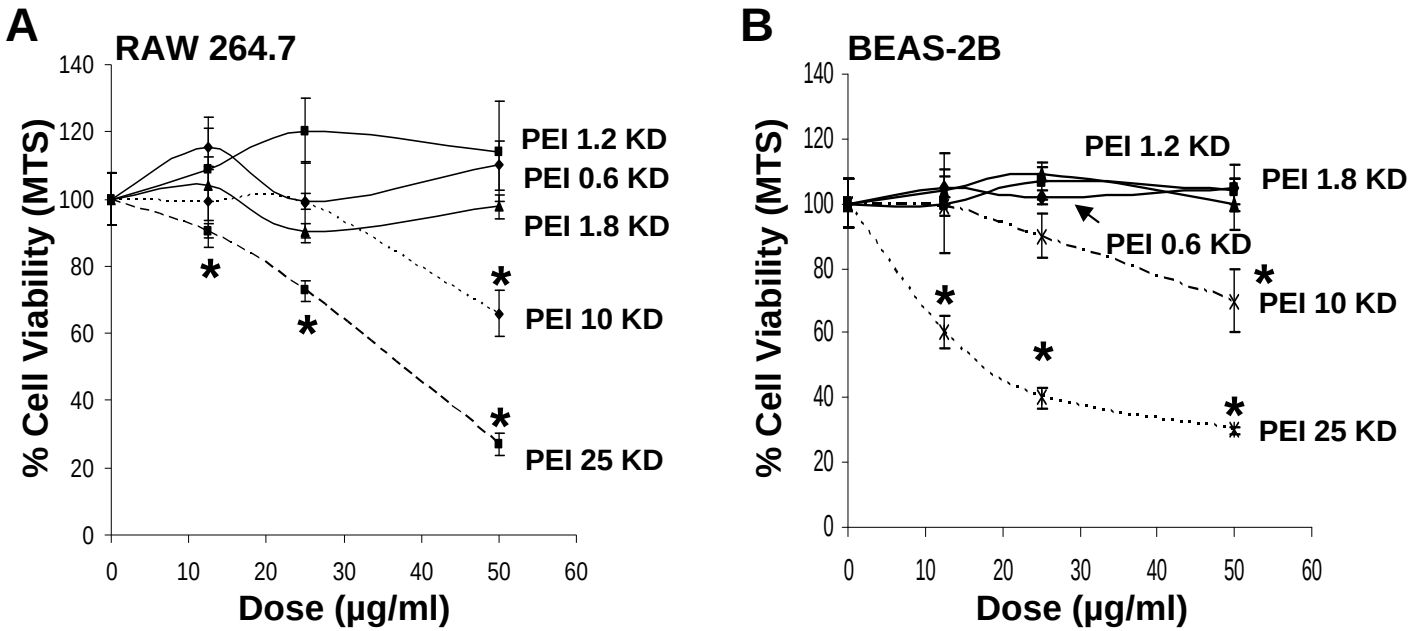
SFig. 4



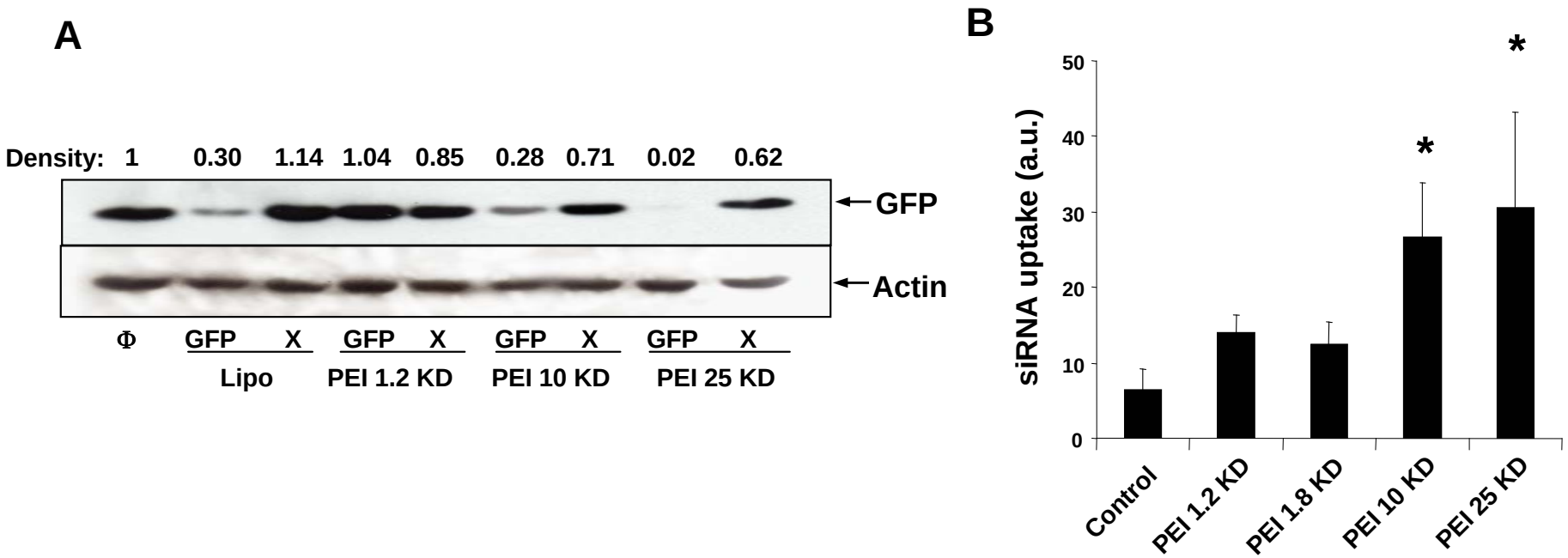
SFig. 5


A
RAW 264.7
Counts
FITC fluorescence
Φ
Phos
PEI 1.2 KD
PEI 25 KD
Fold ↑ in MFI
FITC NP
RITC NP Control
Control
Phos
OH
PEG
PEI 1.2 KD
PEI 25 KD
B
RAW 264.7
MSNP-OH
MSNP-Phos
MSNP-PEG
MSNP-PEI-1.2 KD
MSNP-PEI-25 KD

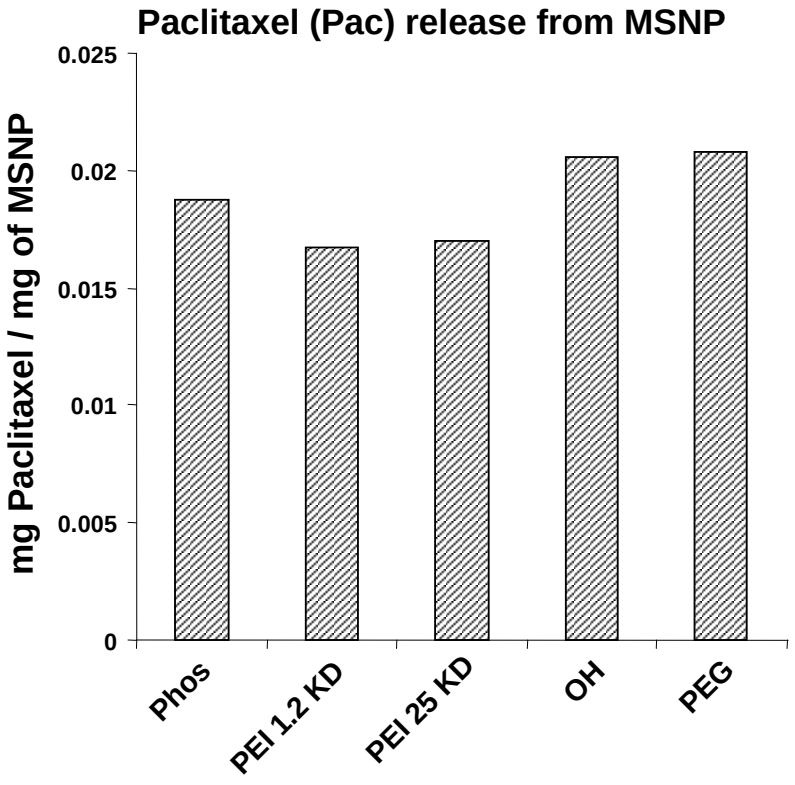
SFig. 6


A
RAW 264.7
% Cell Viability (MTS)
Dose (µg/ml)
PEI 1.2 KD
PEI 0.6 KD
PEI 1.8 KD
PEI 10 KD
PEI 25 KD
B
BEAS-2B
% Cell Viability (MTS)
Dose (µg/ml)
PEI 1.2 KD
PEI 1.8 KD
PEI 0.6 KD
PEI 10 KD
PEI 25 KD

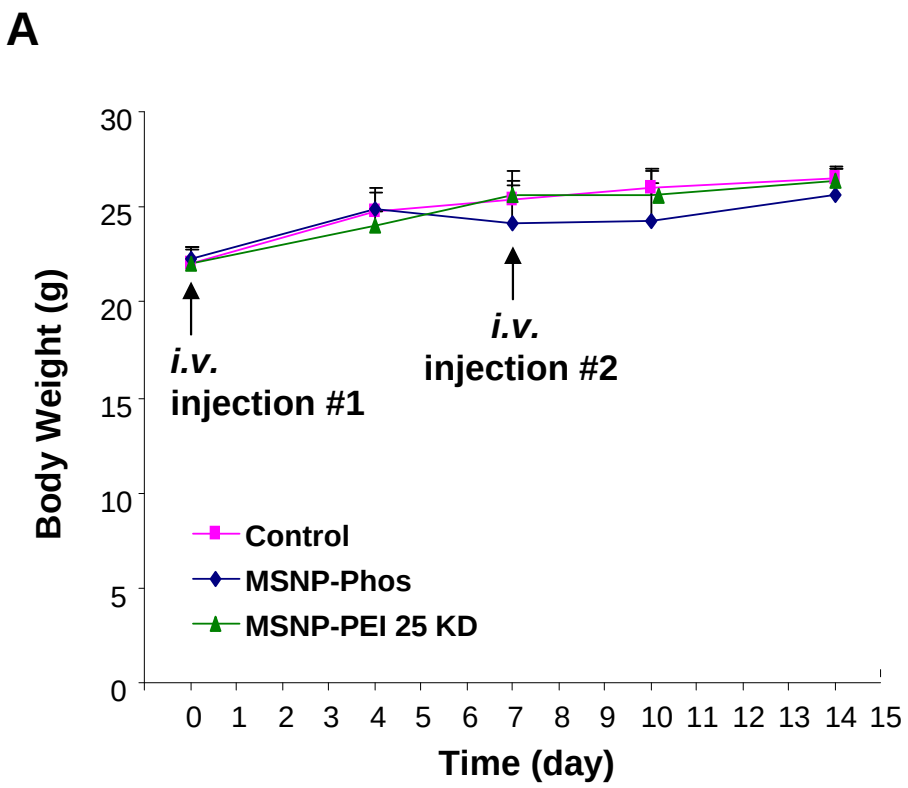
SFig. 7

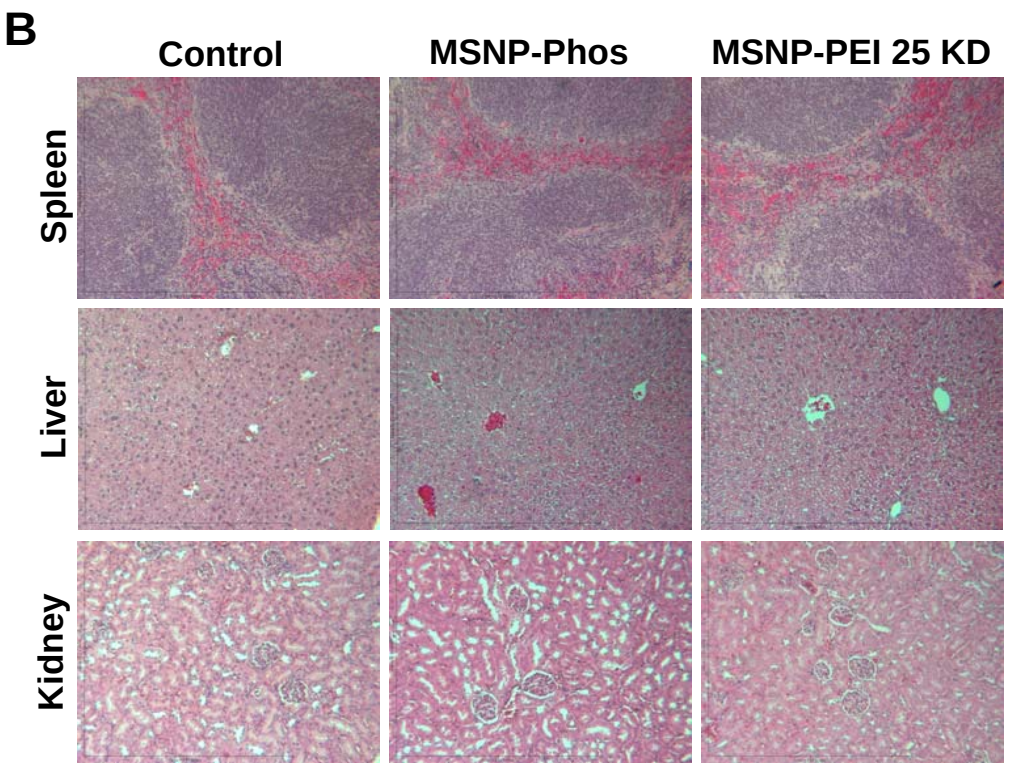

A
Density: 1 0.30 1.14 1.04 0.85 0.28 0.71 0.02 0.62
GFP
Actin
Φ GFP X GFP X GFP X GFP X
Lipo
PEI 1.2 KD
PEI 10 KD
PEI 25 KD
B
siRNA uptake (a.u.)
50
40
30
20
10
0
*
*
Control
PEI 1.2 KD
PEI 1.8 KD
PEI 10 KD
PEI 25 KD

SFig. 8


Paclitaxel (Pac) release from MSNP
mg Paclitaxel / mg of MSNP
0.025
0.02
0.015
0.01
0.005
0
Phos
PEI 1.2 KD
PEI 25 KD
OH
PEG

SFig. 9


A
Body Weight (g)
30
25
20
15
10
5
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
Time (day)
i.v.
injection #1
i.v.
injection #2
Control
MSNP-Phos
MSNP-PEI 25 KD


B
Control
MSNP-Phos
MSNP-PEI 25 KD
Spleen
Liver
Kidney