Supporting Information for:

Silica Coated Paclitaxel Nanocrystals Enable Neural Stem Cell Loading For Treatment of Ovarian Cancer

Pamela Tiet[1,4,#], Jie Li[1,#], Wafa Abidi[1,#], Rachael Mooney[2,3], Linda Flores[2,3], Soraya Aramburo[2,3], Jennifer Batalla-Covello[2,3,4], Joanna Gonzaga[2,3], Lusine Tsaturyan [2,3], Yanan Kang[1,4], Yvonne R. Cornejo[1,4], Thanh Dellinger[5], Ernest Han[5], Karen S. Aboody [2,3,4‡*], Jacob M. Berlin[1,4‡*]

[1]Department of Molecular Medicine, [2]Department of Developmental and Stem Cell Biology, [3]Division of Neurosurgery, [4]Irell and Manella Graduate School of Biological Sciences, Beckman Research Institute at City of Hope, [5]Department of Surgery, City of Hope, 1500 East Duarte Road, Duarte, CA, 91010, United States.

[‡]Principal Investigators K. S. Aboody and J. M. Berlin contributed equally to this manuscript
*Corresponding Authors:
Jacob M. Berlin, PhD.
Associate Professor, Division of Molecular Medicine
City of Hope, 1500 East Duarte Rd, Duarte, CA 91010
Phone [626/256-4673] Email: jberlin@coh.org
Karen Aboody, MD
Professor, Department of Developmental and Stem Cell Biology
City of Hope, 1500 East Duarte Rd, Duarte, CA 91010
Phone [626/256-4673] Email: kaboody@coh.org

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Neural Stem Cells, Ovarian Cancer, Targeted Drug Delivery, Silica Nanoparticles, Paclitaxel, Chemotherapy

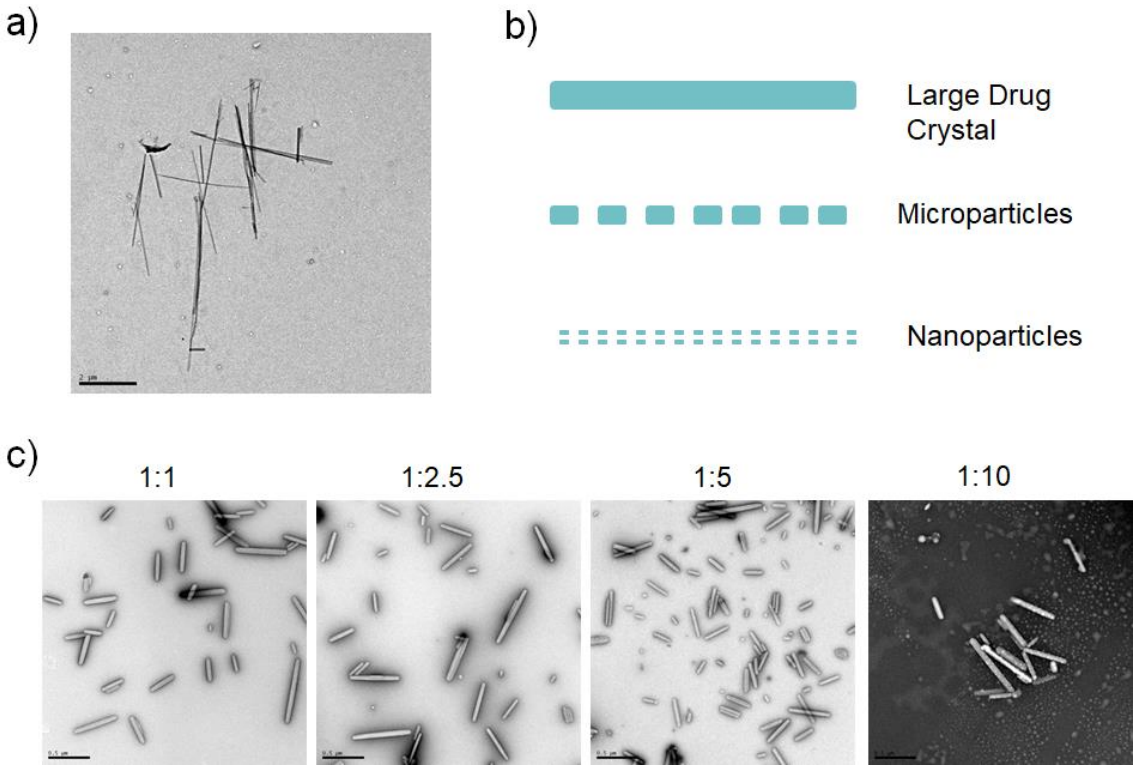


Figure S1. a) TEM image of whole Paclitaxel crystals (scale bar: 2µm). Schematic of large drug crystals being broken down into small nanoparticles/nanocrystals by sonication. c) TEM images of PTX nanocrystals prepared using various PTX to F127 ratios (1:1, 1:2.5, 1:5, and 1:10) with negative staining by uranyl acetate (scale bar: 0.5 µm).

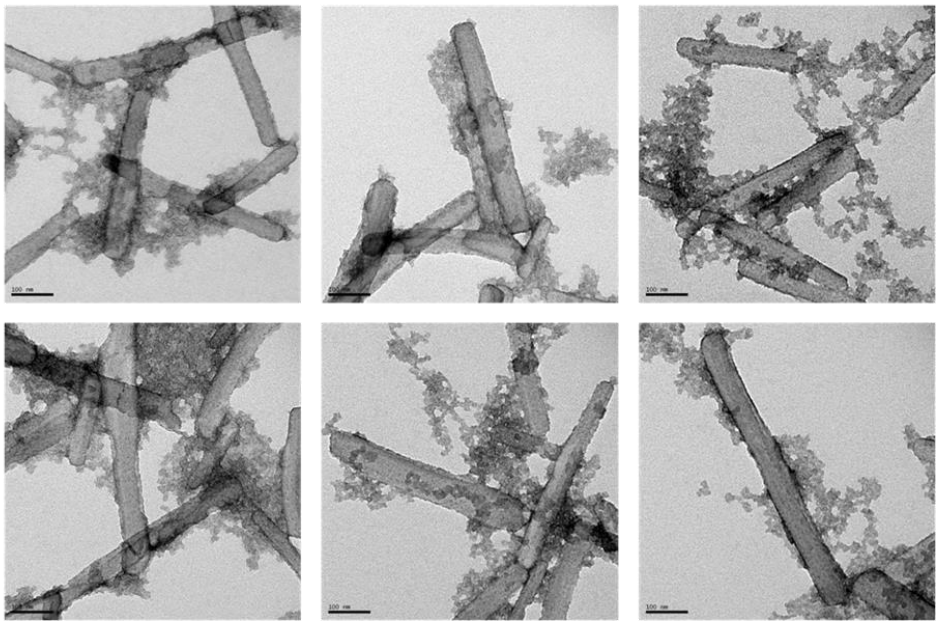


Figure S2. TEM images of intial attempt to grow a silica shell around PTX-NCs using TEOS and NaOH. The addition of TEOS and NaOH caused spontaneous networks of silica to form in solution. The silica networks trapped many of the PTX-siNCs, causing aggregation (scale bar: 100 nm).

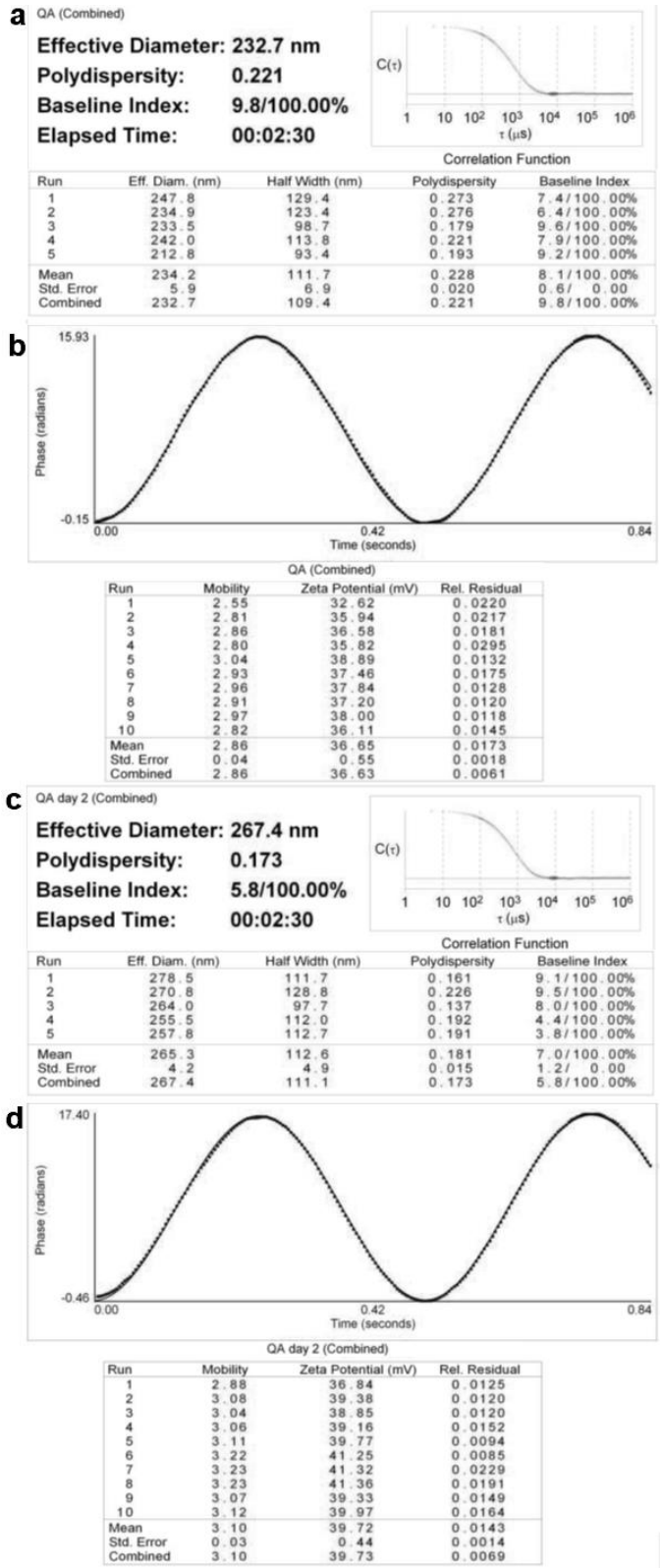
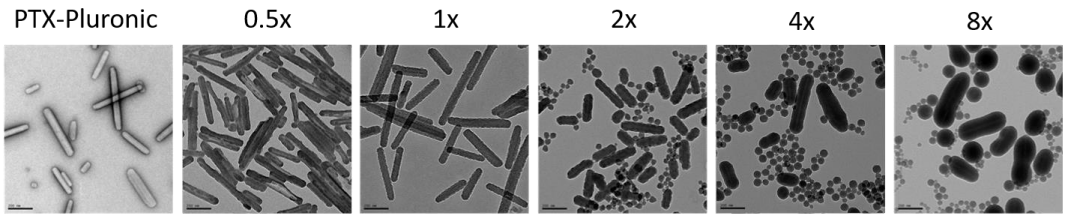


Figure S3. Si-PTX-NCs were immediately characterized after synthesis by measuring a) size by DLS and b) zeta potential. Si-PTX-NCs stored at room temperature for 24 hours were analyzed again for c) size and d) zeta potential.

a)



b)

	0.5x	1x	2x	4x	8x
PTMS (mM)	3.59	7.17	14.35	28.69	57.38
TEOS (mM)	2.40	4.80	9.60	19.19	38.39
APTES (mM)	3.57	7.14	14.29	28.57	57.14
Shell thickness (nm)	n/a	36 ± 8	49.4 ± 13	64.3 ± 8	113.1 ± 12

Figure S4. The thickness of the silica shell can be controlled. **a)** The amount of silica precursors can be adjusted to increase or decrease the silica shell. When PTMS, TEOS, and APTES were reduced, a very thin, spotty layer of silica was produced in the 0.5x Si-PTX-NCs condition. The 1x formulation yielded a uniform silica layer around the PTX-NCs. As PTMS, TEOS, and APTES were further increased in the 2x, 4x, and 8x PTX-siNC conditions, the thickness of the silica shell increased as well, however, spherical silica nanoparticles also formed in the background (scale bar: 200 nm). **b)** Final molar concentration of silica precursors added for each condition.

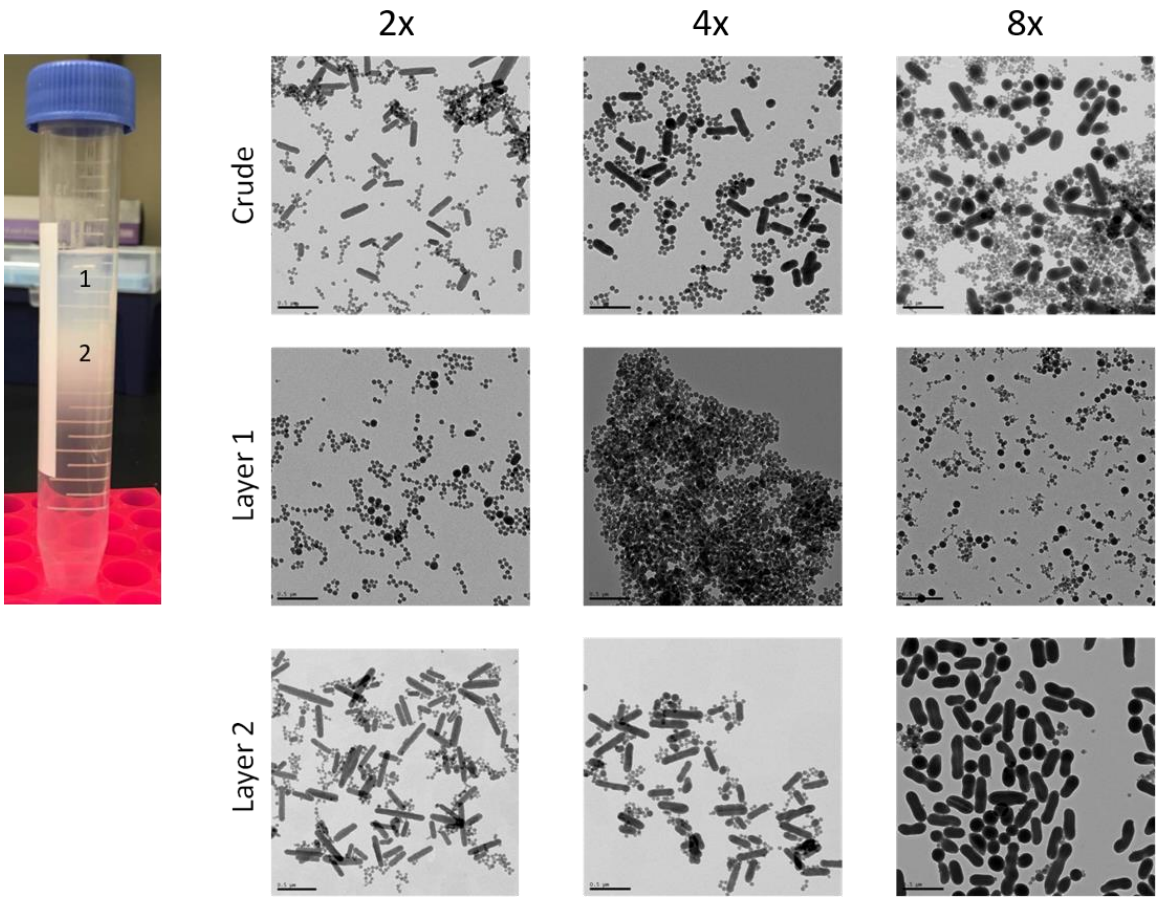


Figure S5. The sucrose gradient isolated Si-PTX-NCs from spherical silica nanoparticles. In the 2x and 4x Si-PTX-NC formulations, there were some carry-over of spherical nanoparticles. However, for the 8x Si-PTX-NC formulation, pure Si-PTX-NCs can be isolated with minimal carry-over of spherical nanoparticles (scale bar: 0.5 µm)

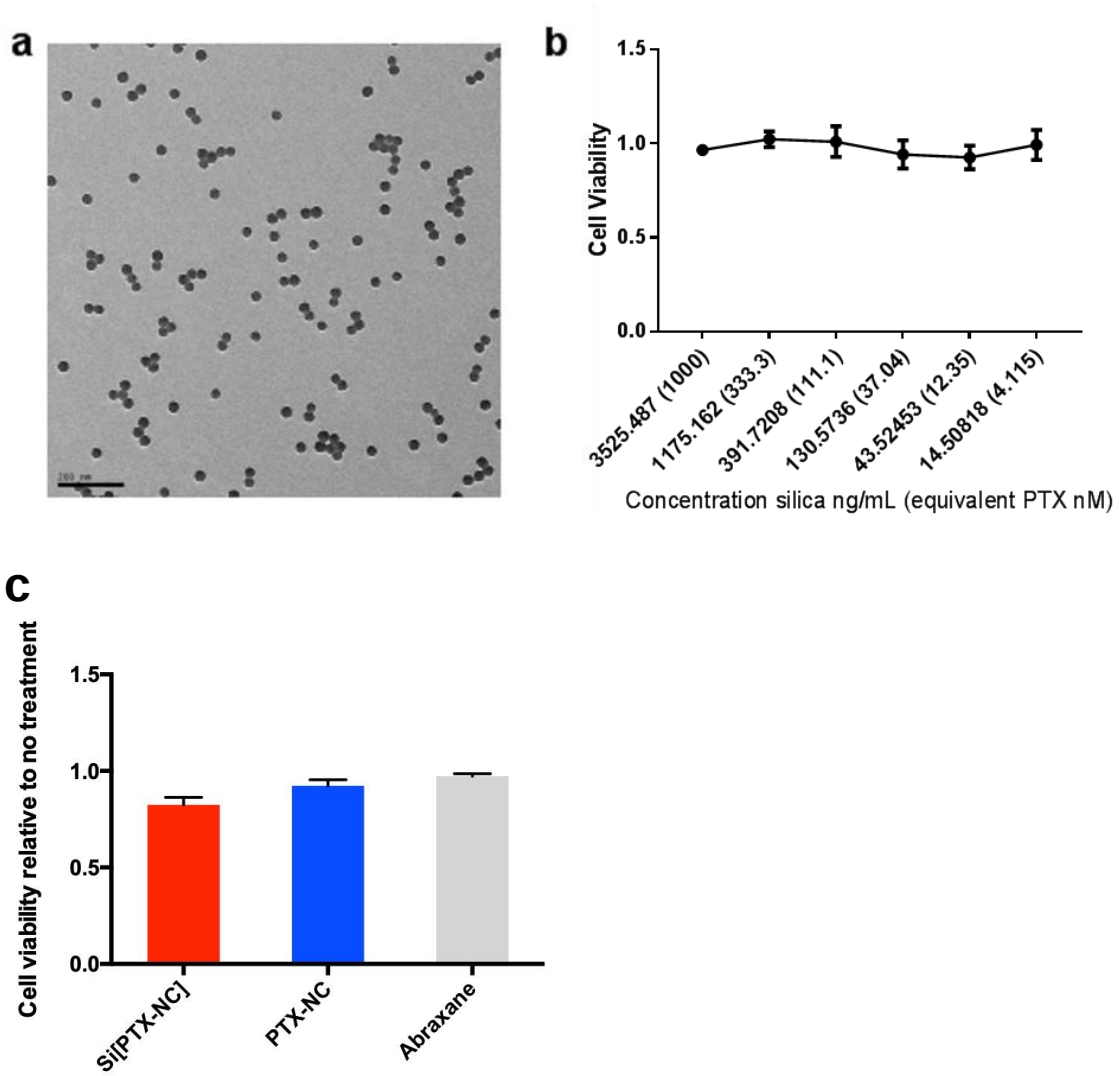


Figure S6. a) TEM image of empty silica nanoparticles (scale bar: 200 nm). b) Cytotoxicity to OVCAR8 cells of empty silica particles. In order to aid comparison to Figure 3, the x axis indicates the amount of silica and the dose of PTX contained in Si[PTX-NC]s containing the same amount of Si. c) viability of NSCs after exposure to the different formulations.

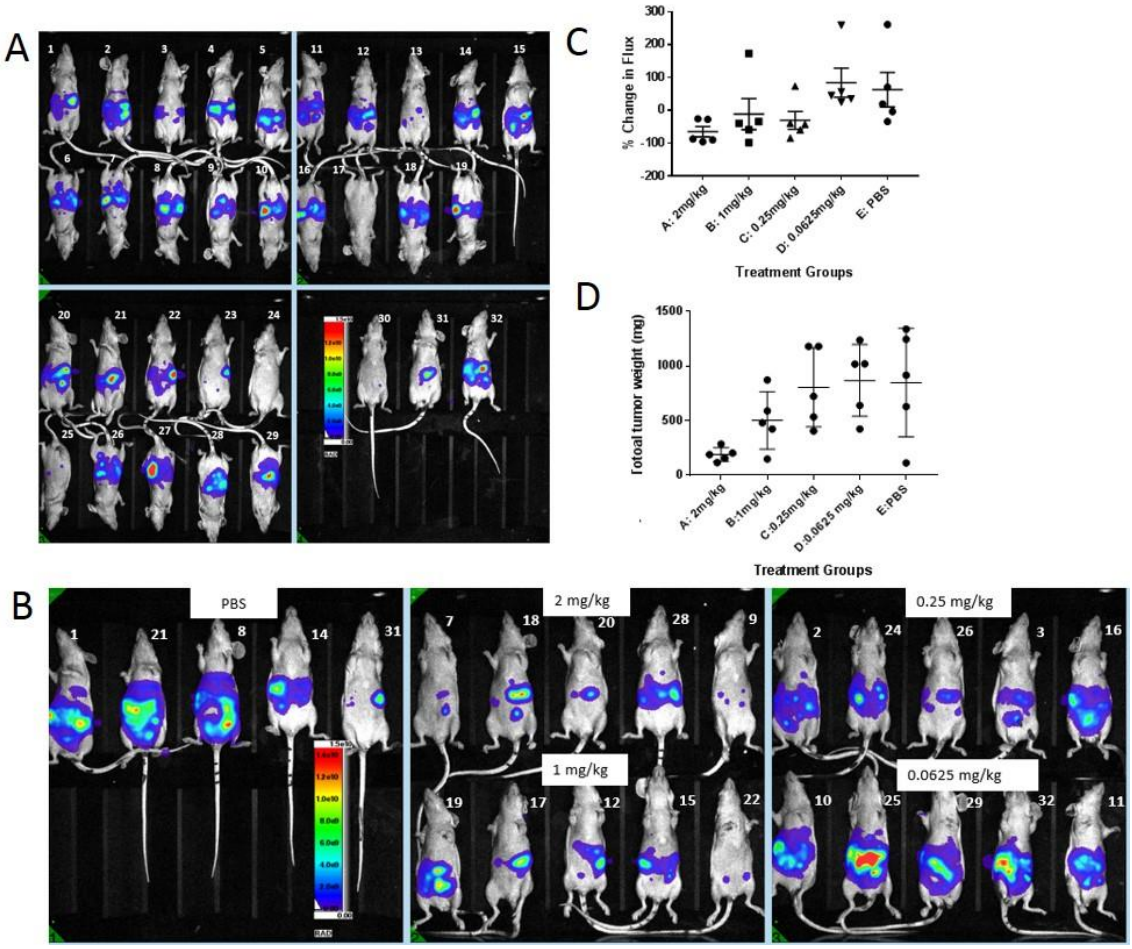


Figure S7. Luminescent images of mice before (A) and after (B) treatment for 3 weeks, 2 times a week, with Free PTX-NC at increasing doses (0.0625 mg/kg, 0.25 mg/kg, 1 mg/kg, 2 mg/kg and PBS control group). C- Quantified analysis of luminescent imaging: % of flux increase. D) Total tumor weight collected after sacrificing mice at the end of the treatment. Treatment here started at 3 weeks after tumor injection. After the pre-treatment imaging (in A), all mice were repartitioned into groups based on the mean intensities (with exclusion of mice with low to no signal) then randomly treated with the mentioned treatments.

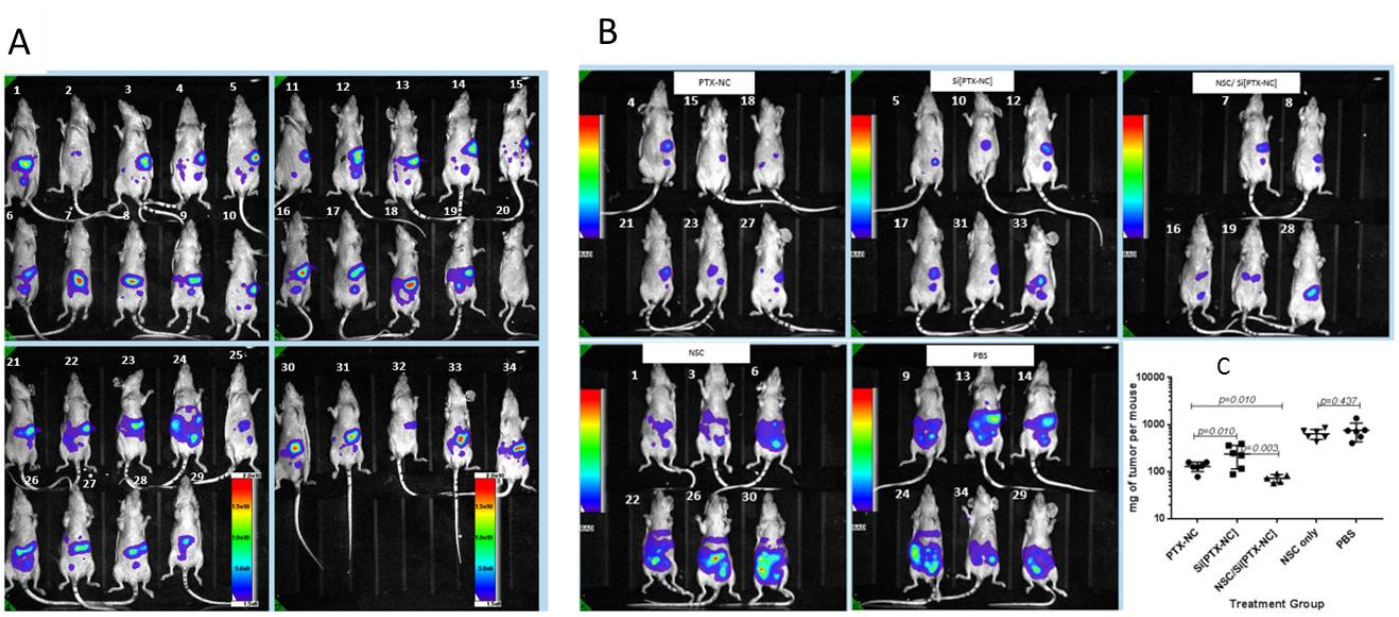


Figure S8. Luminescent imaging of mice (A) before and (B) after treatment with: PTX-NC, Si[PTX-NC], NSC/Si[PTX-NC], NSC and PBS. C) Total tumor weight collected after sacrificing mice at the end of the treatment. Treatment here started at early time point: 12 days after tumor injection (2.10E6 OVCAR8 cells, injected IP) and the dose of the PTX administrated was kept constant: 0.5 mg/kg two times a week for 3 weeks. After the pre-treatment imaging (in A), all mice were repartitioned into 5 groups of 6 mice each, based on the mean intensities (with exclusion of mice with low to no signal) then randomly treated with the mentioned treatments.

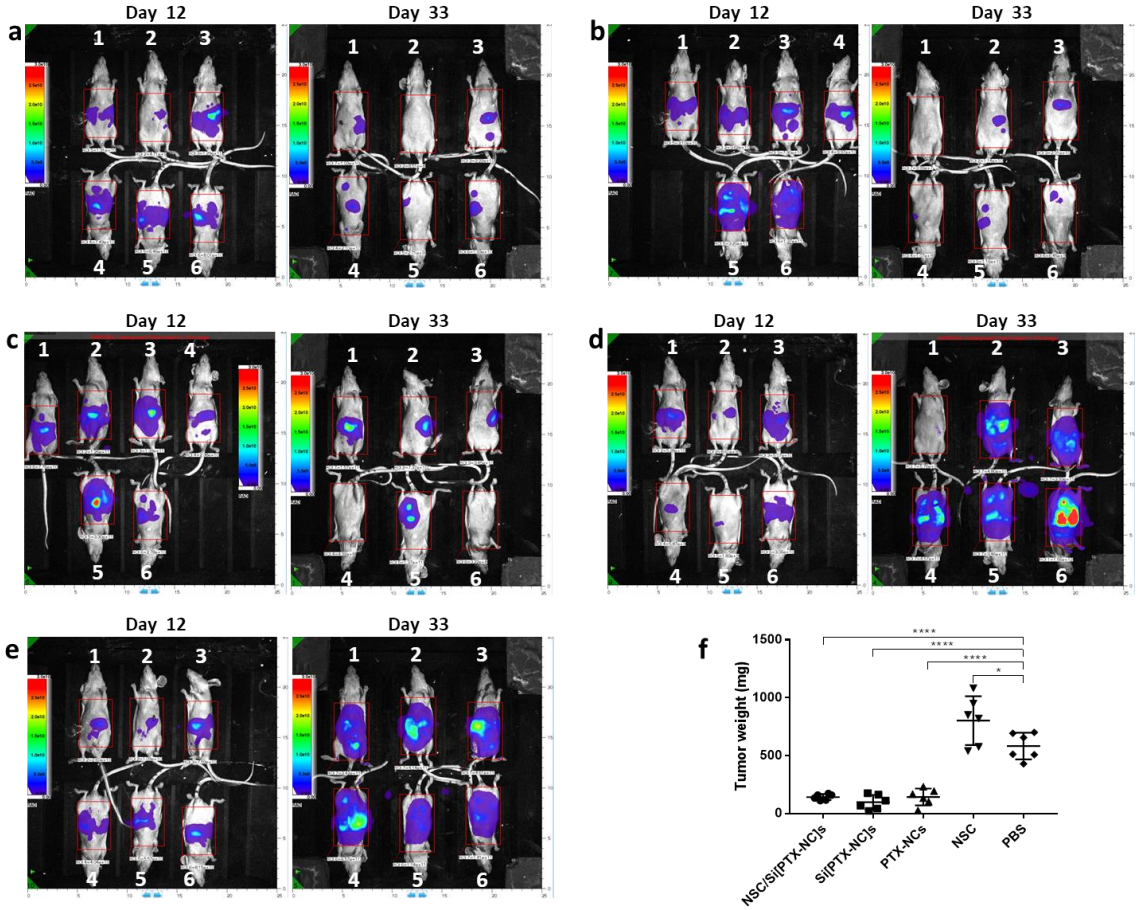


Figure S9. Luminescent imaging of mice before (day 12) and after (day 33) treatment with a) NSC/Si[PTX-NC]s, b) Si[PTX-NC]s, c) PTX-NCs, d) NSC, e) PBS. f) Total tumor weight collected after sacrificing mice (day 34) at the end of the treatment. Treatment here started at early time point (14 days) after tumor injection and the dose of the PTX administrated was: 4.72 mg/kg on day 14, 3.33 mg/kg on day 16, 2.73mg/kg on day 21, 4.2 mg/kg on day 23, 2.34 mg/kg on day 28 and 3 mg/kg on day 30.. Mice showed in all images at day 12 are repartitioned into groups based on the mean intensities after exclusion of mice with low to no signal (not showed here)