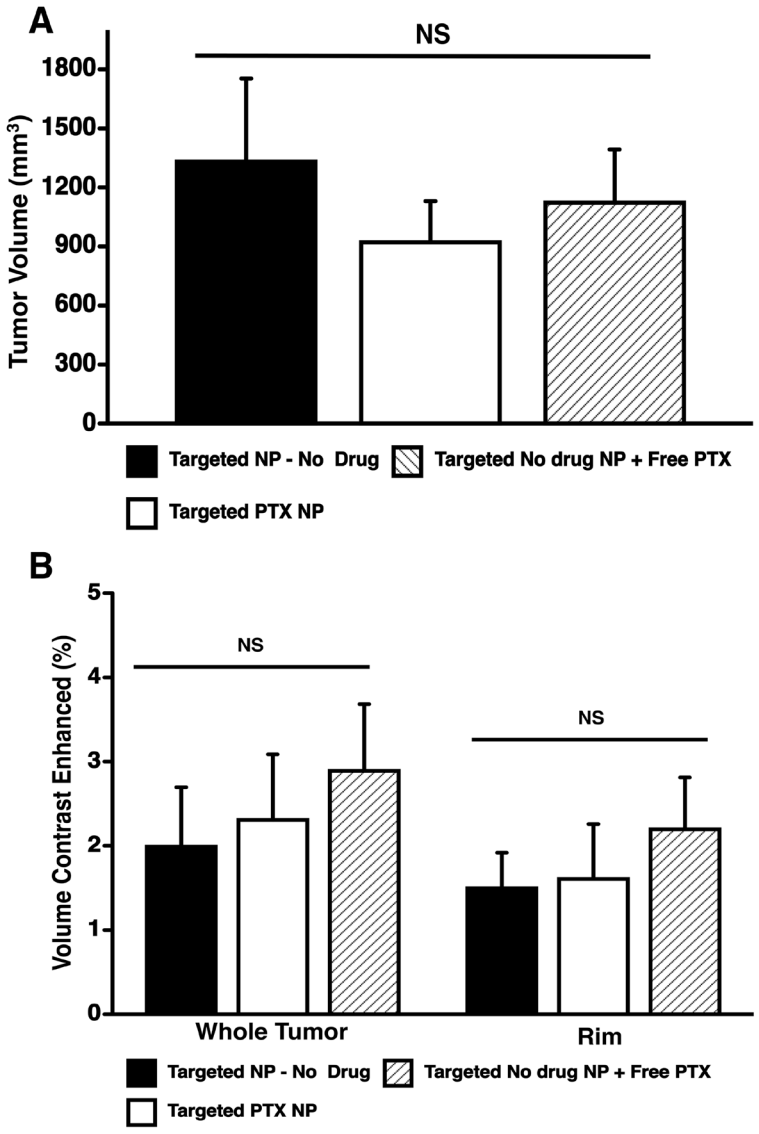
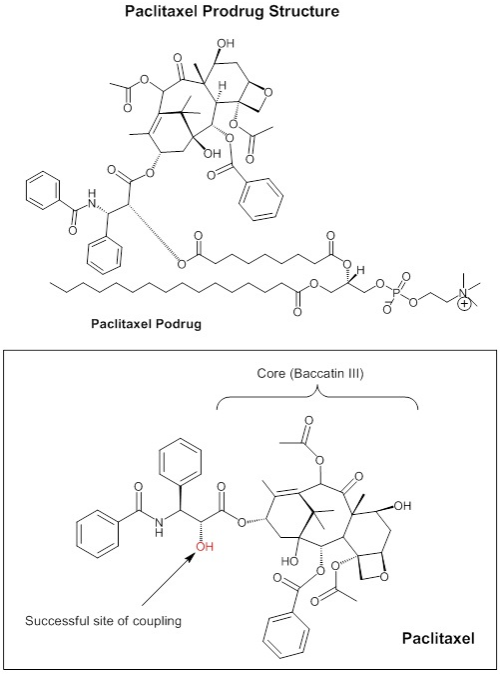
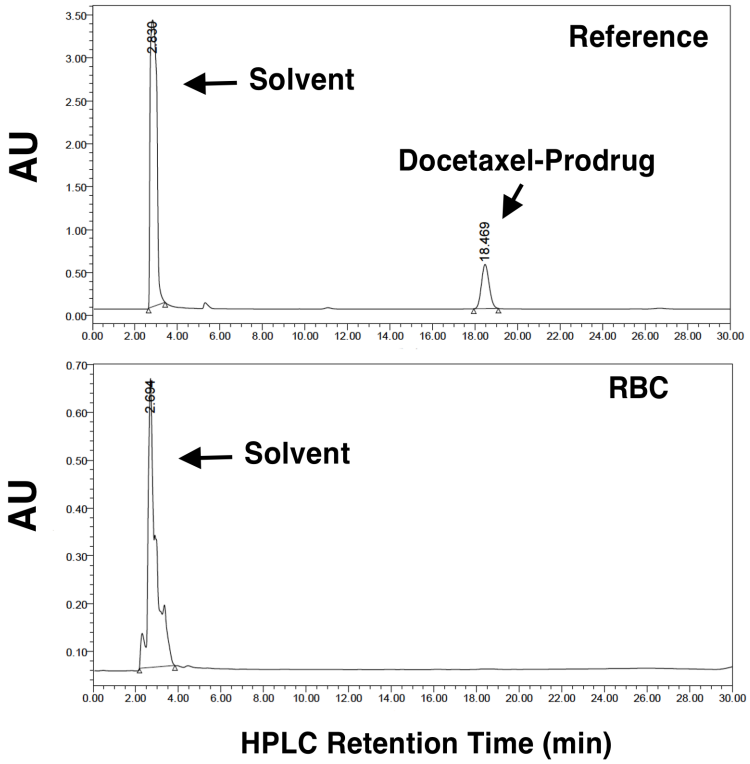


Supplemental Figure 1. A) $\alpha_v\beta_3$-targeted paclitaxel (PTX) PFC nanoparticles (NP) had no impact on tumor volume. No difference ($p>0.05$) was noted between animals given $\alpha_v\beta_3$-targeted PFC nanoparticles (no drug) or $\alpha_v\beta_3$-targeted PFC nanoparticles plus dose equivalent Taxol®. B) No effect ($p>0.05$) of $\alpha_v\beta_3$-targeted paclitaxel PFC nanoparticles noted on Vx2 angiogenesis as a whole tumor or on the tumor periphery versus controls.

Supplemental Material and Supplemental Figure 2. Paclitaxel is a clinically relevant broad-spectrum anticancer agent, which was utilized in the present study for site-specific anti-angiogenesis therapy. Paclitaxel has a low solubility in water (<0.1 µg/ml) and from the synthetic stand point, chemistries involving esterification of the 2'-hydroxyl group are feasible providing a site for functionalization. **(Supplemental Figure 2)** The 2'-hydroxy group is the most reactive of the hydroxy groups in paclitaxel. For the synthesis of paclitaxel prodrug, several reagents were attempted for conjugating the PAzPC (1-palmitoyl-2-azelaoyl-sn-glycero-3-phosphocholine) through the 2"-hydroxyl group that included dicyclohexyl carbodiimide (DCC)/dimethylaminopyridine (DMAP) and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide/ dimethylaminopyridine (EDCI/DMAP). Between these reagents, DCC/DMAP were found to be the most efficient coupling agents and produced the desired compound in 87% yield. The compound was isolated and purified by flash chromatography utilizing a Biotage Flash+ system and the structure was confirmed by

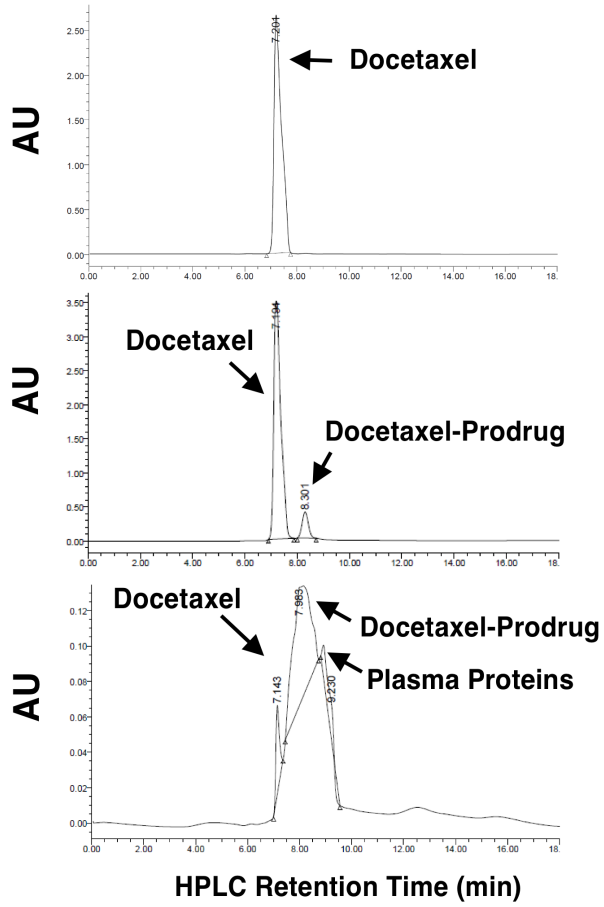




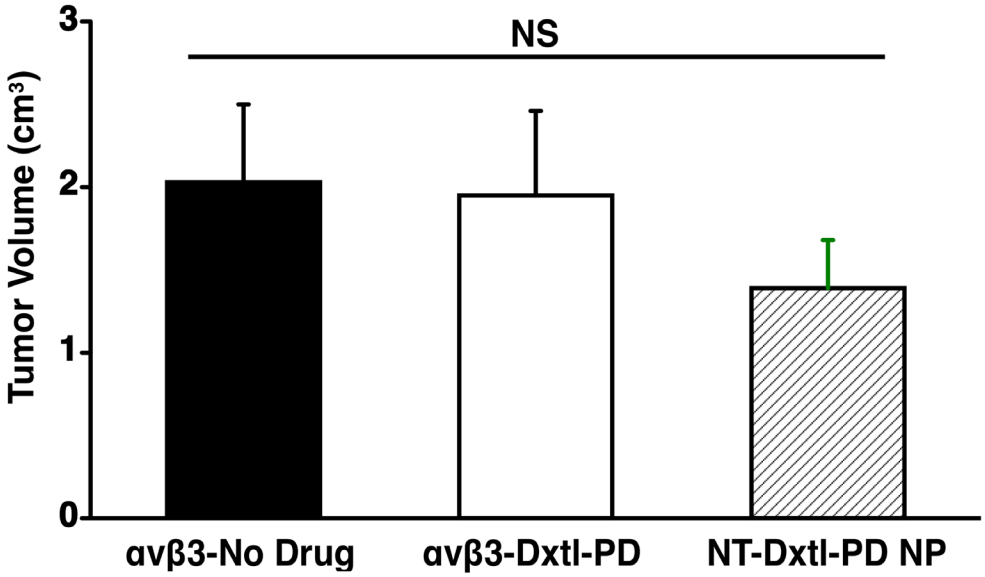
Supplemental Figure 3. HPLC assessment of the passive transfer of Dxtl-PD from nanoparticles to erythrocytes (RBCs) during co-incubation in vitro. No transfer of Dxtl-PD was detectable in the RBC fraction of the whole blood.

Procedure: 0.2 mL PFOB NPs containing 0.2 mole% Dxtl-PD was spiked into 1ml whole blood in 4 ml PBS and incubated at 37 ºC for 2-3 hours. Next, sample was centrifuge at 1000 rpm for 10 min. An aliquot from RBC fraction located above the dense PFOB NPs was washed 3X 4 ml PBS. 100 microliter of the washed RBC were mixed with 2-propanol (0.2 ml) and deionized water (0.2 ml), then centrifuge at 11000 rpm for 5 min. The supernatant (200µl) was used for HPLC analysis. No peak was observed at RT 18 min

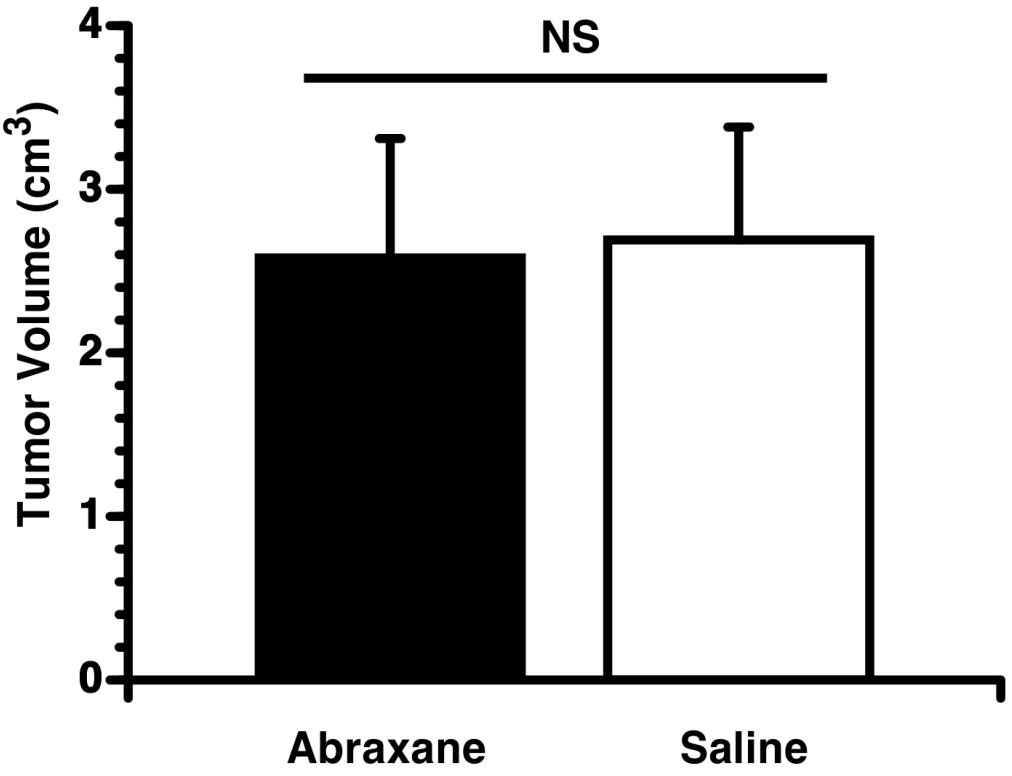
HPLC analysis: Mobile phase: A 0.2 M NH4Ac pH 4.5; B: 100% MeOH; Condition: 70% B, isocratic; Column: Phenomenex c18 5 u 100 A 4.6X250 mm; Detection: UV 227 nm; Flow rate: 1 ml/min; Run time: 30 min



Supplemental Figure 4. Shown are the relative retention times of free docetaxel, Dxtl-PD, and the metabolism of Dxtl-PD in methanol added to phospholipase enriched plasma. As expected, docetaxel retention is somewhat less than the HPLC retention of Dxtl-PD. When Dxtl-PD was added to lipase rich plasma, docetaxel was liberated and differentiated from the parent prodrug. Not the column and conditions in this run differ from those used in **Figure 5**. **Procedure:** Dxtl-PD was dissolved in 0.25 ml chloroform and alcohol and mixed with 0.25 ml fresh human plasma, 0.25 ml lipase 0.278 mg and15 mM calcium in saline and allowed to incubate at 37°C overnight. The mixture was centrifuged at 14,000 rpm for 30 min, 20 µl of the supernatant was injected and analyzed by HPLC. **HPLC analysis:** Column: PHOLIPIDEC LC Column from Astec; Mobile phase: methanol 100%; Running condition: Isocratic; Flow rate: 0.5 ml/min; Detection: UV 227 nm



Supplemental Figure 5. Vx2 tumor volume changes following treatment with $\alpha_v\beta_3$-Dxtl-PD NP versus controls showing no significant differences (NS, $p>0.05$).



Supplemental Figure 6. Vx2 tumor volume changes following treatment with Abraxane versus saline controls showing no significant differences (NS, p>0.05).