Electronic Supplementary Material (ESI) for Chemical Science.

Supplementary Results

Antiangiogenic Platinum Through Glycan Targeting

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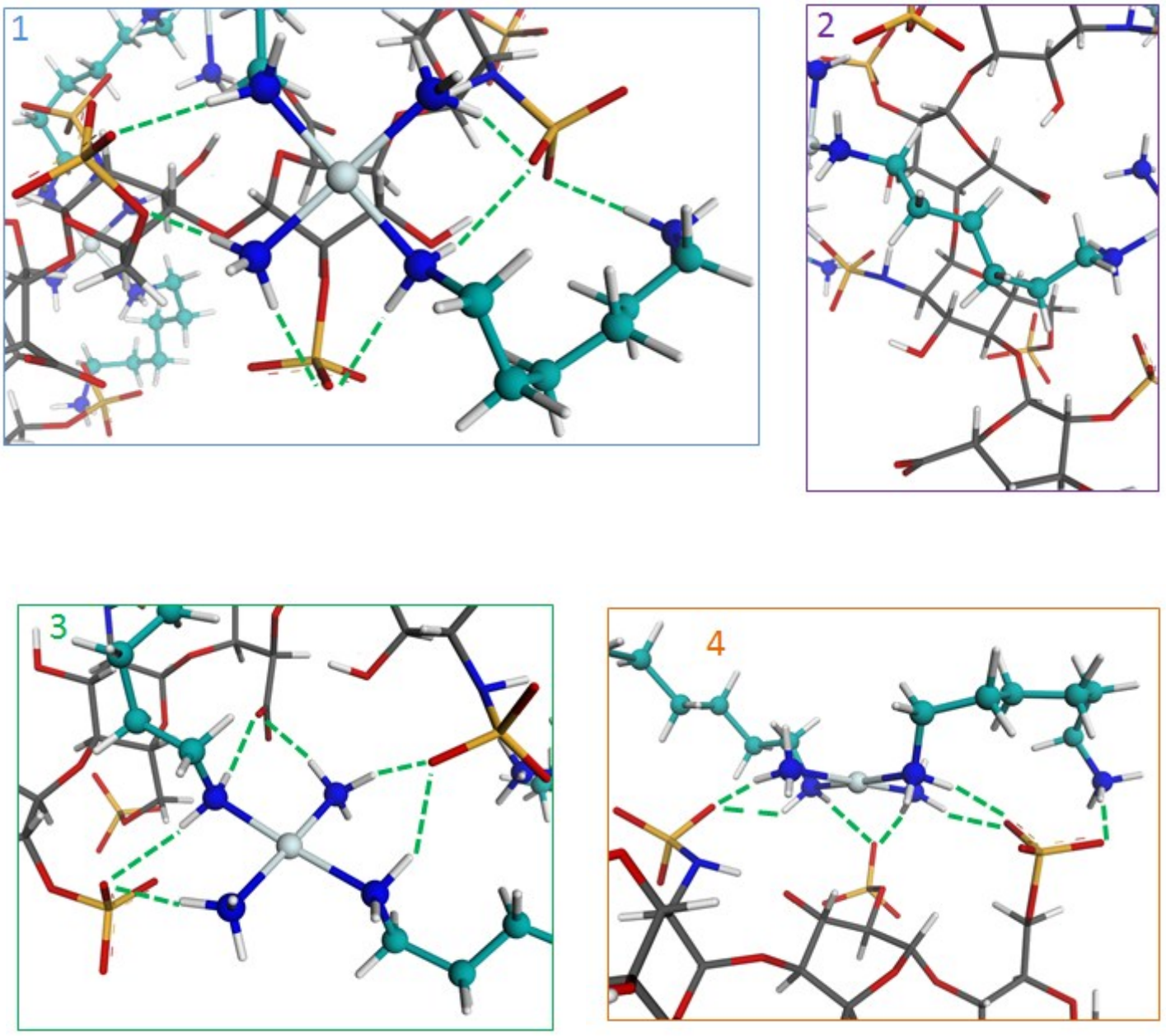
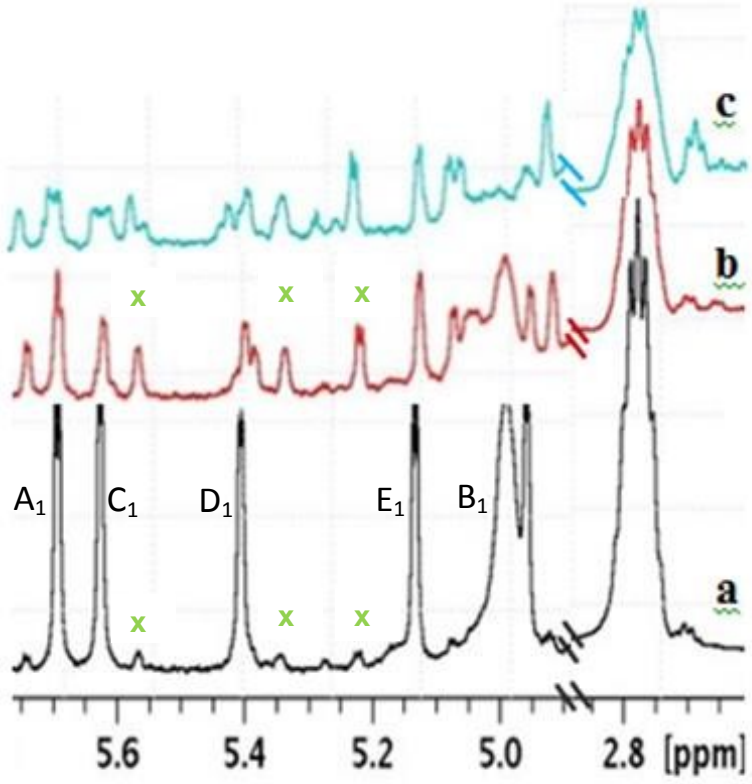
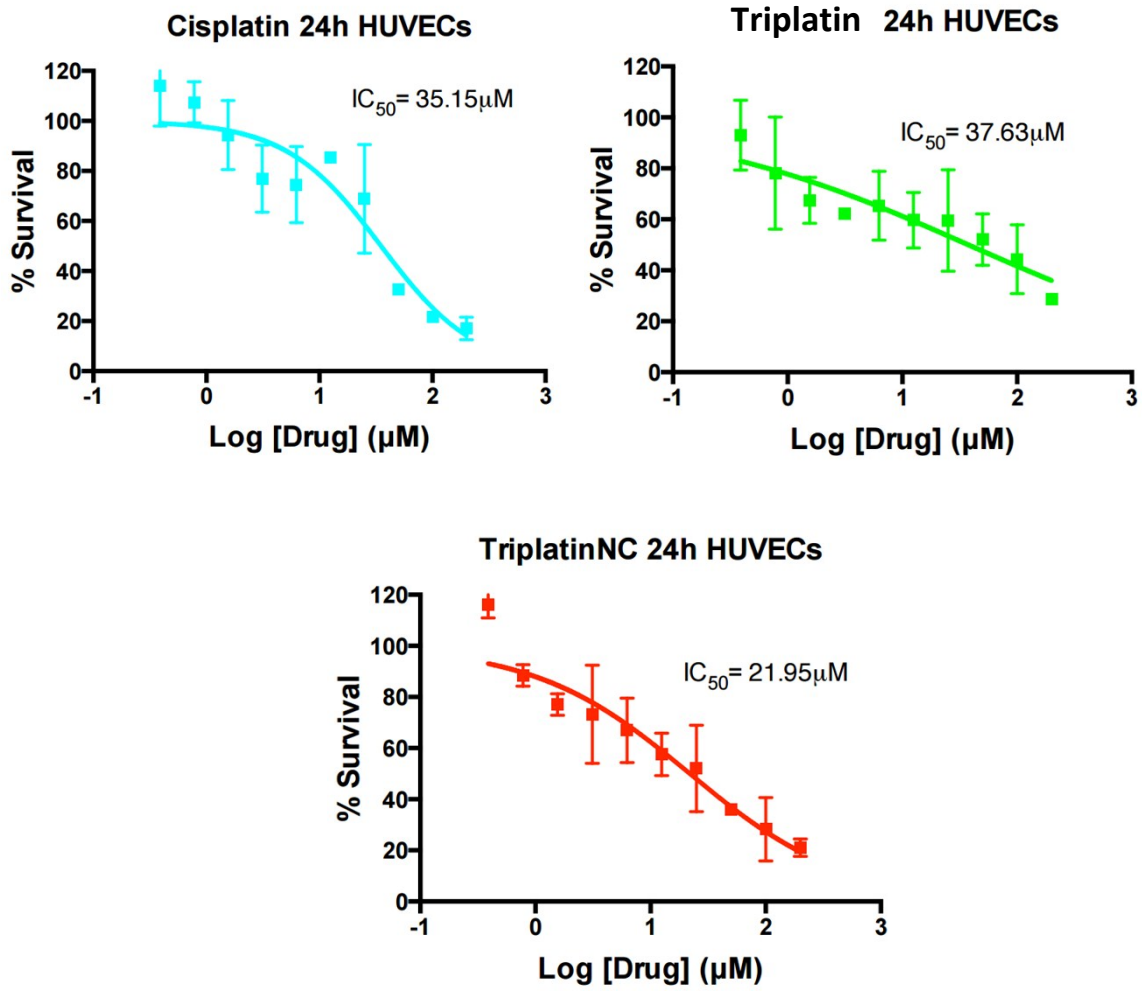


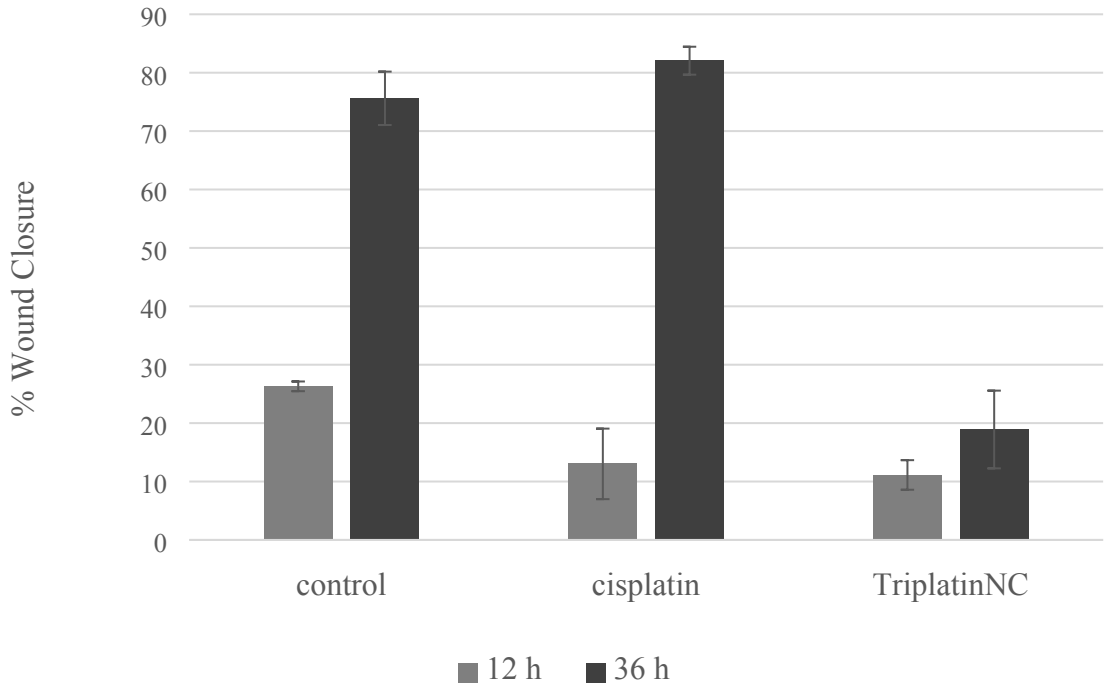
Supplementary Figure 1. Highlighted individual regions from the DFT calculations of the optimized structure of TriplatinNC with a heparin hexamer [IdoA(2S)-GlcNS(6S)]$_3$ from **Figure 2c**. Sulfate clustering of individual platinum coordination spheres is apparent in Regions 1,3 and 4 while a diamine linker (Pt-$NH_2(CH_2)_6NH_2$-Pt) – oligosaccharide (sugar) backbone contact is seen in Region 2.



Supplementary Figure 2. ^{1}HNMR spectra of Triplatin+ FPX + heparanase in anomeric region and the Pt–H_2NCH_2 protons of Triplatin in 2.5 – 3.00 ppm region. (a) Triplatin + FPX no enzyme. Note the non-covalent contribution with A_1 notations etc. from **Fig. 3a**. The major chemical shift changes of the spectrum are identical to **Fig. 3b (i)**. (b) Spectrum after 1h in presence of heparanase. (c) Spectrum after 24h in presence of heparanase. Note the appearance of upfield peaks in 2.8ppm region indicating formation of covalent FPX-Pt-NH_2CH_2 species through Pt-Cl displacement. Peaks labelled **x** initially grow with time (a -> b) but anomeric region becomes complicated over time possibly dues to presence of multiple species with different environments for the proposed Pt-sulfate covalent binding.



Supplementary Figure 3. Sensitivity of human umbilical vein epithelial cells (HUVECs) to cisplatin, Triplatin, and TriplatinNC treatments determined by the MTT growth inhibition assay. HUVECs were seeded in a 96-well plate in 100 µl of media and allowed 24 h to attach. Cells were drug treated for a period of 24 h. After drug removal, cells were incubated with 0.5 mg/mL MTT reagent (3,4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) in media for 3 h at 37 °C. After reagent was removed, 100 µl of DMSO was added to each well. The plate was then incubated on a shaker at room temperature in the dark. The spectrophotometric reading was taken at 570 nm using a microplate reader. The average ± s.d. of two independent repeats is shown.



Supplementary Figure 4. Effects of cisplatin and TriplatinNC on serum-induced wound closure in HCT116 cells. 5 x 10^5 HCT116s were seeded in a 24-well plate containing 1 ml media (RPMI containing 10% FBS). After cells reached confluence, a scratch was made on the monolayer using p10 pipette tips. The wells were washed 2x with PBS. The media was replaced with or without 2μM cisplatin or TriplatinNC. The extent of closure of the scratch at 12 and 36 h was compared to the control by light microscopy, digital imaging, and analysis by ImageJ software. The results are reported as the average of two independent experiments.