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Internet that contain copyrighted material. The use of this website constitutes agreement to our US copyright policies.Modulation of the Efficacy of Therapies for Prostate Cancer by the Enhanced Interfacial Effect.

The influence of cell-substrate and cell-cell interactions on the efficacy of therapies in vitro and in vivo is poorly understood. The effectiveness of drug delivery was investigated with a prostate cancer model

consisting of PTEN-negative PC3 cells and normal prostate RWPE-1 cells. Cells were plated on either tissue culture plastic or a surface previously modified with synthetic peptides. The toxicity of camptothecin and

paclitaxel was evaluated by live-cell staining and flow cytometry, whereas the dose-response to Taxol and camptothecin was determined by MTT assays. Intracellular drug distribution was assessed by confocal microscopy. In vivo

studies were conducted with murine prostate cancer cells and immunocompetent mice. Administration of Taxol to PTEN-negative PC3 cells reduced the number of cells by >90% on tissue culture plastic; however, PTEN-positive RWPE-1 cells

were highly resistant. Camptothecin was more toxic in RWPE-1 cells, which were more sensitive to paclitaxel. Cell-substrate interactions enhanced the intracellular distribution and enhanced the efficacy

of Taxol and camptothecin in PTEN-positive RWPE-1 cells, but not in PTEN-negative PC3 cells. The efficacy of Taxol and camptothecin increased on the modified surface of RWPE-1 cells compared with tissue culture

plastic, and the maximum tolerated dose of Taxol increased at least five-fold. Similarly, the antitumor activity of Taxol and camptothecin increased approximately 10-fold on the modified surface of PC3 cells.

Tumor regression was observed in all of the drug treatment groups, but the number of tumor-free mice was increased five-fold in the group that received Taxol plus the peptide modified surface. These studies show that the cell-

substrate interaction modulates the efficacy of drug delivery, resulting in improved efficacy of Taxol and cam 2d92ce491b