Researchers at the University of South Florida have derived a membrane estrogen receptor bound multimodal nanoparticle for the targeted co-delivery of mitotic inhibitor and a BH3 mimetic polymeric conjugate for the potential use in breast adenocarcinoma.

Breast adenocarcinoma is a malignant cancer that can move aggressively and become difficult to treat. Pharmaceuticals such as paclitaxel (PTX) have become the new “gold-standard” for breast cancer treatment. Although PTX is one of the most effective anticancer agents for the treatment of breast, ovarian, and lung cancer, it has substantial shortcomings including acquired drug resistance, myelosuppression, neurotoxicity. The acquired PTX drug resistance has been linked to Bcl-2 overexpression. Bcl-2 regulates apoptosis; overexpression of the oncogene leads to unwanted replication of cells. To combat these challenges, the inventors have developed a multimodal nanoparticle by interpolating a Bcl-2 inhibitor (BH3 mimic) and gossypol (G) into a PTX drug delivery system. This effective drug nanodelivery system provides therapeutic efficacy and amelioration of drug resistance, as well as ratiometric release in specific tumor site.

The invention entails construction of a novel targeting moiety β-cyclodextrin conjugated estrone (CDE1) that has been synthesized and integrated in a polymeric nanoparticle. The integration of CDE1 increases uptake by the tumor and decreases the side effects of the encapsulated cytotoxic drugs. The enhanced anti-tumor activities with improved targeting efficacy have been achieved in vitro and in vivo. The systemic toxicity associated with the solvent of the cytotoxic drugs is minimal due to the hydrophilic nano-formulation. Moreover, the molecular mechanism for the cell death induced by the nanoparticle has been explored thoroughly by a systematic proteomics study. The results suggest that enhanced G2/M cell cycle arrest and PI3K/Akt/mTOR mediated autophagy, account for the exceedingly potent anti-tumor activity of this convergent nanoparticle.

ADVANTAGES:
- Improve targeting efficacy
- BH3 mimic has anti-neoplastic activities
- Induces cell death
- Effectively deliver Paclitaxel
- Counters Paclitaxel drug resistance

Multimodal Nanoparticle Combats Drug Resistant Breast Cancer

Schematic of the novel nanoparticle

Targeted multifunctional Nanoparticles formulated by functionalized PEG-PLA and synergetic chemotherapeutics, for improved anticancer activity

The various modifications to the PEG-PLA polymer allow the nanoparticle to be capable of targeted co-delivery of therapeutics

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