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Remotely Triggered Polymeric Nanoparticles for the Treatment of Triple Negative Breast Cancer.

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Triple Negative Breast Cancer (TNBC) has the worst prognosis among all the sub-types of breast cancer. Currently no targeted treatment has been approved for TNBC management. While TNBC does not overexpress hormone receptors, it has been found to over express certain receptors like transferrin (TfR) or folate receptors. The aim of this research is to synthesize targeted polymeric nanoparticles for TNBC. MDA-MB-231 cells are used as a representative TNBC cell line in this study. Active targeting of TNBC is achieved by conjugating the nanoparticles to a peptide (Tr) that binds to the TfR. Photodynamic Therapy (PDT) using polymeric nanoparticles was explored for TNBC treatment. PDT utilizes a secondary form of targeting by remotely triggering benzoporphyrin derivative monoacid (BPD) using near infrared light. When irradiated at 690nm, BPD induces cytotoxicity via generation of reactive oxygen species. The polymeric nanoparticles were characterized for size, zeta potential, and drug release at 37°C. The morphology of the nanoparticles was confirmed using electron microscopy and cell uptake was monitored *in vitro* using fluorescent microscopy. PDT was carried out at 500nM BPD concentration using a 690nm laser. Cytotoxicity of these targeted polymeric nanoparticles was assessed using a standard colorimetric viability assay (MTT). The nanoparticles synthesized were fairly monodisperse and the release studies demonstrated sustained BPD release from the nanoparticles. Receptor mediated endocytosis of the active nanoparticles was studied by using FITC conjugated peptide and the FITC signal was observed using fluorescent microscopy. Stronger BPD fluorescent signal for the active targeting nanoparticles (PLGA-PEG-Tr) compared to the passive (PLGA-PEG) nanoparticles. Significant cell death following PDT was observed in all the treatment groups, which was also confirmed by imaging the cells post-treatment using standard live-dead stain. PDT is a fairly versatile and non-invasive form of treatment and using targeted nanoparticles it can be adapted for other drugs and diseases.

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