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Cytotoxicity of Gemcitabine- and Paclitaxel-loaded Poly(lactic-co-glycolic acid) Microparticles Against Human Pancreatic Adenocarcinoma Cell Lines

Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer death in the United States. Most patients are not surgical candidates due to the advanced stage of their disease at diagnosis and current systemic treatments have not been effective at increasing surgical candidacy or extending survival.

Poly(lactic-co-glycolic acid) (PLGA) is an FDA approved polymer for the preparation of sustained release injectable microparticles. PLGA microparticles (MPs) can be loaded with chemotherapeutics like gemcitabine and paclitaxel for local injection into tumors. PLGA undergoes hydrolytic cleavage allowing drug-loaded MPs to consistently release the drug.

Treatment of PDAC with local injection of drug-loaded MPs would provide new options for patients who present with unresectable tumors. Because the MPs are injected directly into the tumor, a higher dose of the chemotherapeutic should reach the cancer cells and less should enter the patient's systemic circulation, which should increase efficacy and decrease systemic toxicity compared to systemic drug infusions.

Methods: Gemcitabine-loaded MPs (GMPs), Paclitaxel-loaded MPs (PMPs), and blank (no drug)-loaded MPs were formulated using a water in oil in water (W/O/W) emulsion. The human PDAC cell lines MIA PaCa-2 and PANC-1 were treated with GMPs only, PMPs only, and PMPs and GMPs concurrently for six days. After six days, cells were collected for protein and RNA isolation and cell viability assays were be performed to assess the cytotoxicity of the different treatments.

Results: Treatment of both cell lines with the different MPs regiments results in significant cell death and cleaved-caspase-3 protein expression as compared to the controls.

Conclusions: Using an in vitro assay, we assessed the effects of the drug-loaded MP treatments on the viability of the PDAC cell lines. Next steps will involve protein and gene expression data analysis of the two cell lines after exposure to the MPs treatment conditions.