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Evaluation of Drug-loaded Microparticles In Human Pancreatic Ductal 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 release the drug over time. Treatment of PDAC with local injection of drug-loaded MPs would provide new options for patients who present with unresectable tumors. Since the MPs are injected directly into the tumor, a higher dose of the chemotherapeutic should reach the cancer cells and almost no drug 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 technique. The human PDAC cell lines MIA PaCa-2 and PANC-1 were treated with GMPs only, PMPs only, and PMPs and GMPs concurrently. After treatment, cells were collected for RNA isolation and flow cytometry analysis, and cell viability assays were performed to assess the cytotoxicity of the different treatments. Results: Treatment with the different MPs regimens resulted in significant cell death in both cell lines 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 flow cytometry and gene expression analysis of the two cell lines after exposure to the MPs treatments to understand differences observed.