Dr. Paul Oberstein

Pancreatic ductal adenocarcinoma (PDA) is an aggressive malignancy and a large public health burden in the United States. 80% of PDA patients suffer from a cachexia syndrome, characterized by muscle and weight loss and weakness, leading to diminished quality of life and intolerance of chemotherapy but there are no effective therapies for this syndrome. My mentor, Dr. Kenneth Olive has developed an advanced experimental platform with a genetically engineered model called the KPC mouse for translational studies of pancreatic cancer. We propose to use this model to identify factors that lead to the development of cachexia.

In previous work, we studied the effect of depleting stromal cells from pancreatic tumors and found that this led to the development of aggressive and highly lethal tumors. Subsequently, we have learned that KPC mice depleted of tumor stroma rapidly develop debilitating cachexia with 100% penetrance. We hypothesize that epithelial pancreatic cancer cells secrete soluble factors that lead to cachexia. Here we propose utilizing this validated system, advanced imaging techniques, genomics, proteomics, and metabolomics to identify tumor associated factors that cause cachexia. We will validate these studies in our large cohort of human samples with the goal of identifying targets to reverse this devastating complication of pancreatic cancer.