Pancreatic Adenocarcinoma is the deadliest form of cancer with a 5 year mortality rate of 94%. Nearly 40,000 people die of pancreatic cancer in the US each year, making the disease the 4th leading cause of cancer-related death in the US. Pancreatic cancer has the poorest prognosis among all cancers because it often metastasizes before detection. Metastasis is the migration of invasive tumor cells from the primary tumor to other organs in the body. Primary tumor cells are organized in a tight epithelial manner, expressing epithelial properties. In order to gain the motility and invasive properties required for metastasis, metastatic pancreatic tumor cells must undergo Epithelial-Mesenchymal Transition (EMT). The literature describes EMT as the loss of epithelial protein and RNA, and the upregulation of mesenchymal RNA resulting in mesenchymal protein and invasive properties. As EMT is a quintessential process for cancer plasticity and metastatic progression, a thorough understanding of the genetic mechanisms by which it occurs is imperative to developing treatments and methods for early detection.

My project seeks to determine the genetic mechanisms by which pancreatic tumor cells undergo EMT. I will employ a new and highly publicized technique called CRISPR-Cas to introduce loss of function mutations into cultured human pancreatic cancer cell lines. CRISPR-Cas technology uses a virus to introduce a double strand break in a gene of choice, effectively deleting the gene and eliminating its function. Using this technology I have designed viruses targeting a number of possible drivers of EMT. I will infect human pancreatic cancer cells with viruses targeting different genes of interest and assess the effects that these mutations have on cell motility, invasiveness and epithelial or mesenchymal identity.