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Analysis of cell growth and therapeutic efficacy of pancreatic cancer cells under varying oxygen environments

Pancreatic cancer is more difficult to treat than most other cancers because it is usually diagnosed at a late stage. This is due to the fact that pancreatic cancer does not cause symptoms until it is too late. The common symptoms for pancreatic cancer are weight loss, abnormal pain, back pain, nausea, vomiting, jaundice (yellowing of skin from toxic buildup in the liver).

Only about 10-15 percent of pancreatic cancer patients are diagnosed in a time frame considered for surgery. Even then the prognosis is poor, because 85 percent of the time the cancer will come back. In the best-case scenario only 25-30 percent of patients are alive five years after surgery.¹ The current therapy for surgery (early stages) is removing 95 percent of the pancreas including the tumor, but leaving 5 percent to serve as the insulin-producing functions. The commonly used drugs for pancreatic cancer (FDA approved) are Cisplatin, Capecitabine, Erlotinib (an EGFR inhibitor and targeted therapeutic drug), Fluorouracil, Gemcitabine, Irinotecan, Leucovorin, Nab-paclitaxel, Nanoliposomal irinotecan, and Oxaliplatin. Chemotherapy is used if the cancer is locally advanced or metastatic (late stage of cancer) pancreatic cancer.

Studies show that tumors are very well adapted at the hypoxia, low nutrient environment and are able to metastasize in that environment. Previous studies conducted to measure oxygenation in the pancreatic cancer tumor by probing into the exposed organ during surgery have shown that oxygen level is between 0-.03% in the pancreatic tumor. Normally the pancreas oxygen level is around 1%. Tumor cells farthest from the blood supply will have less oxygen. Hypoxia triggers a metabolic switch that drives growth. HIF-1 and HIF-2 induction induce drug resistance and metastasis. Hypoxic chamber is used in this experiment to mimic the pancreas in the human body since the oxygen level is only 1% in our body.

In our experiment design, we tested pancreatic cancer cells line PANC-1 in hypoxic environment using (Hypoxic chamber) as well as in normal conditions (incubator 37C) to document the grow rates. The choice of drugs we tested were Cisplatin and 5-Fluorouracil at concentrations between 1-100 μmol. Cisplatin is a platinum
base drug, and its mode of action is apoptosis by causing mispairing of nucleotides. The mechanism of action for 5-Fluorouracil is forming a complex to inhibit DNA replication and repair. To reduce the oxygen concentration on the treatment group, the AnaeroPack system (Mitsubishi Chemicals) allowed us to create the oxygen-deprived and hypoxic environments that we need for the experiment without shifting any pressures or reducing possible confounding variables. Additionally, the anaerobic indicator strips will permit us to measure our atmosphere conditions without the extra and unnecessary expense of any sort of gauge. The analysis of the growth rates were measured over 72 hours (by Fiji Program) with the media being replaced (along with the drugs) on a daily basis. Based on our time course data, 5-Fluorouracil inhibited PANC-1 growth more effectively under the hypoxia environment compared to the normoxia environment. Additional, Cisplatin inhibited cell growth more effectively in the hypoxia environment compared to the normoxia environment.