Altering Metabolic Pathways To Override Drug Resistance in Cancer

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Pancreatic Ductal Adenocarcinoma (PDAC) is a highly lethal and aggressive form of pancreatic cancer with a 5-year survival rate of 8%. This form of cancer is particularly hard to treat due to late diagnosis, the rapid development of drug resistance, and the dense microenvironment surrounding the cancer cells. Increasing evidence has shown that the reprogrammed metabolism of pancreatic cancer may play a role in tumor progression, prognosis, and treatment. Two transmembrane proteins that play an important role in cancer metabolism are syndecan-1 and glut-1. Glut-1 is a transmembrane protein that facilitates cellular glucose uptake, providing glucose for glycolysis and other complex metabolic pathways. Syndecan-1 is a transmembrane proteoglycan that has high levels of expression in cancer cells. This protein is a critical mediator of macropinocytosis. Macropinocytosis (“cell-scavenging”) is the uptake of nutrients from the extracellular matrix through the cell membrane. Both syndecan-1 and glut-1 are promising candidates that could affect the metabolic pathways of pancreatic cancer and potentially decrease cell viability if inhibited. Due to pancreatic cancer’s ability to resist treatment, combination therapies hold the greatest promise in therapeutic effect. Previous studies have forged a link between the starvation of cancer cells and increased chemosensitivity. Therefore, if both syndecan-1 and glut-1 are selectively inhibited and then treated with a chemotherapeutic agent, PDAC cells will demonstrate decreased proliferation and decrease ability to develop drug resistance. This study will investigate if inhibition of both syndecan-1 and glut-1could starve pancreatic cancer cells and promote chemosensitivity.

Awards Won: