

MUC1 as a Biomarker for TGF- β 1 Inhibition: Investigating the Role of MUC1 in the Switch of TGF- β 1 Function from a Tumor Suppressor to a Tumor Promoter in Pancreatic Ductal Adenocarcinoma

Ashkin, Emily

With a 5-year survival rate of only 6%, pancreatic ductal adenocarcinoma (PDA) is the 4th leading cause of cancer related deaths in the United States. Transforming Growth Factor- β 1 (TGF- β 1), a growth factor commonly over-expressed in PDA, can act both as a tumor suppressor and a promoter of tumor progression. At early stages of tumorigenesis, TGF- β 1 acts as tumor suppressor via inducing apoptosis of cancer cells. However, as the tumor progresses, biochemical changes within the tumor microenvironment allow TGF- β 1 to stimulate tumor progression by initiating epithelial-to-mesenchymal transition (EMT). This allows cancer cells to invade into neighboring healthy tissues and also metastasize to distant organs. In parallel, mucin 1 (MUC1), a circulatory, transmembrane glycoprotein, is frequently over-expressed in more than 90% of PDA patients. I hypothesize that signaling through MUC1 supports TGF- β 1 induced EMT and invasion and inhibits TGF- β 1 induced apoptosis. Western blotting technique was used to determine the endogenous expression of MUC1 and TGF- β 1 receptor I and II with a panel of cell lines. Migration Assay and Flow Cytometry Cell Cycle Analysis with Propidium Iodide staining were used to test the effects of MUC1 on TGF- β 1 induced apoptosis and EMT with a panel of cell lines. These results showed that signaling through MUC1 leads to down regulation of TGF- β 1-induced apoptosis and up regulation in TGF- β 1-induced invasion. These results support my hypothesis that MUC1 regulates TGF- β 1 signaling pathways, switching TGF- β 1 from a tumor suppressor to a tumor promoter. Thus, MUC1 up regulation in PDA could help deduce the efficacy of therapeutic reagents that target TGF- β 1 and its downstream partners by determining TGF- β 1 as either tumor suppressive or promoting.

Awards Won:

Second Award of \$2,000