

AB107. P081. Metabolic oligosaccharide engineering of pancreatic cells: measurement of sialylation and identification of sialylated glycoproteins

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Abstract: Pancreatic cancer (PC) accounts for 7% of all cancer related deaths in the US. The 5-year survival rate is only 7%. This poor prognosis is attributed to the fact that in over 80% of cases, PC is diagnosed at a stage of malignancy where surgical removal is not an option. In cases where the cancer is detected early enough that surgical removal is possible, the survival rates go up to 25%. Thus, it is imperative to identify selective biomarkers that can distinguish precancerous lesions or an early stage cancer from pancreatitis and other gastroenterological cancers. The currently used FDA approved serum biomarker CA19-9 [the tetrasaccharide sialyl Lewis a (sLe^a)] brings

forth the importance of glycans as biomarkers, although it lacks the specificity to screen for pancreatic cancer and is currently used to monitor treatment response. Metabolic oligosaccharide engineering (MOE) has been used by our lab to supply patented 'high-flux' analogs of carbohydrates to intercept intracellular metabolic pathways and provide a means to track their incorporation on the cell surface. In this study, we utilize MOE to screen a non-neoplastic pancreatic cell line and a panel of pancreatic cancer cell lines with varying degrees of genetic complexity for the production of 'free' monosaccharide sialic acid when treated with the N-acetylmannosamine analog, 1,3,4-O-Bu₃-ManNAc, at different doses and time points. We also utilized this difference in the flux through the sialic acid biosynthetic pathway as a tool to screen the secretome of the non-neoplastic cell line against an early stage cancer cell line, as a means to identify serum glycoproteins for detecting early-stage pancreatic cancer.

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