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RE-EXPRESSION OF PTF1A IN HUMAN PANCREATIC CANCER CELL LINES

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Pancreatic Cancer is the 3rd deadliest cancer in the U.S., despite only accounting for 3% of all cancers. The majority of malignant pancreatic cancer is in the form of Pancreatic Ductal Adenocarcinoma (PDAC), which presents itself in acinar cells of the exocrine pancreas. Over 90% of PDAC has an oncogenic Kras mutation. Kras is often considered "undruggable," which necessitates the need for further understanding and the discovery of possible new drug targets. In previous studies, PDAC was shown to be initiated through the de-differentiation of mature acinar cells into a more duct-like phenotype. Research in our lab specifically points to the downregulation of Ptf1a, the master regulator of acinar cell differentiation, as the rate-limiting step of Kras-driven pancreatic cancer initiation. By using a Cre- and doxycycline-dependent Ptf1a gain-of-function mouse model, we saw that mice expressing transgenic Ptf1a and oncogenic Kras mutation exhibited significantly less precancerous lesions compared to that of mice expressing only oncogenic Kras. In addition, sustained expression of Ptf1a resulted in both the rescue and reversion of precancerous lesions *in vivo*. We sought to further investigate the mechanism of sustained Ptf1a expression in fully malignant PDAC. By infecting human pancreatic cancer cell lines with inducible lentiviral Ptf1a vectors, a model was developed through which re-expression of Ptf1a could be examined in malignant cells. Sustained Ptf1a expression in the cell lines resulted in a wide range of response. By and large, cell lines that had an upregulation of Ptf1a's downstream genes displayed a significant growth inhibition. This indicates that Ptf1a effectively turned back on its normal cellular machinery. Future studies will attempt to elucidate the mechanism through which Ptf1a re-expression acts in cancer cells, hopefully leading to the discovery of potential new drug targets.