Investigating the Role of Nicotinamide Adenine Dinucleotide Precursors in Pancreatic Cancer Prevention

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Pancreatic Ductal Adenocarcinoma (PDAC) remains one of the most lethal cancers with a significantly low 5-year survival rate. PDAC is typically diagnosed in individuals over 65, suggesting that the malignancy may be associated with age-related metabolic and physiological decline. A critical and relevant metabolic change that occurs as a result of aging is a decline in Nicotinamide Adenine Dinucleotide (NAD+) levels. NAD+ is an integral part of energy metabolism in cells, including sustaining mitochondrial function, promoting DNA repair, and maintaining redox balance. Consequently, disruption of NAD+ pathways may be a source of cancer initiation. We hypothesize that supplementation of NAD+ precursors may prevent the malignant transformation of pancreatic ductal cells in the presence of carcinogens by reducing reactive oxygen species (ROS) and increasing DNA repair. The methods used for this experiment include Colony Formation, PicoGreen, DCFDA, Mitosox, and Seahorse assays. Cells from the HPNE cell line were grown in two conditions: 1% FBS media only or 1% FBS Media and NMN, a precursor to NAD+. Assays were performed with Phenformin (a mitochondrial poison) and Oxaliplatin (a mutagen) at treatments of varying concentrations in both the presence and absence of NMN to assess the impact of NAD+ in reducing cellular ROS and cell death. Results show relatively increased cellular viability and decreased mitochondrial and total cellular ROS in pancreatic cells treated with NMN in the presence of carcinogens, validating the hypothesis. Future directions may include furthering experimentation with a broader range of cell lines and NAD precursors.

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