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“Evaluation of RhoA Activation in RSK2-Mediated Invasion in Pancreatic Cancer.”

Pancreatic Ductal Adenocarcinoma (PDAC) is one of the most aggressive and deadliest forms of pancreatic cancer, covering around 90% of all cases. Mutations in the oncogene KRAS are amongst the earliest and common genetic changes in pancreatic cancer and contribute to the overall development and progression of the disease. This is reflected by behaviors such as increased cellular invasion, metastasis, and cell proliferation. This creates the importance of investigating therapeutic targets within the KRAS signaling cascade, such as RSK2. Previous studies have demonstrated that RSK2 promotes aggressive cancer cell behaviors by regulating the RhoA signaling pathway. RhoA functions as a molecular switch to control cytoskeleton remodeling, cell motility, and division. Therefore, investigating RhoA activation and downstream signaling will help elucidate how RSK2 contributes to the invasiveness of PDAC. My experiment utilized the Miapaca2 cell line that had been transfected with anti-RSK2 shRNA and non-targeted shRNA to examine the hypothesis that RSK2 inhibition reduces RhoA activation, potentially contributing to lower rates of cellular invasion. My approach to test this was immunocytofluorescence to quantify overall RhoA-GTP (active RhoA) expression, and western blots to quantify activation of targets that are downstream of RhoA (pMYPT1 and pMCL2). Following confirmation of efficient RSK2 knockdown by Western blot analysis, fluorescence imaging revealed a stronger RhoA-GTP signal in RSK2-knockdown cells. The phosphorylation of downstream RhoA signaling targets was increased following RSK2 depletion. These findings suggest that RSK2 negatively regulates RhoA activity in MiaPaCa-2 cells, and that RSK2 loss enhances RhoA-GTPase activation.