Rethinking Pancreatic Ductal Adenocarcinoma (PDAC) Prognosis: Analysis of KRAS-Dependent Biomarkers Across Subtypes

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Pancreatic cancer is among the world's deadliest cancers with a 5-year survival rate below 9%. Pancreatic ductal adenocarcinoma (PDAC) encompasses >90% of all pancreatic cancers, and >95% are initiated by a mutation in the KRAS proto-oncogene; KRAS is a clear target for investigation. Up-regulated KRAS-dependent genes expressed in both “Classical” (resectable) and “Basal” (non-resectable) pancreatic tumors were identified in literature (n=13). The most clinically relevant of the KRAS-dependent genes (n=6) may play a role in transforming pancreatic cancer into the invasive phenotype, allowing for use in prognosis and targeted therapy. In my previous investigation, KRAS-dependent genes AMIGO2, PMEPA1, and TGM2 were identified to be upregulated in the Basal subtype; their increased RNA expression portended a worse 5-year survival probability. This study’s purpose was to evaluate KRAS-dependent genes’ expression as biomarkers stratified by PDAC subtypes. Previous work within the Tuveson CSH Lab by Miyabayashi et. al used xenotransplanted human-derived PDAC tumor organoids in immunodeficient mice. The remnant tissue was later gifted to this project for adjunct analysis and stained for AMIGO2, PMEPA1, and TGM2 protein expression. Slides were then analyzed via light microscopy and images were deconvoluted using Image JTM to isolate protein staining. A trend of greater protein expression in Basal tumors when compared to Classical tumors was exemplified in AMIGO2 (21.58 v. 7.72, p=0.194) and TGM2 (12.85 v. 2.85, p=0.149). Identification and use of the KRAS-dependent biomarkers can lead to targeted therapy and positively influence treatment and PDAC patient outcomes.

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