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Unveiling Aquaporin-5 Contribution in Pancreatic Ductal Adenocarcinoma: Tumor Microenvironment Dynamics and Prognostic Biomarker Potential

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Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive malignancy driven by its immunosuppressive tumor microenvironment (TME). Despite advances in immunotherapy, its efficacy against PDAC remains limited. Aquaporins (AQPs), a family of membrane water channels, are aberrantly expressed in PDAC. This study explores AQPs' role in cancer immunotherapy, evaluating their impact in modulating TME components, to further predict its application as potential target or prognosis factor. For that purpose, two mouse PDAC cell lines, Panc02 and KPC, were established and characterized. AQP expression was assessed by qPCR, WB and immunofluorescence, and functional activity measured using Stopped-Flow Spectroscopy. In qPCR and WB, Panc02 showed high AQP5 levels. However, in immunofluorescence and functional assays, KPC cells seemed to have superior AQP5 expression, exhibiting increased permeability rates than Panc02, suggesting differences in protein turnover between the models. Since AQP5 was the most significant isoform in the cell lines, we are generating AQP5-overexpressing and -silenced variants, which will be implanted in murine models to evaluate tumor growth and immune responses. Understanding AQP5's influence on immune infiltration and therapeutic response may unveil novel biomarkers and improve personalized immunotherapy strategies for PDAC patients.