A Novel, Tumor-Suppressive Role for Adhesion Molecule PLEKHA7 in Pancreatic Cancer

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With a dismal five-year survival rate of 8%, pancreatic cancer remains one of the most lethal epithelial cancers. A growing body of evidence suggests that deformities in cell-cell junctions play a critical role in the formation of many such epithelial cancers. Recently, the adhesion molecule PLEKHA7 was discovered as a central component of apical adherens junctions with proposed tumor-suppressive functions. This study aimed to elucidate the role of PLEKHA7 in pancreatic cancer. PLEKHA7's molecular function was first examined across three pancreatic cancer cell lines (BxPC3, PANC-1, Capan-2). In each, endogenous expression of PLEKHA7 was knocked down using lentiviruses and ectopically overexpressed using retroviruses. Subsequent changes to proliferation were measured as a marker for tumor aggression. Results indicated that the knockdown of functional PLEKHA7 led to significantly increased proliferation, while overexpression led to significantly lessened proliferation. Next, the expression phenotype of PLEKHA7 was characterized in 150+ tissue samples from human patients with precancerous pancreatic lesions (PanINs) and adenocarcinomas (PDAC). Results indicated a strong trend between cancer progression and PLEKHA7 function; as the cancer advanced through its precancerous lesions, the molecule became increasingly lost or mis-localized from cellular junctions. Upon reaching the adenocarcinoma phase, PLEKHA7 was dysfunctional in the vast majority of cases. These observations are consistent with PLEKHA7's proposed tumor suppressive function and suggest a novel role for the protein in the progression of pancreatic cancer. In the future, PLEKHA7 can be used as a biomarker for early detection and as a target for gene-therapies to reverse cancer progression.

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