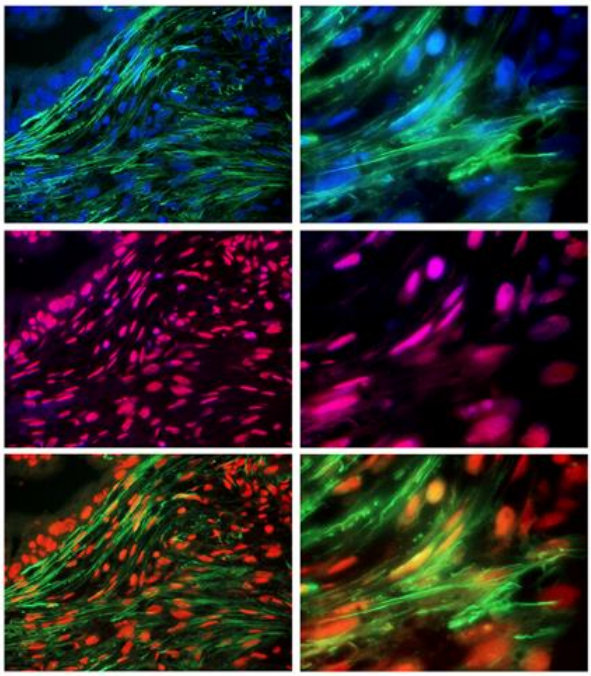
Investigating the role of BET family proteins in regulating pancreatic cancer fibrosis

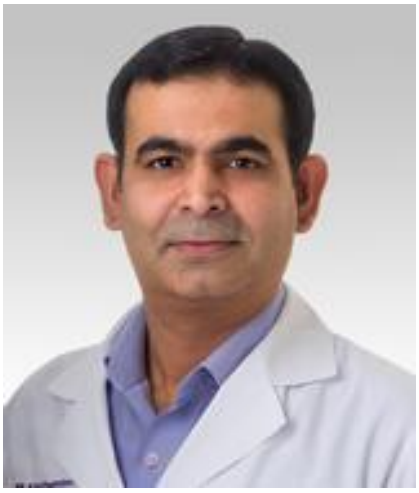


Human PDAC tumor sections were stained for α-SMA (green) and BRD4 (red) by immune-fluorescence, and the nuclei counterstained using DAPI (blue) to show that human pancreatic stellate cells express BRD4. The stained sections were examined at 40x (left) and 100x (right) magnifications.

Northwestern Medicine scientists showed how bromodomain and extra-terminal (BET) family proteins regulate collagen I production and fibrosis in pancreatic ductal adenocarcinoma (PDAC), one of the deadliest cancer.

Fibrosis is particularly pronounced in human PDAC tumors and can account for as much as 70-80% of the tumor tissue. This dense fibrotic stroma, mediated by pancreatic stellate cells (PSCs), can limit drug delivery and also mediate oncogenic signals to the cancer cells. Research study published in JCI Insight showed that bromodomain and extra-terminal (BET) family of proteins regulate collagen I production and fibrosis. Genetic and pharmacological inhibition of BET proteins decreased collagen I production in primary PSCs isolated from human pancreatic tumors. In the murine model of pancreatic cancer, BET inhibitors significantly reduced fibrosis, and collagen I production. This study suggests that BET inhibitors could potentially be used to therapeutically modulate pancreatic tumor stroma.

This study was co-lead by Krishan Kumar in the Munshi Lab. Other Northwestern Medicine co-authors include Brian DeCant and Kazumi Ebine, members of the Munshi Lab, David Bentrem, MD, Associate Professor of Surgery, and HG Munshi, MD, Associate Professor of Medicine.



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