Researcher unlocks new approach for possible pancreatic cancer treatment

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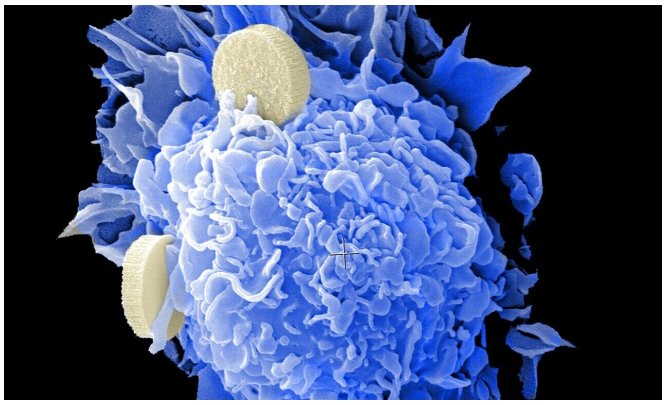

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Researchers at the Indiana University Melvin and Bren Simon Comprehensive Cancer Center have identified how restoring a missing molecule in pancreatic fibrosis could help deliver treatments to cancer cells.

Pancreatic cancer is one of the deadliest cancers with only 10.8 percent of people surviving five years after diagnosis. One risk factor for pancreatic cancer is chronic pancreatitis, a fibroinflammatory disease. In response to internal injury or damage, the body produces a fibrous connective tissue—much like scar tissue—in a process called fibrosis. Pancreatic fibrosis occurs in both pancreatic cancer and chronic pancreatitis.

"These pancreatic cancer cells are very smart; they develop this thick, fibrotic tissue around the tumors. That poses a major barrier for the drug delivery when clinicians try to target these tumors because the therapies cannot penetrate these tumors," said Janaiah Kota, Ph.D., assistant professor of medical and molecular genetics at IU School of Medicine and a researcher at the IU Simon Comprehensive Cancer Center.

Kota and colleagues found that a molecule called microRNA-29a (miR-29a) functions as an anti-fibrosis and anti-inflammatory in the pancreas. Using this molecule in drug therapy could help stop fibrosis so that treatments could reach the cancer cells. Currently, there are no FDA-approved therapies to reduce fibrosis.

"This tiny molecule is missing in the pancreas and, more broadly, the fibrotic tissue. When we put this molecule back in cells, it significantly reduces the potential for cancer cells to develop fibrotic tissue around the tumors," Kota said.

In findings published in *JCI Insights*, researchers established the role of miR-29a as a therapeutic agent in mouse models. Now Kota is developing methods to deliver the molecule back into the pancreas. He is using a pancreas targeted gene delivery approach called adeno-associated virus (AAV) space region therapy, which could carry the molecule directly to the pancreas.

"When we delete the molecule in mouse models with pancreatitis, they develop a significant fibrosis and inflammation, mimicking the human disease," said Kota, senior author on the study. "This is providing compelling evidence for us to use this molecule as a potential therapeutic agent both in cancer patients as well as in pancreatitis patients."

"The study of pancreatic fibrosis serves an unmet clinical need as there is currently no FDA-approved drug which might halt or reverse this process. This patient population is at high risk for developing pancreas cancer, and potentially stopping or reversing the fibrosis may reduce this risk. Physicians worldwide continue to struggle with management of patients with chronic pancreatitis and pancreas cancer. We are optimistic that miR-29a has the potential to fill an important gap and reduce pancreatic fibrosis, with a broader application for other fibrotic diseases," said Evan Fogel, MD, a cancer center researcher and co-

author on the publication. Fogel is also a professor of medicine at IU School of Medicine.

Future therapies for chronic pancreatitis could potentially prevent those patients from developing pancreatic cancer. Additionally, the development of an anti-fibrotic therapy could have applications beyond the pancreas. Fibrosis also causes complications in lung and liver diseases.

More information: Shatovisha Dey et al, Loss of miR-29a/b1 promotes inflammation and fibrosis in acute pancreatitis, *JCI Insight* (2021). DOI: 10.1172/jci.insight.149539

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