

Bacteria may promote pancreatic cancer by suppressing the immune system

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Bacterial load was significantly higher in pancreatic tumor samples from patients with pancreatic ductal adenocarcinoma compared with pancreatic tissue from normal individuals, and in studies using mice, eliminating certain "bad" bacteria slowed the growth of pancreatic cancer, reversed immune suppression, and upregulated the immune checkpoint protein PD1.

The study is published in *Cancer Discovery*, a journal of the American Association for Cancer Research, by George Miller, MD, HL Pachter Professor in the Departments of Surgery and Cell Biology at New York University School of Medicine; Deepak Saxena, PhD, associate professor in the Department of Basic Science and Craniofacial Biology at New York University College of Dentistry.

"The [gut microbiome](#) has been studied in many different cancers, including liver and colorectal [cancer](#), and is shown to affect cancer progression," said Miller. "Because the pancreas is remote from the gut, it is considered a sterile organ, and there haven't been many studies that looked at the role of the gut microbiome in [pancreatic](#) cancer."

How the Study Was Conducted and Results: The researchers also compared fecal samples from 32 [patients](#) with pancreatic ductal adenocarcinoma with fecal samples from 31 normal individuals and found that the bacterial composition of cancer patients was distinct from that of normal individuals. "The bacterial composition was more diverse in the [fecal samples](#) than from cancer patients," noted Miller.

"The dysbiosis [imbalance] in the gut microbiome can potentially be used as a biomarker to define a high-risk population," noted Saxena. Among the more abundant strains of bacteria found in pancreatic cancer patients were Proteobacteria, Bacteroidetes, and Firmicutes.

In mouse studies, the team demonstrated that bacteria translocate from the gut to the pancreas during pancreatic cancer. With further studies, the researchers showed that eliminating these bacteria using antimicrobial treatment slowed the progression of pancreatic cancer and lowered the [tumor](#) burden by about 50 percent. This process also affected T-cell differentiation, leading to increased T-cell infiltration into the tumor and reduction in myeloid-derived suppressor cell (MDSC) population. Antimicrobial treatment also resulted in increased expression of PD1 on CD4+ and CD8+ T cells within the tumors.

Reintroduction of bacteria in antimicrobial treated mice reversed the tumor protection and reduced the immunogenicity of the tumors, suggesting that the microbiome promotes pancreatic ductal adenocarcinoma by inducing [immune suppression](#) in the tumor.

The researchers also found that combining [antimicrobial treatment](#) with an anti-PD1 immunotherapy resulted in enhanced CD4+ and CD8+ T-cell activation in mice, suggesting that such a combination is a potential treatment option for pancreatic ductal adenocarcinoma.

The team is preparing to launch a clinical trial to test a combination of antibiotics (ciprofloxacin and metronidazole) and an anti-PD1 antibody in patients with [pancreatic ductal adenocarcinoma](#).

"We were surprised to see that the human pancreatic tissue samples had an active microbiome," said Saxena. "And we found that not only are there bacteria in the pancreas but the bacterial load is significantly higher in pancreatic cancer tissue compared to normal pancreas tissue."

"Our studies show that the bacteria may serve both as biomarkers of increased risk for pancreatic cancer as well as potential therapeutic targets," said Miller. "We believe that targeting the microbiome in patients with [pancreatic cancer](#) can make immunotherapy effective."

Saxena noted, "Pancreatic cancer is a very aggressive disease with a five-year survival rate of a dismal 8.2 percent. Extending the life of these patients by manipulating the microbiome and decelerating tumor progression would be a significant step forward in managing this deadly disease."

A limitation of the study is the small sample size used for the human pancreatic cancer studies. As noted by Miller, identifying beneficial bacteria that could potentially be utilized to slow the progression of pancreatic cancer or decrease risk is important in future studies.

Provided by American Association for Cancer Research

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