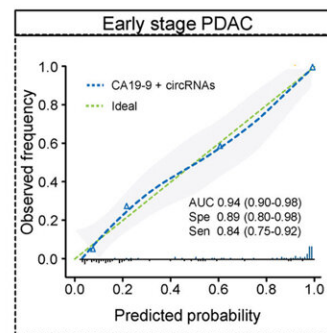
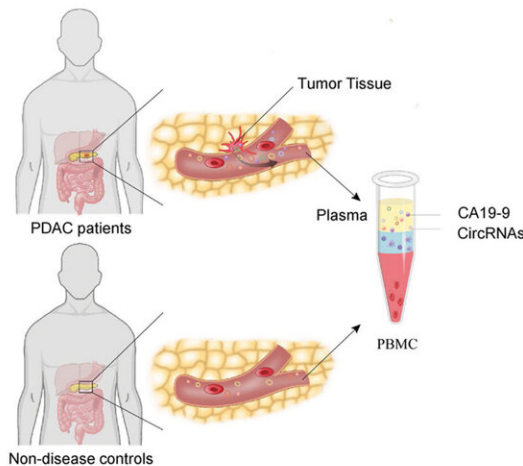


# Creating a 'robust' early-detection method for pancreatic cancer

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Graphical abstract. Credit: *Gastroenterology* (2023). DOI: 10.1053/j.gastro.2023.09.050

In a significant breakthrough that could eventually extend the survival of patients with one of the deadliest of all malignancies, an international team of researchers have devised an investigational blood test that might one day help doctors detect pancreatic cancer earlier.

The team from the U.S., China, South Korea and Japan created and tested a biomarker panel that detects small amounts of RNA [genetic material](#) that breaks off from [pancreatic cancer](#) cells and circulates in the bloodstream, known as circular RNA or circRNA, according to results

of a study published in the journal *Gastroenterology*.

The U.S. team members include City of Hope; Translational Genomics Research Institute (TGen), part of the City of Hope; and HonorHealth Research Institute.

More than 50,500 Americans are predicted to die this year from pancreatic cancer, making it the third leading cause of cancer-related death behind lung and colon cancers. Both the number of cases and deaths due to pancreatic cancer continue to increase year after year. Only about [11%](#) of those diagnosed with this type of cancer survive more than 5 years.

One of the primary reasons for the dismal survival rates in pancreatic cancer is that most patients are usually diagnosed in late stages when the disease has already spread to other parts of the body. Because the pancreas is deep within the abdominal cavity, this type of cancer usually does not cause pain or inflammation in its early stages, symptoms that might otherwise reveal the presence of disease. Fewer than 15% of pancreatic cancer patients are diagnosed at a stage when the cancer can be surgically removed, the study said.

## **'Urgent' need for early detection test**

"These data highlight the urgent, unmet clinical need to identify and develop diagnostic methods that could precisely detect pancreatic cancer at its earliest stages, when the disease is still confined to the pancreas and surgical resection is still an option," said Ajay Goel, Ph.D., AGAF, the study's senior author.

Dr. Goel is professor and founding chair of the Department of Molecular Diagnostics and Experimental Therapeutics at the Beckman Research Institute of City of Hope and associate director of basic

science for City of Hope Comprehensive Cancer Center.

Previous diagnostic efforts using imaging and blood levels of CA 19-9, a cancer antigen, have proved inadequate and misleading. Pancreatic cancer does not always produce detectable amounts of CA 19-9 in early stages, leading to false negatives. It also is elevated in other gastrointestinal cancers and conditions.

"We hypothesized that circRNAs might offer diagnostic potential in pancreatic cancer. Recent evidence indicates that circRNAs might have untapped potential as biomarkers for cancer diagnosis and prognosis," said Caiming Xu, M.D., Ph.D., the study's lead author and a visiting post-doctoral fellow in Dr. Goel's lab. Dr. Caiming also is part of the First Affiliated Hospital of Dalian (China) Medical University.

Because they form in a circle, circRNAs are more stable and have longer half-lives compared with linear RNAs, and circRNAs are abundantly expressed in the bloodstream. It has only been in recent years that genetic sequencing technology has advanced sufficiently to precisely detect, process and analyze circRNA.

Using genome-wide expression profiling, researchers undertook a systematic and comprehensive review of patient samples to discover pancreatic cancer biomarkers based on circRNA that could distinguish pancreatic cancer tumors from adjacent normal tissue specimens, especially among those patients with early-stage disease.

## **Blood panel had 'robust diagnostic accuracy'**

Five candidate biomarkers were used to devise a blood-based panel test—a non-invasive, liquid biopsy-based assay—for early detection of pancreatic cancer; a test that "exhibited robust diagnostic accuracy," according to the study. The predictive performance of these biomarkers

"improved remarkably" when analyzed in conjunction with CA 19-9, the study said.

Blood-based liquid biopsies have multiple advantages over tissue-based traditional biopsies, including their noninvasiveness, ease of sample collection, and accurate results, which can be exploited as an important tool in the early detection of cancers and patient disease management.

"When pancreatic cancer is caught early, the chance of survival is so much greater than when diagnosed in the advanced stage. Therefore, there is a great need to develop novel ways to detect pancreatic cancer," said Erkut Borazanci, M.D., research director of the Cancer Research Division at HonorHealth Research Institute, and one of the study's authors.

"By collaborating with City of Hope, TGen and other centers working together, we are making strides where we hope for a future reality in which pancreatic cancer is detected early, and that we are talking about cures for more people," Dr. Borazanci said.

Study researchers, all part of the Pancreatic Cancer Detection Consortium, concluded that additional tests should be conducted to determine if there are any differences due to patients' age, sex or other factors: "Although the performance seems promising, further investigation is warranted for our circRNA-based panel of biomarkers to be found eligible as a reliable clinical test."

## **Nearly a decade in the making**

Still, the results of this study go a long way toward achieving the goal of better cancer diagnostics, said Daniel Von Hoff, M.D., a Distinguished Professor at the Translational Genomics Research Institute (TGen), part of City of Hope, and one of the study's authors. Dr. Von Hoff has

worked for nearly a decade with Dr. Borazanci to discover a way to detect pancreatic cancer in its early stages.

"Perfecting a method of early detection for this extremely aggressive cancer would be a substantial step in providing better care for patients with pancreatic [cancer](#)," Dr. Von Hoff said. "It could also be the basis for eventually developing early-detection tests for other cancers, as well."

The study—"[A circulating panel of circRNA biomarkers for the noninvasive and early detection of pancreatic ductal adenocarcinoma](#)"—was published Oct. 13.

**More information:** Caiming Xu et al, A circulating panel of circRNA biomarkers for the noninvasive and early detection of pancreatic ductal adenocarcinoma, *Gastroenterology* (2023). [DOI: 10.1053/j.gastro.2023.09.050](#)

Provided by The Translational Genomics Research Institute

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