Study finds genes associated with improved survival for pancreatic cancer patients

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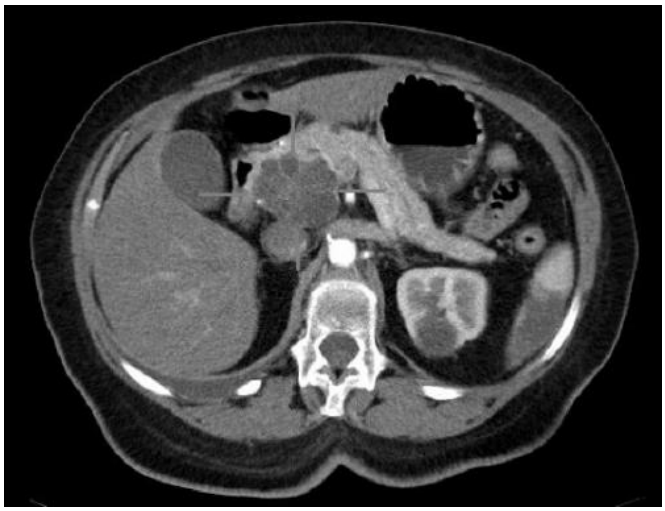

Axial CT image with i.v. contrast. Macrocystic adenocarcinoma of the pancreatic head. Credit: public domain

A study by the Translational Genomics Research Institute (TGen) and other major research institutes, found a new set of genes that can indicate improved survival after surgery for patients with pancreatic cancer. The study also showed that detection of circulating tumor DNA in the blood could provide an early indication of tumor recurrence.

In conjunction with the Stand Up To Cancer (SU2C) Pancreatic Cancer Dream Team, the study was published in the prestigious scientific journal *Nature Communications*.

Using whole-exome sequencing—looking at the DNA protein-coding regions of 24 tumors—and targeted genomic analyses of 77 other tumors, the study identified mutations in chromatin-regulating genes MLL, MLL2, MLL3 and ARID1A in 20 percent of patients associated with improved survival.

In addition, using a liquid biopsy analysis, the study found that 43 percent of pancreatic cancer patients had circulating tumor DNA (ctDNA) in their bloodstream at the time of diagnosis.

Very importantly, the study also found that detection of ctDNA following surgery predicts clinical relapse of the cancer and poor outcomes for patients. In addition, using a liquid biopsy detected the recurrence of cancer 6.5 months earlier than using CT imaging.

"These observations provide predictors of outcomes in patients with pancreatic cancer and have implications for detection of tumor recurrence, and perhaps someday for early detection of the cancer," said Dr. Daniel D. Von Hoff, TGen Distinguished Professor and Physician-In-Chief, Co-Director of TGen's SU2C Pancreatic Cancer Dream Team, and Chief Scientific Officer at the Virginia G. Piper Cancer Center Clinical Trials at HonorHealth (formerly Scottsdale Healthcare). Dr. Von Hoff was one of the authors of the study.

The pancreatic cancers analyzed in the study were stage II tumors from patients who underwent potentially curative surgery. Only 15-20 percent of patients are candidates for tumor resection, because pancreatic cancer is difficult to detect and usually is not diagnosed until its late stages when surgery is no longer an option. The 5-year survival rate for those diagnosed with pancreatic cancer is less than 10 percent.

The study's results found that a significant number of early-stage pancreatic cancers could be diagnosed non-invasively using liquid biopsy blood analysis that focuses on a few specific genetic alterations.

"We have identified MML genes as markers of improved prognosis for patients with pancreatic cancer," Dr. Von Hoff said. "We have also shown that ctDNA in the blood of pancreatic cancer

patients may provide a marker of earlier detection of recurrence of the disease."

The study—Clinical implications of genomic alterations in the tumor and circulation of pancreatic cancer patients—was published July 7.

This analysis suggests that additional studies should "evaluate more intensive therapies" for patients without MLL mutations or with detectable ctDNA following surgical removal of their tumors, as well as interventional clinical trials, the study said.

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