Scientists link pancreatic cancer survival to four genes

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Alterations in four main genes are responsible for how long patients survive with pancreatic cancer, according to a new study in *JAMA Oncology*.

Before now, the presence and patterns between the genes and disease progression was not clearly established. One key difference in this study is the relatively large size: it involved 356 patients who all had pancreatic

adenocarcinoma that could be surgically removed.

Adenocarcinoma is by far the most common type of pancreas tumor.

Ninety of the patients were treated at the University of Rochester Medical Center's Wilmot Cancer Institute; the others at Dana Farber/Brigham and Women's Cancer Center in Boston and Stanford Cancer Institute. In all cases after the tumors were removed, scientists extracted DNA from the cancerous tissue and nearby normal tissue, and conducted next-generation DNA sequencing on the specimens.

The analysis centered on the activity of the KRAS, CDKN2A, SMAD4, and TP53 genes. Results showed that patients who had three or four of the altered genes had worse disease-free survival (the time between surgery and when the cancer returns), and overall survival (from surgery to death), compared to patients with a single or two altered genes. A more detailed breakdown of survival and specific gene activity is available in the full study.

"The research helps us to understand how the molecular features of pancreatic cancer impact prognosis on an individual level and gives us more facts to guide patients, and importantly, to design future research studies," said study co-author Aram Hezel, M.D., a gastrointestinal cancer expert and chief of the Division of Hematology/Oncology at Wilmot.

Pancreatic cancer is aggressive and generally has poor survival odds. Patients who can undergo surgery as part of treatment often survive longer and some patients fare best when they can receive chemotherapy prior to surgery. But having customized, molecular information will provide an even greater understanding of how the disease is likely to progress in each patient, Hezel said.

The team of investigators from Wilmot, Dana Farber and Stanford are continuing to collaborate and recently published in the British Journal of Cancer, showing that an accurate classification of pancreatic cancer's spread to the lymph nodes is also an effective tool to predict disease survival in surgery-eligible patients.

More information: Zhi Rong Qian et al. Association of Alterations in Main Driver Genes With Outcomes of Patients With Resected Pancreatic Ductal Adenocarcinoma, *JAMA Oncology* (2017). DOI: 10.1001/jamaoncol.2017.3420

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