Medical Xpress

Glitches in DNA repair genes predict prognosis in pancreatic cancer

January 14 2009

Variations in mismatch repair genes can help predict treatment response and prognosis in patients with pancreatic cancer, according to research from The University of Texas M. D. Anderson Cancer Center presented today in advance of the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium.

In the study, single nucleotide polymorphisms (SNPs) in genes involved in DNA mismatch repair were associated with response to gemcitabine (Gemzar)-based preoperative chemoradiation, tumor resectability (the likelihood of removing the entire tumor), and overall survival.

"Gemcitabine is a major chemotherapeutic agent used to treat pancreatic cancer, but we don't understand why some patients respond and most patients do not," said Donghui Li, Ph.D., the study's lead author and professor in M. D. Anderson's Department of Gastrointestinal Medical Oncology. "There has been no biomarker for pancreatic cancer used in the clinic to predict response. Our research interest has been to determine whether genetic variation in DNA repair can be a predictor of treatment response or a prognosis factor for patient survival."

DNA repair is a complicated process, Li noted, with various mechanisms responsible for identifying and correcting different types of DNA damage. Mismatch repair genes correct mistakes in DNA replication or trigger cell death (apoptosis) if repair is not possible. Ensuring cell death is critical to preventing the runaway cell division that occurs in malignant tumors.

In the study, Li's group obtained DNA samples from 154 patients with potentially resectable pancreatic adenocarcinomas who were participating in phase II clinical trials of preoperative gemcitabine-based chemoradiation. The researchers evaluated 15 SNPs (also called genotypes) among eight mismatch repair genes (EXO1, MLH1, MSH2, MSH3, MSH6, PMS1, TREX1, and TP73) and correlated them with tumor response to gemcitabine, the likelihood of achieving complete tumor resection, and overall survival.

Individually, five genotypes were associated with tumor response to preoperative gemcitabine-based chemoradiation; six were associated with tumor resectability, and ten were associated with overall survival. However, the combined effects of several genotypes on patient survival were dramatic. For example, 20 of 25 patients with 0 to 1 abnormal genotype were alive at the completion of the study (after a median follow-up time of 49.9 months). In contrast, median survival times were 36.2 months for patients with 2 adverse genotypes; 23.9 months for those with 3; 16.3 months for those with 4; 13 months for those with 5; and 8.3 months for those with 6 - 7.

If confirmed by other researchers, these findings could have a profound effect on how pancreatic cancer is treated. Having established biomarkers like abnormal mismatch repair genes, for example, would make choosing which patients might benefit from surgery much easier, Li explained.

"The doctor always faces a tough choice," Li said. "Among the pancreatic tumors that are technically respectable, 25-30 percent might have very small tumors that have already metastasized to the liver or other organs. For these patients, the tumors recur very shortly after surgery, so these patients actually do not benefit from the traumatic and difficult surgery."

The study results also suggest that variations in mismatch repair genes could be useful in determining which patients will respond best to gemcitabine-based chemoradiation. Having this information would allow physicians to move more quickly to give alternative drugs to a patient unlikely to respond to gemcitabine, Li explained.

"We hope that in the future we will be able to run a genetic test that will help doctors predict a patient's outcome and help them select the best therapy for each patient," Li concluded.

Source: University of Texas M. D. Anderson Cancer Center

Citation: Glitches in DNA repair genes predict prognosis in pancreatic cancer (2009, January 14) retrieved 3 May 2024 from
https://medicalxpress.com/news/2009-01-glitches-dna-genes-prognosis-pancreatic.html