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Eliminating cellular stroma could enable anti-cancer drugs to penetrate tumor tissues, improve survival

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Like a stealth jet cloaks itself from radar, cancer cells cloak themselves within tumors by hiding behind a dense layer of cellular material known as stroma.

According to a new study by the Translational Genomics Research Institute (TGen), drugs that target and strip away the stroma would pave the way for drugs to reach the cancerous cells within the tumor, which could have a beneficial effect on the survival of pancreatic cancer patients.

Targeting stroma could potentially extend patient survival even among those with advanced stage cancer that has spread to other organs, said the TGen study in the journal *Clinical Cancer Research*, published online Feb. 18 by the American Association for Cancer Research. AACR is the world's largest cancer research organization, representing more than 35,000 investigators.

The accumulation of stroma - the supporting connective tissue that includes hyaluronan and several types of collagen - prevents therapeutic anti-cancer drugs from reaching and destroying cancer cells, the study said, not only in the primary tumors in the pancreas but also in metastatic lesions when the cancer spreads to distant organs such as liver and lung.

"If we can target and reduce stroma, new cancer therapeutics could

prove more effective and patients could experience longer survival," said Dr. Haiyong Han, a TGen Associate Professor, head of TGen's pancreatic cancer research unit, and the study's senior author.

In what is believe to be the first study of its kind, the TGen paper found that metastatic lesions can have the same high level of stromal content as the primary tumors in the pancreas. And, significantly, these high levels of stroma correlate with poor patient survival.

The study examined the stromal content of primary tumors and metastatic lesions from among 50 patients with pancreatic ductal adenocarcinoma, which represents about 95 percent of all pancreatic cancer.

Among patients with low hyaluronan in their primary tumors, median survival was 24.3 months, compared to only 9.3 months for patients with high levels of hyaluronan. Likewise, among patients with low collagen in their primary tumors, median survival was 14.6 months, compared to only 6.4 months for patients with high levels of collagen.

The pancreas is an organ behind the stomach that produces digestive juices and several key hormones. This year, nearly 49,000 Americans will be diagnosed with pancreatic cancer, and more than 40,000 will die from this disease, making it the fourth leading cause of cancer-related death in the U.S.

Median survival for patients with advanced disease is less than 6 months following diagnosis, and the 5-year survival rate is less than 6 percent for all patients.

Pancreatic cancer's lethal nature stems from its propensity to rapidly spread to distant organs. Because there is no early screening test, it usually is not diagnosed until its late stages, often when surgery is no

longer an option, making it difficult to treat.

The TGen study shows by targeting and eliminating the stroma surrounding the cancer cells, anti-cancer drugs - as well as immunologic approaches - should be more effective not only within the pancreas, but also more effective on tumors throughout the body where the cancer may have spread.

"We are hopeful that in the future new therapeutics that target stroma will have a significant benefit for our patients, and lead to better outcomes," said Dr. Daniel D. Von Hoff, TGen's Distinguished Professor and Physician-In-Chief, and an author of the study.

More information: "Desmoplasia in primary tumors and metastatic lesions of pancreatic cancer" *Clin Cancer Res* clincanres.1051.2014; Published OnlineFirst February 18, 2015; DOI: 10.1158/1078-0432.CCR-14-1051

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