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Early Biomarker for Pancreatic Cancer Identified

Researchers at the University of California, San Diego School of Medicine and Moores Cancer Center have identified a new biomarker and therapeutic target for pancreatic cancer, an often-fatal disease for which there is currently no reliable method for early detection or therapeutic intervention. The paper will be published May 15 in *Cancer Research*.

Pancreatic ductal adenocarcinoma, or PDAC, is the fourth-leading cause of cancer-related death. Newly diagnosed patients have a median survival of less than one year, and a 5-year survival rate of only 3 to 5 percent. Therefore, biomarkers that can identify early onset of PDAC and which could be viable drug targets are desperately needed.

“We found that a kinase called PEAK1 is turned on very early in pancreatic cancer,” said first author Jonathan Kelber, PhD, a postdoctoral researcher in the UCSD Department of Pathology and Moores Cancer Center. “This protein was clearly detected in biopsies of malignant tumors from human patients – at the gene and the protein levels – as well as in mouse models.”

PEAK1 is a type of tyrosine kinase – an enzyme, or type of protein, that speeds up chemical reactions and acts as an “on” or “off” switch in many cellular functions. The fact that PEAK1 expression is increased in human PDAC and that its catalytic activity is important for PDAC cell proliferation makes it an important candidate as a biomarker and therapeutic target for small molecule drug discovery.

In addition to showing that levels of PEAK1 are increased during PDAC progression, the scientists found that PEAK1 is necessary for the cancer to grow and metastasize.

“PEAK1 is a critical signaling hub, regulating cell migration and proliferation,” said Kelber. “We found that if you knock it out in PDAC cells, they form significantly smaller tumors in preclinical mouse models and fail to metastasize efficiently.”

The research team, led by principal investigator Richard Klemke, PhD, UCSD professor of pathology, studied a large, on-line data base of gene expression profiles to uncover the presence of PEAK1 in PDAC. These findings were corroborated at the protein level in patient biopsy samples from co-investigator Michael Bouvet, MD, and in mouse models developed by Andrew M. Lowy, MD, both of the UCSD Department of Surgery at Moores Cancer Center.

While many proteins are upregulated in cancers of the pancreas, there has been limited success in identifying candidates that, when inhibited, have potential as clinically approved therapeutics. However, the researchers found that inhibition of PEAK1-dependent signaling sensitized PDAC cells to existing chemotherapies such as Gemtamine, and immunotherapies such as Trastuzumab.

“Survival rates for patients with pancreatic cancer remain low,” said Bouvet. “Therefore, earlier detection and novel treatment strategies are very important if we are going to make any progress against pancreatic cancer. Since current therapies are often ineffective, our hope is that the findings from this research will open up a new line of investigation to bring a PEAK1 inhibitor to the clinic.”

Additional contributors to the study include Theresa Reno, Sharmeela Kaushal, Cristina Metildi, Tracy Wright, Konstantin Stoletov, Jessica M. Weems, Frederick D. Park, Evangeline Mose, UC San Diego; Yingchun Wang, Chinese Academy of Science, Beijing; and Robert M. Hoffman, UC San Diego and AntiCancer, Inc., San Diego.

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