Gene Mutation Found for Aggressive Form of Pancreatic Cancer

Discovery may prove useful in future diagnoses and in developing new therapies

May 27, 2014 |

Researchers at the University of California, San Diego School of Medicine have identified a mutated gene common to adenosquamous carcinoma (ASC) tumors – the first known unique molecular signature for this rare, but particularly virulent, form of pancreatic cancer.

The findings are published in the May 25 advance online issue of *Nature Medicine.*

Pancreatic cancer is the fourth leading cause of cancer-related death in the United States, with roughly 45,220 new cases diagnosed and more than 38,400 deaths annually. Both numbers are rising. ASC cases are infrequent, but typically have a worse prognosis than more common types of pancreatic cancer.

"There has been little progress in understanding pancreatic ASC since these aggressive tumors were first described more than a century ago," said co-senior author Miles F. Wilkinson, PhD, professor in the Department of Reproductive Medicine and a member of the UC San Diego Institute for Genomic Medicine. "One problem has been identifying mutations unique to this class of tumors."

In their paper, Wilkinson, co-senior author Yanjun Lu, PhD, of Tongji University in China, and colleagues report that ASC pancreatic tumors have somatic or non-heritable mutations in the UPF1 gene, which is involved in a highly conserved RNA degradation pathway called nonsense-mediated RNA decay or NMD. It is the first known example of genetic alterations in an NMD gene in human tumors.

NMD has two major roles. First, it is a quality control mechanism used by cells to eliminate faulty messenger RNA (mRNA) – molecules that help transcribe genetic information into the construction of proteins essential to life. Second, it degrades a specific group of normal mRNAs, including those encoding proteins promoting cell growth, cell migration and cell survival. Loss of

NMD in these tumors may "release the brakes on these molecules, and thereby driving tumor growth and spread," said Wilkinson.

Co-first author Rachid Karam, MD, PhD, a postdoctoral fellow in Wilkinson's laboratory said the findings will create new opportunities for the development of novel diagnostic approaches and therapeutic strategies for targeting pancreatic cancer. "Currently, pancreatic cancer is detected far too late in most cases for effective treatment, and therapeutic options are limited," Karam said.

Co-authors include Chen Liu, Fang Su, GuoTong Xu, LiXia Lu, ChongRen Wang, MeiYi Song, JingPing Zhu, YiRan Wang and YiFan Zhao, Tongji University School of Medicine; YingQi Zhou and Gang Li, Second Military Medical University; Yuan Ji, Fudan University; Wai Chin Foo, Mingxin Zuo and Milind Javie, University of Texas MD Anderson Cancer Center.

Funding for this research came, in part, from The National Key Basic Research Program of China, the National Natural Science Foundation of China and the National Institutes of Health.

# # #

Media contact: Scott LaFee, 619-543-6163, slafee@ucsd.edu

Related Specialties

Cancer

Share This Article

Related News

Study Uses Precision Medicine to Speed Drug Testing for Pancreatic Cancer
4/15/2021

Pancreatic Cancer Risk Linked to Weak Sunlight
4/29/2015

UC San Diego Named Stem Cell "Alpha Clinic"
10/23/2014

Promise Put to the Test
10/20/2014

View All News >

Follow Us

Follow @ucsdhealth