MedicalXpress

Experts identify critical genes mutated in stomach cancer

April 8 2012

An international team of scientists, led by researchers from the Duke-NUS Graduate Medical School (Duke-NUS) in Singapore and National Cancer Centre of Singapore, has identified hundreds of novel genes that are mutated in stomach cancer, the second-most lethal cancer worldwide.

The study, which appears online on April 8, 2012 in Nature Genetics, paves the way for treatments tailored to the genetic make-up of individual stomach tumors.

Stomach cancer is the second leading cause of cancer death globally with more than 700,000 deaths each year, and is particularly common in East Asia. Treatment of this deadly disease is often difficult and unsuccessful because of late detection of tumors and a poor understanding of the causes. In the United States, less than a quarter of patients survive more than five years after diagnosis, even after treatment.

"Until now, the genetic abnormalities that cause stomach cancers are still largely unknown, which partially explain the overall poor treatment outcome," said Patrick Tan, M.D., Ph.D., senior author of the study and associate professor in the Cancer and Stem Cell Biology Program at Duke-NUS. Tan also leads the Genomic Oncology Program at the Cancer Sciences Institute of Singapore and is a group leader at the Genome Institute of Singapore.

Using state-of-the-art DNA sequencing technology, the research team analyzed tumor and normal tissue from stomach cancer patients, which

led to the discovery of the novel gene mutations.

"This technology allows us to read the DNA sequence of the genes in each cancer genome," said co-senior author Steven G. Rozen, Ph.D., who heads the Computational Systems Biology and Human Genetics Laboratory in Duke-NUS. "This is also a major team effort involving both basic scientists and clinicians."

The team included scientists and clinicians from three research groups affiliated with Duke-NUS, including one headed by co-senior author Teh Bin Tean, M.D., Ph.D., director of the NCCS-VARI Translational Research Laboratory at the National Cancer Center Singapore.

"Our study is one of the first gastric cancer studies to investigate the vast majority of human genes at the single nucleotide level," Teh said. "We screened 18,000 human genes and identified over 600 genes that were previously unknown to be mutated in stomach cancer."

Two of the 600 genes identified that were associated with stomach cancer, FAT4 and ARID1A proved to be particularly interesting. A further analysis of about 100 stomach tumors found these genes to be mutated in 5 percent and 8 percent of stomach cancers, respectively. In some patients, portions of the chromosome containing the two genes were found to be missing, providing further evidence that genetic defects affecting these genes occur frequently in stomach cancer.

Lab experiments demonstrated the importance of these two genes in driving stomach cancer, as manipulation of FAT4 and ARID1A function altered the growth of stomach cancer cells.

"More research is required to realize the clinical implications of these findings. ARID1A and FAT4 are likely also involved in many other cancer types, not just stomach cancer," noted Tan, whose research team

is actively working on translating the results of this study into clinical applications.

With more than 100,000 new cases worldwide of stomach cancer each year likely to be caused by mutations in FAT4 or ARID1A, drugs against these targets may someday lead to more effective treatment of stomach tumors and other cancers.

Provided by Duke University Medical Center