MedicalXpress

Gene fusion in lung cancer afflicting never-smokers may be target for therapy

December 22 2011

Smoking is a well-known risk factor for lung cancer, but nearly 25% of all lung cancer patients have never smoked. In a study published online today in *Genome Research*, researchers have identified a previously unknown gene fusion event that could explain a significant proportion of lung cancer cases in never-smokers, and might serve as a target for new therapies.

Recent strides have been made to identify gene mutation events driving cases of lung adenocarcinoma in never-smokers, but the underlying genetic events leading to these lung cancers still remain unknown in a large number of cases. In this report, using a combination of genome sequencing and RNA sequencing, a team of researchers in South Korea has characterized a previously unknown gene fusion event in a case of lung adenocarcinoma striking a 33-year-old Korean male with no history of smoking or cancer within his family.

The group sequenced and compared the genome of the patient's cancer and normal tissue (blood), but they found no mutations in known-cancer related genes, such as *EGFR*, *KRAS*, and *EML4-ALK* mutations, that were likely to explain this case. Delving deeper, they also sequenced RNA isolated from the cancer cells, which when analyzed, can reveal gene rearrangement events that are difficult to detect by genome sequencing and may be driving the cancer.

From the RNA sequencing analysis they built a list of candidate gene fusions, narrowing it down to a single gene fusion that could be a cancer-

causing event. A genomic inversion event occurred on chromosome 10 in the cancer, fusing the *KIF5B* and *RET* genes. This fusion was particularly interesting because *RET* has been previously implicated in other gene fusion events known to drive thyroid cancers, and although it is normally expressed at low levels in the lung, chimeric *RET* in this patient is highly expressed. Furthermore, *KIF5B* contains a protein domain that is necessary for activation of the fusion gene.

They then confirmed that the *KIF5B-RET* fusion occurs in other lung cancer cases, finding two instances in twenty additional cases of lung cancer, indicating that this fusion event is not rare. The authors suggest that the *KIF5B-RET* fusion occurs in about 6% of all lung adenocarcinoma cases. The authors note that although further epidemiological studies are needed to accurately define the frequency of *KIF5B-RET* in lung cancers, they expect that the fusion gene may be a promising molecular target for treatment.

"We showed that genome sequencing technology could reveal a previously hidden cause of human cancer, which can be used as a therapeutic target for personal cancer therapy", said Dr. Jeong-Sun Seo, director of the Genomic Medicine Institute-Seoul National University, chairman of Macrogen Inc., and senior author of the study.

More information: Ju YS, Lee W, Shin J, Lee S, Bleazard T, Won J, Kim YT, Kim J, Kang J, Seo J. Fusion of KIF5B and RET transforming gene in lung adenocarcinoma revealed from whole-genome and transcriptome sequencing. *Genome Res* doi: 10.1101/gr.133645.111

Provided by Cold Spring Harbor Laboratory

Citation: Gene fusion in lung cancer afflicting never-smokers may be target for therapy (2011,

December 22) retrieved 16 April 2024 from https://medicalxpress.com/news/2011-12-gene-fusion-lung-cancer-afflicting.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.