Researchers identify genetic mutation for rare cancer

January 15 2013

This image shows Dan R. Robinson, Michigan Center for Translational Pathology, a research fellow. Credit: University of Michigan Health System

By looking at the entire DNA from this one patient's tumor, researchers have found a genetic anomaly that provides an important clue to improving how this cancer is diagnosed and treated.

Researchers at the University of Michigan Comprehensive Cancer Center sequenced the tumor's genome through a new program called MI-ONCOSEQ, which is designed to identify genetic mutations in tumors that might be targeted with new therapies being tested in clinical trials.

The sequencing also allows researchers to find new mutations. In this case, an unusual occurrence of two genes – NAB2 and STAT6 – fusing together. This is the first time this gene fusion has been identified.

"In most cases, mutations are identified because we see them happening again and again. Here, we had only one case of this. We knew NAB2-STAT6 was important because integrated sequencing ruled out all the known cancer genes. That allowed us to focus on what had been changed," says lead study author Dan R. Robinson, research fellow with the Michigan Center for Translational Pathology.

Once they found the aberration, the researchers looked at 51 other tumor samples from benign and cancerous solitary fibrous tumors, looking for the NAB2-STAT6 gene fusion. It showed up in every one of the samples. Results are published online in Nature Genetics.

"Genetic sequencing is extremely important with rare tumors," says study co-author Scott Schuetze, M.D., associate professor of internal medicine at the U-M Medical School. "Models of rare cancers to study in the laboratory are either not available or very limited. The sequencing helps us to learn more about the disease that we can use to develop better treatments or to help diagnose the cancer in others."

The NAB2-STAT6 fusion may prove to be a difficult target for therapies, but researchers believe they may be able to attack the growth signaling cycle that leads to this gene fusion.

"Understanding the changes induced in the cell by the NAB2-STAT6 gene fusion will help us to select novel drugs to study in patients with advanced solitary fibrous tumors. Currently this is a disease for which there are no good drug therapies available and patients are in great need of better treatments," Schuetze says.

No treatments or clinical trials are currently available based on these findings. Additional testing in the lab is needed to assess the best way to target NAB2-STAT6. The gene fusion could also potentially be used to help identify solitary fibrous tumors in cases where diagnosis is

challenging.

More information: *Nature Genetics,* published online Jan. 13, 2013, DOI: 10.1038/ng.2509