Researchers open 'Pandora's box' of potential cancer biomarkers

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Arul Chinnaiyan, M.D., Ph.D. Credit: University of Michigan Health System

A new analysis opens the door to discovery of thousands of potential new cancer biomarkers.

Researchers at the University of Michigan Comprehensive Cancer Center analyzed the global landscape of a portion of the genome that has not been previously well-explored - long non-coding RNAs. This vast portion of the human genome has been considered the dark matter because so little is known about it. Emerging new evidence suggests that lncRNAs may play a role in cancer and that understanding them better could lead to new potential targets for improving cancer diagnosis, prognosis or treatment.

"We know about protein-coding genes, but that represents only 1-2 percent of the genome. Much less is known about the biology of the non-coding genome in terms of how it might function in a human disease like cancer," says senior study author Arul M. Chinnaiyan, M.D., Ph.D., director of the Michigan Center for Translational Pathology and S.P. Hicks Professor of Pathology at the University of Michigan Medical School.

The researchers pulled together 25 independent datasets totaling 7,256 RNA sequencing samples. The data was from public sources such as The Cancer Genome Atlas project, as well as from the Michigan Center for Translational Pathology's archives. They applied high-throughput RNA sequencing technology to identify more than 58,000 lncRNA genes across normal tissue and a range of common cancer types.

Results of the study appear online in *Nature Genetics*.

"We used all of this data to decipher what the genomic landscape looks like in different tissues as well as in cancer," Chinnaiyan says. "This opens up a Pandora's box of all kinds of lncRNAs to investigate for biomarker potential."

The complete dataset, named the MiTranscriptome compendium, has been made available on a public website,

http://www.mitranscriptome.org, for the scientific community to explore.

The researchers also identified one lncRNA, SChLAP1, as a potential biomarker for aggressive prostate cancer. SChLAP1 was more highly expressed in metastatic prostate cancer than in early stage disease. SChLAP1 was found primarily in prostate cancer cells, not in other cancers or normal cells, which gives researchers hope that a non-invasive test could be developed to detect SChLAP1. Such a test could be used to help patients and their doctors make treatment decisions for early stage prostate cancer.

"Some long non-coding RNAs tend to be exquisitely specific for cancer, while protein-coding genes are often not. That's what makes lncRNAs a very promising target for developing biomarkers," Chinnaiyan says. "We hope that researchers will investigate the MiTransciptome compendium and begin to nominate lncRNAs for further study and development. It's likely that only a subset of these have true function but as a previously untapped area, it holds great promise."

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