

## **Reducing NOVA1 gene helps prevent tumor growth in most common type of lung cancer**

August 6 2018



Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia



Researchers have identified a gene that when inhibited or reduced, in turn, reduced or prevented human non-small cell lung cancer tumors from growing.

When mice were injected with non-small cell <u>lung cancer cells</u> that contained the gene NOVA1, three of four mice formed tumors. When the mice were injected with <u>cancer cells</u> without NOVA1, three of four mice remained tumor-free.

The fourth developed a tumor, but it was very small compared to the mice with the NOVA1 tumor cells, said Andrew Ludlow, first author on the study and assistant professor at the University of Michigan School of Kinesiology.

The research appears online today in *Nature Communications*. Ludlow did the work while a postdoctoral fellow at the University of Texas Southwestern Medical Center, in the shared lab of Woodring Wright, professor of cell biology and internal medicine, and Jerry Shay, professor of cell biology.

The study found that in cancer cells, the NOVA1 gene is thought to activate telomerase, the enzyme that maintains telomeres—the protective caps on the ends of chromosomes that preserve genetic information during cell division (think of the plastic aglets that prevent shoelace ends from fraying).

Telomerase isn't active in healthy adult tissues, so telomeres degrade and shorten as we age. When they get too short, the body knows to remove those damaged or dead cells.

In most cancers, telomerase is reactivated and telomeres are maintained, thus preserving the genetic material, and these are the cells that mutate and become immortal.



Telomerase is present in most cancer types, and it's an attractive therapeutic target for cancer. However, scientists haven't had much luck inhibiting telomerase activity in cancer, Ludlow said.

Ludlow's group wanted to try a new approach, so they screened <u>lung</u> cancer cell lines for splicing genes (<u>genes</u> that modify RNA) that might regulate telomerase in cancer, and identified NOVA1.

They found that reducing the NOVA1 gene reduced <u>telomerase activity</u>, which led to shorter telomeres, and <u>cancer cells</u> couldn't survive and divide.

Researchers only looked at non-small cell lung cancers, and NOVA1 was present in about 70 percent of them.

"Non-small cell lung cancer is the most prevalent form of age-related cancer, and 80 to 85 percent of all lung cancers are non-small cell," Ludlow said. "But there really aren't that many treatments for it."

According to the American Cancer Society, lung cancer causes the most cancer deaths among men and women, and is the second most common cancer, aside from skin cancer.

Before researchers can target NOVA1 or telomerase splicing as a serious potential therapy for non-small cell lung cancer, they must gain a much better understanding of how telomerase is regulated. This research is a step in that direction.

Ludlow's group is also looking at ways to directly impact <u>telomerase</u> splicing, in addition to reducing NOVA1.

**More information:** Andrew T. Ludlow et al, NOVA1 regulates hTERT splicing and cell growth in non-small cell lung cancer, *Nature* 



## Communications (2018). DOI: 10.1038/s41467-018-05582-x

## Provided by University of Michigan

Citation: Reducing NOVA1 gene helps prevent tumor growth in most common type of lung cancer (2018, August 6) retrieved 3 May 2024 from https://medicalxpress.com/news/2018-08-nova1-gene-tumor-growth-common.html

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