

Study shows that smoking 'stops' cancer-fighting proteins, causing cancer and making it harder to treat

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Scientists at the Ontario Institute for Cancer Research (OICR) have uncovered one way tobacco smoking causes cancer and makes it harder to treat by undermining the body's anti-cancer safeguards.

Their new study, [published](#) in *Science Advances*, links [tobacco smoking](#) to harmful changes in DNA called 'stop-gain mutations' that tell the body to stop making certain proteins before they are fully formed.

They found that these stop-gain mutations were especially prevalent in genes known as 'tumor-suppressors,' which make proteins that would normally prevent [abnormal cells](#) from growing.

"Our study showed that [smoking](#) is associated with changes to DNA that disrupt the formation of tumor suppressors," says Nina Adler, a University of Toronto Ph.D. student who led the study during her postgraduate research in Dr. Jüri Reimand's lab at OICR. "Without them, abnormal cells are allowed to keep growing unchecked by the cell's defenses and cancer can develop more easily."

Adler, Reimand and colleagues used powerful computational tools to analyze DNA from more than 12,000 tumor samples across 18 different types of cancer. Their analysis showed a strong link between stop-gain mutations in [lung cancer](#) and the telltale 'footprint' that smoking leaves in DNA.

The researchers then looked at whether how much someone smoked had an impact. Sure enough, their analysis showed that more smoking led to more of these harmful mutations, which can ultimately make cancer more complex and harder to treat.

"Tobacco does a lot of damage to our DNA, and that can have a major impact on the function of our cells," says Reimand, an OICR Investigator and Associate Professor at the University of Toronto. "Our study highlights how tobacco smoking actually deactivates critical proteins, which are the building blocks of our cells, and the impact that can have on our long-term health."

The study also identified other factors and processes responsible for creating large numbers of stop-gain mutations, which are also called 'nonsense' mutations.

Some, like a group of enzymes called APOBEC that is strongly linked to stop-gain [mutations](#) in [breast cancer](#) and other cancer types, occur naturally in the body. Other factors like unhealthy diet and [alcohol consumption](#) are also likely to have similar damaging effects on DNA, but Reimand says more information is needed to fully understand how that works.

As for smoking, Adler says the findings from this study are an important piece of the puzzle behind a leading cause cancer in the world.

"Everyone knows that smoking can cause cancer, but being able to explain one of the ways this works at a [molecular level](#) is an important step in understanding how our lifestyle affects our risk of cancer," Adler says.

OICR President and Scientific Director Dr. Laszlo Radvanyi says these new insights should reinforce that tobacco smoking is one of the biggest threats to our health.

"This is further proof of the immense damage smoking has on our bodies, and further evidence that stopping smoking is always the right choice," Radvanyi says.

More information: Nina Adler et al, Mutational processes of tobacco smoking and APOBEC activity generate protein-truncating mutations in cancer genomes, *Science Advances* (2023). [DOI: 10.1126/sciadv.adh3083](#). www.science.org/doi/10.1126/sciadv.adh3083

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