Study finds a new way that tobacco smoke can cause cancer

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Credit: University of Kentucky

A recent study led by University of Kentucky researchers illuminates a new way that tobacco smoke may promote the development of lung cancer: inhibiting a DNA repair process called nucleotide excision repair

(NER). The results of the study were published in the journal *PLoS ONE*.

Many components of tobacco smoke are carcinogens that can damage DNA. This damage must be removed by DNA repair processes to prevent the development of genetic mutations. In this way, DNA repair processes such as NER are crucial for blocking the accumulation of the DNA mutations that ultimately drive lung cancer development.

"It is well established that the carcinogens in tobacco smoke can produce mutations," said Isabel Mellon, an associate professor in the Department of Toxicology and Cancer Biology at UK and the principal investigator of the study. "But relatively few researchers have investigated the effects of tobacco smoke on DNA repair pathways."

Mellon and her research team examined the effects of cigarette smoke condensate (CSC) – a commonly-used surrogate for tobacco smoke – on the function of the NER process in cultured human lung cells. They found that exposure of these cells to CSC significantly reduces NER efficiency. Additionally, the researchers showed that CSC exposure stimulates the destruction of a key NER protein known as XPC. The reduced abundance of XPC that follows might explain how CSC suppresses NER.

The study's results point to a twofold effect of tobacco smoke on DNA integrity: it not only damages DNA, but it also suppresses a key process that repairs DNA damage.

"Inhibition of NER would likely increase the production of mutations and cancer incidence, particularly in cases of chronic DNA damage induction, as occurs in the lung issue of smokers," Mellon explained.

If this is the case, then the capacity of cells within the lung of a given person to repair damaged DNA could be used to predict that person's

risk of developing lung cancer as a result of tobacco smoke exposure.

"In the future, we hope to determine how the efficiency of the NER pathway differs among different people," said Mellon. "We are also continuing to evaluate how the efficiency of DNA repair in people is negatively impacted by exposure to environmental agents. Whether due to genetic or environmental factors, reduced DNA repair could increase a person's risk for developing cancer."

More information: Nathaniel Holcomb et al. Exposure of Human Lung Cells to Tobacco Smoke Condensate Inhibits the Nucleotide Excision Repair Pathway, *PLOS ONE* (2016). DOI: 10.1371/journal.pone.0158858

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