

First genome-wide comparison of vapers and smokers finds similar DNA changes linked to disease risk

August 13 2024, by Zara Abrams



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In the most comprehensive study of its kind, researchers from the Keck School of Medicine of USC compared epigenetic changes across the

genome in young adults who vaped, smoked or did not use nicotine products, finding a tumor-suppressor gene among the top affected genes in vapers and smokers.

Young adults who vape show chemical changes in their DNA similar to those found in [young adults](#) who smoke—changes known to be linked to the development of cancer—according to a study published in the [*American Journal of Respiratory Cell and Molecular Biology*](#).

A team of researchers from the Keck School of Medicine of USC measured DNA methylation, a chemical modification of DNA that can effectively turn genes "on" or "off," in the oral cells of young adult vapers, smokers and non-users.

DNA methylation is vital to normal cellular processes but if it goes awry it can lead to cancer and other diseases. Using a state-of-the-art genetic sequencing technique, they analyzed virtually the entire genome in the cells of study participants, compared to previous studies that analyzed just two to three percent of genetic regions in vapers or smokers.

The researchers found substantial overlap in DNA methylation patterns, a type of epigenetic modification, between people who vaped versus those who smoked.

"Our findings indicate that the changes in DNA methylation observed in vapers may contribute to the development of disease, including cancer," said Stella Tommasi, Ph.D., an associate professor of research population and public health sciences at the Keck School of Medicine and the study's lead author.

"Electronic cigarettes are not as safe as some people claim that they are, even if the level of most toxicants and carcinogens present in e-liquid and vapor is generally much lower than that found in [cigarette smoke](#),"

she said.

The study, supported in part by the National Institutes of Health, contributes to a growing evidence base on the [health risks](#) of vaping. It also provides a basis for future research that seeks to identify a molecular signature to assess the disease risks associated with vaping.

In the meantime, the research team hopes the study can further emphasize the potential harms of vaping as new products continue to hit the market.

"These findings have significant implications for public health and tobacco regulation that aim to keep vaping products away from young people, who are a particularly vulnerable population," Tommasi said.

Comparing DNA methylation

The study included 30 young adults, average age 23.5 years, divided into three groups: vapers (people who vaped at least three times a week for at least six months, but did not smoke), smokers (people who smoked at least three times a week for at least one year, but did not vape) and non-users (people who neither vaped nor smoked).

Researchers matched the groups by age, race and gender. They also accounted for potential confounding factors, including how much alcohol or grilled food each participant consumed.

After collecting oral cell samples from the cheeks of each participant, the researchers used a high-resolution sequencing technique, known as whole genome bisulfite sequencing, to study more than 25 million sites across the genome.

They searched for differentially methylated regions (DMRs), or areas in

the genome that were more or less methylated in one group of participants compared to the others. They found 831 DMRs in vapers and 2,863 in smokers.

Next, the researchers looked for DMRs that were shared between smokers and vapers, finding 346 (46% of all DMR-associated genes in vapers) that overlapped between the two groups. These methylated regions were on gene sites known to regulate important biological signaling pathways that drive disease development.

This indicates that DNA methylation in vapers, much like in smokers, can contribute to the development of diseases such as cancer, Tommasi said.

A key finding from the study was that the most significant DMR most shared between vapers and smokers was located within HIC1, a tumor-suppressor gene named Hypermethylated In Cancer 1 because of the extensive research base linking it with various cancers, including those linked to tobacco use.

HIC1 is altered by methylation at a very early stage in cancer development. Methylation of HIC1 has also been found in blood samples of smokers who are at high risk of cancer and other chronic diseases. This means it may be useful as a predictive biomarker to help identify people who need to be monitored closely so cancer can be diagnosed early on when it is easiest to treat.

"This is an exciting discovery because the methylation of this gene has never before been identified in vapers," Tommasi said.

Of significance, more than half of the DMRs found in vapers were not detected in smokers. That finding is consistent with the fact that e-cigarettes produce a wide range of harmful or potentially harmful

chemicals, some of which are not found in tobacco cigarettes, the researchers said.

Drilling down on the impact of vaping

The research team is now examining a separate, larger group of participants to learn more about the impact of vaping on DNA methylation. They want to know whether the types of flavors and additives in e-cigarettes, as well as the duration and intensity of vaping, impact DNA methylation.

Their goal is to establish a molecular signature for vaping that can be used to assess the risks associated with vaping in the general population.

"This study presents a lot of opportunities," she said. "It shows us that there are a multitude of candidate genes that can be explored for assessing the risk of disease in vapers."

More information: Stella Tommasi et al, Epigenomic Dysregulation in Youth Vapers: Implications for Disease Risk Assessment, *American Journal of Respiratory Cell and Molecular Biology* (2024). [DOI: 10.1165/rcmb.2024-0207OC](https://doi.org/10.1165/rcmb.2024-0207OC)

Provided by Keck School of Medicine of USC

Citation: First genome-wide comparison of vapers and smokers finds similar DNA changes linked to disease risk (2024, August 13) retrieved 13 August 2024 from <https://medicalxpress.com/news/2024-08-genome-wide-comparison-vapers-smokers.html>

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