

DNA's organization influences the risk of smoking-induced lung cancer

The Hebrew University of Jerusalem

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The study from The Hebrew University of Jerusalem, led by Prof. Sheera Adar and her graduate student Elisheva Heilbrun-Katz from The Institute for Medical Research Israel-Canada in the Faculty of Medicine in collaboration with Prof. Raluca Gordan from Duke University and the University of Massachusetts, has uncovered how the structure and chemical modifications of DNA affect the damage caused by cigarette smoke and the body's ability to repair it. This breakthrough helps explain how smoking leads to lung cancer.

The research focuses on benzo[a]pyrene, a harmful chemical in cigarette smoke. When processed by the body, this chemical becomes Benzo[a]pyrene diol epoxide (BPDE), which can bind to DNA, disrupt its normal function, and lead to cell damage.

Using advanced genomic tools, the researchers discovered that:

- **DNA's environment matters:** Certain regions of DNA, especially ones that are more open and active, are more prone to damage but are also repaired better by the cells.
- **Transcription factors can help or harm:** Proteins that regulate gene activity can sometimes protect DNA from damage, but in other cases, they make it more vulnerable.
- **Efficient repair is key:** The areas of DNA that are better repaired tend to accumulate fewer mutations, even if they suffered from more damage initially.

The study highlights that the body's ability to fix DNA damage is more important than the amount of damage when it comes to determining whether mutations will form. These findings provide new insights into how smoking-related mutations occur and may help guide future cancer prevention and treatment strategies.

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