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Faulty DNA repair could be a risk factor for lung cancer in nonsmokers

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People who have never smoked but whose cells cannot efficiently repair environmental insults to DNA are at higher risk of developing lung cancer than those with effective genomic repair capability, according to researchers from the Department of Epidemiology at The University of Texas M. D. Anderson Cancer Center.

"About 15 percent of lung cancers occur in lifetime never smokers. Risk factors for lung cancer in people who have never smoked are poorly understood, but this study demonstrates that poor DNA repair capacity is an important predictor of lung cancer risk in never smokers," said the study's lead author, Olga Gorlova, Ph.D., an assistant professor in the Department of Epidemiology.

In the June issue of *Cancer Epidemiology, Biomarkers and Prevention*, a journal of the American Association for Cancer Research, the researchers say that, overall, nonsmokers with suboptimal DNA repair capacity (DRC) are almost twice as likely to develop lung cancer, compared with nonsmokers with normal DRC. Study participants with the lowest ability to repair their DNA had a more than a threefold increased risk, compared with individuals with efficient DRC.

Secondhand smoke exposure is another established risk factor; in participants with inefficient DRC who also reported such exposure, the risk of lung cancer was almost fourfold.

Although the research team has not pinpointed the gene or genes that

cause suboptimal DRC, their data suggest that the trait is heritable to some degree. Notably they found that first-degree relatives of those with lowest DRC were 2.5 times more likely to develop lung cancer than were first-degree relatives of people with efficient DRC.

"Our findings demonstrate that suboptimal DNA repair capacity together with secondhand smoke exposure are strong lung cancer risk factors in lifetime never smokers," Gorlova said.

This is the first study that has looked at functional DNA repair capacity as a risk factor for lung cancer in nonsmokers. Researchers drew white blood cells from 219 lung cancer patients and 309 matched control participants, all of whom had never smoked. They used the cells to conduct a host-cell reactivation assay, a complicated test that introduced a specific carcinogen, benzo[a]pyrene diol epoxide (BPDE) into the cells. BPDE is a hydrocarbon found in smoke of all kinds (tobacco, wood, etc.) that is highly carcinogenic and mutagenic, capable of changing the composition of DNA.

The study is a continuation of research underway at M. D. Anderson that is looking for genetic and epigenetic components to lung cancer risk. The research group has previously shown that DNA repair capacity as measured by the host cell reactivation assay was significantly lower in lung cancer patients who were current or former smokers than in matched controls.

"Many people think they aren't at risk for lung cancer because they don't smoke, but anyone who has non-smoking relatives with lung cancer should avoid not just tobacco smoke, but all the other carcinogens and mutagens that are products of combustion," Gorlova said.

Source: American Association for Cancer Research