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# Scientists discover link between estrogen and tobacco smoke

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The hormone estrogen may help promote lung cancer— including compounding the effects of tobacco smoke on the disease—pointing towards potential new therapies that target the hormone metabolism, according to new research presented at the AACR Annual Meeting 2012 on Tuesday, April 3 by scientists at Fox Chase Cancer Center in Philadelphia.

"This research provides the link between estrogen and tobacco smoke," says study author Jing Peng, Ph.D., postdoctoral associate in the lab of Margie L. Clapper, Ph.D., also a co-author on the paper.

The researchers found that estrogen is metabolized into toxic derivatives in the mouse lung. The level of these toxic metabolites increased when mice were exposed to tobacco smoke. The results suggest that new therapies which prevent estrogen from being converted into toxins could one day help treat—or even prevent—lung cancer, says Peng. "In the future, we would like to target estrogen-metabolizing pathways as a form of treatment or prevention of lung cancer."

Researchers have long known that tobacco smoke is the number one cause of lung cancer. But recent findings suggest that estrogen may also play a role in the disease. If so, it wouldn't be the first form of cancer linked to estrogen—this hormone is known to promote breast cancer as well as other gynecologic cancers.

To investigate, Peng, Clapper and their colleagues examined the lungs of

healthy mice and found that they contained high levels of estrogen metabolites, known as 4 hydroxy- estrogens (4-OHEs), which are carcinogenic. Specifically, these 4-OHEs help activate processes that promote cell growth, and generate free radicals that damage cells.

When the researchers exposed the mice to tobacco smoke for 8 weeks, they found that the levels of 4-OHEs increased. "We believe that these metabolites of estrogen can damage cells and contribute to lung cancer," says Clapper.

Female mice had twice as much 4-OHE in their lungs compared to male mice after controlling for the level of total estrogen present. Whether this is the same in humans remains to be determined. "While lung cancer is not more common in women, the number of nonsmokers who develop lung cancer is greater for men than for women," explains Clapper.

In the future, Peng and Clapper hope these results will help researchers develop new therapies that target estrogen metabolism as a way to treat or prevent lung cancer. Already, patients are enrolling in clinical trials that are using anti-estrogen drugs to treat lung cancer.

"We believe that levels of these toxic estrogen metabolites may one day be useful in predicting a person's lung cancer risk or prognosis", adds Peng. "If levels are particularly high, for instance, that may suggest the person is more prone to developing the disease, or has a worse prognosis. We'd definitely like to be able to use this information to develop a more personalized treatment approach," she says.

Provided by Fox Chase Cancer Center

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