Estrogen-targeting drug combo may help prevent lung cancer

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A combination of drugs that target estrogen production significantly reduced the number of tobacco carcinogen-induced lung tumors in mice, according to results from a preclinical study.

"Antiestrogens have been shown to prevent breast cancer in some women," said Jill M. Siegfried, Ph.D., professor in the department of pharmacology and chemical biology at University of Pittsburgh Cancer Institute. "If antiestrogens can prevent lung cancer as well, this would be a major advance, because these drugs are safe to give for long periods and there are no approved ways to prevent lung cancer."

Siegfried presented the results at the AACR-IASLC Joint Conference on Molecular Origins of Lung Cancer: Biology, Therapy and Personalized Medicine, held Jan. 8-11, 2012.

Most lung cancers are positive for a type of estrogen receptor that makes lung tumors grow when exposed to estrogen. In addition, an enzyme in the lung called aromatase produces estrogen. Siegfried and colleagues hoped that by blocking this estrogen receptor and the aromatase enzyme, they might be able to prevent estrogen-sensitive lung tumors.

To test this theory, they conducted a study on two groups of female mice : one group that was currently being exposed to a tobacco carcinogen and one that had past exposure to a tobacco carcinogen and in which some precancerous cells had already formed. The mice were assigned to treatment with a placebo, the aromatase inhibitor anastrozole, the

antiestrogen fulvestrant or a combination of anastrozole and fulvestrant.

"The first model asks whether the treatments inhibit the process by which cancer is first started before it is even detectable under the microscope, and the second asks whether the treatments inhibit the process by which microscopic precancers develop into visible tumors," Siegfried said.

In the first model, the combination treatment given during carcinogen exposure resulted in significantly fewer lung cancer tumors compared with placebo or either treatment alone. The tobacco carcinogen was stopped once treatment began to maximize its ability to halt lung cancer development. Combination treatment also resulted in maximum antitumor effects in the second model, where precancerous cells were already present.

According to Siegfried, these results suggest that antiestrogen treatment combined with an aromatase inhibitor prevents lung cancer development during tobacco carcinogen exposure and after carcinogen damage to the airways has already occurred.

Siegfried said that ultimately, the hope is that this research could lead to an approved treatment that could greatly reduce the risk for an ex-smoker to develop lung cancer.

"We may be able to prevent lung cancer in people who have been previously exposed to tobacco carcinogens using some of the same antiestrogen drugs that can prevent breast cancer," Siegfried said. "A lot of work needs to be done to determine who would benefit from this therapy, and these drugs would need to be tested in clinical trials in those at high risk for lung cancer."