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## Vitamin A Derivative Associated with Reduced Growth in Some Lung Cells

Treatment with a derivative of vitamin A called retinoic acid was associated with reduced lung cell growth in a group of former heavy smokers, according to a study published online October 30 in the *Journal of the National Cancer Institute*.

Former smokers remain at elevated risk for lung cancer. According to one hypothesis, lung cells that were damaged during years of smoking may continue to grow and evolve into cancer even after that person has quit smoking. Previous studies have suggested that retinoids, a class of drugs related to vitamin A, may be effective for preventing lung cancer in former smokers. Retinoids have also been shown to slow the growth of cancer cells in laboratory experiments.

Investigators at the University of Texas M.D. Anderson Cancer Center in Houston previously conducted a double-blind lung cancer prevention trial among 225 former heavy smokers. The subjects were randomly assigned to receive a 3-month treatment of 13-*cis*-retinoic acid and vitamin E, or 9-*cis*-retinoic acid, or a placebo. Walter Hittelman, Ph.D., and colleagues later examined biopsy samples of participants' lung tissue taken before and after treatment, then measured the proliferation of the cells using a biomarker called Ki-67.

Both treatments reduced cell proliferation in one layer of the lung cells (the parabasal layer), but not the other (the basal layer), which surprised the researchers.

In patients given 13-*cis*-retinoic acid and vitamin E, there was a statistically significant reduction in parabasal layer cell growth compared with the placebo treatment, but not in those given 9-*cis*-retinoic acid. When the data were analyzed by the biopsy site, both treatments statistically significantly reduced cell growth.

"It will therefore be important to distinguish the effects of molecularly targeted agents on the basal and parabasal [lung cell] layers in proposed lung chemoprevention trials with long follow-up," the authors write.

In an accompanying editorial, Eva Szabo, M.D., of the National Cancer Institute in Bethesda, Md., discusses the appropriateness of using the biomarker Ki-67 as an alternative endpoint in cancer prevention trials. While the biomarker showed that the retinoid agents were able to reduce cell growth, she says it is still too soon to test them in more advanced clinical trials. "We do not have a full understanding of the effects of these agents on [lung cells] or their effects during the full spectrum of carcinogenesis," she writes.

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### Citations:

- Article: Hittelman WN, Liu DD, Kurie JM, Lotan R, Lee JS, Khuri F, et al. Proliferative Changes in the Bronchial Epithelium of Former Smokers Treated With Retinoids. *J Natl Cancer Inst* 2007; 99:1603-1612
- Editorial: Szabo E. Proliferative Changes in Chemoprevention Trials: Learning From Secondary Endpoints. *J Natl Cancer Inst* 2007; 99:1565-1567

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