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EXPRESSION OF CONCERN

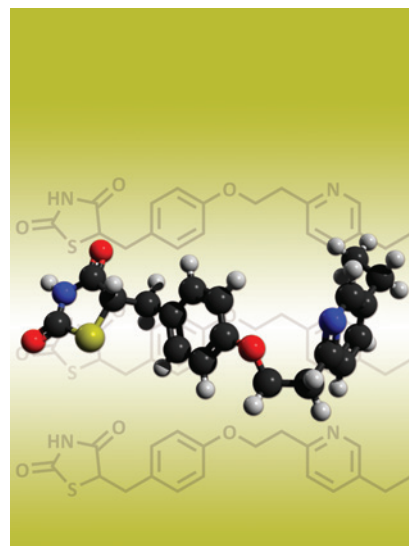
- 733** Expression of Concern: Tobacco-Specific Carcinogens Induce Hypermethylation, DNA Adducts, and DNA Damage in Bladder Cancer

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ABOUT THE COVER

No effective chemopreventive agents for lung cancer exist. Prostacyclin overexpression or administration of the stable prostacyclin analog, iloprost, is highly effective in preventing adenoma formation in multiple murine models of chemical carcinogenesis, including a tobacco smoke-induced tumor model. Oral iloprost is effective in improving premalignant dysplasia in former smokers in a Phase II trial, but the drug is not currently available. Basic studies have supported a PPAR γ -mediated mechanism for iloprost's chemopreventive activity. Pioglitazone is a thiazolidinedione PPAR γ activator and has been shown to be chemopreventive in multiple preclinical models. Keith and colleagues carried out a placebo-controlled Phase II trial (beginning on page 721) of oral pioglitazone in high-risk current or former smokers with sputum cytologic atypia or known endobronchial dysplasia. Although pioglitazone did not show efficacy in improving premalignant dysplasia in either current or former smokers, specific lesions showed histologic improvement. The results suggest that chemopreventive activity of iloprost is not purely mediated through PPAR γ . Further study will be needed to better characterize responsive dysplasia. The cover image depicts the structure of pioglitazone, the drug tested in this study.



Cancer Prevention Research

12 (10)

Cancer Prev Res 2019;12:641-734.

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