

EDITORIAL

373 Validation of PDE5 as a Chemoprevention Target

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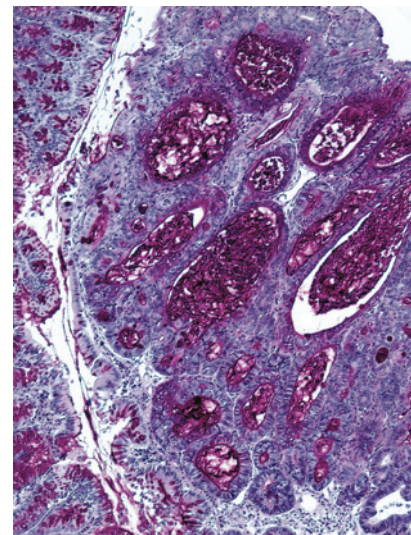
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ABOUT THE COVER

Lesions of the colon and rectum are of the most commonly diagnosed cancers, and chemoprevention is relevant due to large populations with established risk factors, and a poor prognosis for advanced disease. Phosphodiesterase-5 inhibitors are an established pharmacological approach to increase cGMP levels, which a growing body of evidence predicts will be tumor suppressive in the intestine. A study by Islam and colleagues (page 377) has tested the effect of the phosphodiesterase-5 inhibitor sildenafil in an inflammatory carcinogenesis model of colon cancer in mice. The study showed that sildenafil blocked the early carcinogenesis phase to reduce polyp formation and promoted mucus differentiation but otherwise had a minimal effect on suppressing the progression of initiated lesions. The cover image shows large pockets of differentiated tissue in a colonic polyp from a sildenafil-treated mouse that was stained to visualize mucus. Central to primary chemoprevention is a low risk-benefit ratio for drugs given to patients predisposed to disease but are otherwise healthy. This study has clear translational impact because of its use of a human dose-equivalent of sildenafil that is routinely prescribed for long-term daily use in pediatric patients with pulmonary arterial hypertension.



Cancer Prevention Research

10 (7)

Cancer Prev Res 2017;10:373-430.

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