Cancer Prevention Research

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REVIEW

RESEARCH ARTICLES

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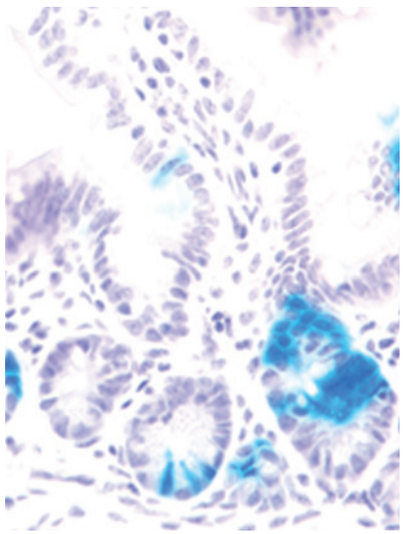
ABOUT THE COVER



Celecoxib, a selective inhibitor of cyclooxygenase-2 (COX-2), has chemopreventive effects in the gastrointestinal (GI) tract. Although celecoxib is believed to possess anti-tumor activity primarily by suppressing COX-2-derived prostaglandin biosynthesis, it may also act by COX-2-independent mechanisms. The GI tract contains trillions of bacteria which can secrete metabolites known to impact GI tumor development. This study demonstrates that celecoxib treatment shifts the luminal bacterial and metabolite profiles in association with reducing stem cell proliferation and polyp burden in $APC^{Min/+}$ mice. The cover image shows results of lineage tracing of Lgr5-positive stem cells in the ileal crypt of an *Lgr5-EGFP-ires-CreERT2/Rosa26-lacZ* mouse given celecoxib. Mice were given either celecoxib-containing diet or control diet for five weeks then tamoxifen was administered and tissues were examined by LacZ staining. The ability of Lgr5-positive cells to give rise to the differentiated cells in the crypt was impaired by celecoxib treatment. Taken together, this study suggests that celecoxib has a previously unrecognized mechanism of action that may contribute to its chemopreventive effects. Namely, altering the microbiota and reducing the growth-promoting metabolites they produce results in decreased stem cell proliferation and reduced polyp burden. See the article by Montrose and colleagues (beginning on page 721) for more information.

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