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CANCER PREVENTION RESEARCH

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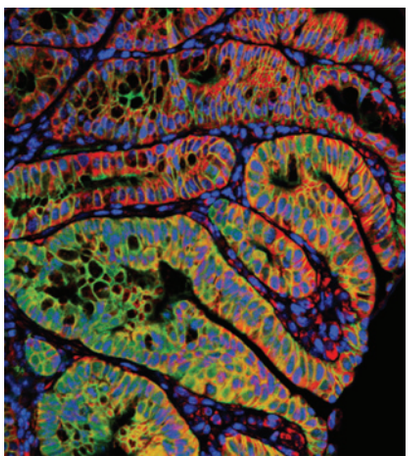
ABOUT THE COVER

Mutations in the adenomatous polyposis coli (*APC*) gene that activates Wnt/β-catenin signaling and drives the transcription of oncoproteins (e.g., MYC) essential for malignant progression, occur in over 80% of patients with colorectal cancer. Mutations in *APC* or other members of the Wnt/β-catenin signaling cascade impair β-catenin degradation and promote translocation of β-catenin to the nucleus, where it mediates a proliferative/survival transcriptional program. Novel compounds that inhibit Wnt/β-catenin signaling can block the effect of such mutations and are attractive drug candidates for cancer chemoprevention or therapy. In a publication starting on page 995 of this issue, Lee and colleagues report that a novel phosphodiesterase 10A (PDE10) inhibitor (ADT 061) suppresses the formation of colorectal adenomas in the $Apc^{+/Min\text{-}FCCC}$ mouse model, where tumorigenesis is driven by an *APC* mutation and nuclear accumulation of β-catenin. PDE10 inhibition activates cGMP/PKG signaling and phosphorylates the oncogenic pool of β-catenin, resulting in its degradation and mitigation of proliferative/survival transcription. The cover shows the colocalization of PDE10 (red) and β-catenin (green) in colon adenomas from $Apc^{+/Min\text{-}FCCC}$ mice.



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