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Canonical Wnt/β-catenin Signaling Drives Human Schwann Cell Transformation, Progression, and Tumor Maintenance 674

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GSK-3α Promotes Oncogenic KRAS Function in Pancreatic Cancer via TAK1–TAB Stabilization and Regulation of Noncanonical NF-κB 690
D. Bang, W. Wilson, M. Ryan, J.J. Yeh, and A.S. Baldwin

Précis: GSK3α but not GSK3β enhances pancreatic cell growth downstream of mutant KRAS via coordinate activation of both canonical and noncanonical NF-κB signaling.

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- Next-Generation Screening Goes National in UK
- Anti-HER2 Drugs May Benefit Some Lung Cancer Patients
- Outreach Cuts Disparities in Colorectal Cancer Deaths
- Debating Drug Approval Decisions
- FDA Struggles with Spending Uncertainties
- Lighting Up Discussion on Tobacco Use

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Killian and colleagues found that gastrointestinal stromal tumors (GIST) with mutations in succinate dehydrogenase (SDH) complex genes exhibited a distinct methylation signature relative to the profile of KIT-mutant tumors and normal reference tissues. This methyl-divergent profile was distinguished by increased global DNA hyper-methylation, particularly at DNase hypersensitive sites, and was also present in other SDH-mutant tumor lineages, including paraganglioma and pheochromocytoma, supporting the oncogenotype dependence of this signature. In addition, a similarly perturbed methylation profile was detected in gliomas harboring mutations in another Krebs cycle enzyme, isocitrate dehydrogenase (IDH). These findings identify a strong association between the mitochondrial Krebs cycle and cancer epigenomic reprogramming. For details, please see the article by Killian and colleagues on page 648.