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EPAH2 Is a Mediator of Vemurafenib Resistance and a Novel Therapeutic Target in Melanoma


Précis: EPAH2 upregulation confers BRAF inhibitor resistance in melanoma, which can be overcome by treatment with small-molecule inhibitors targeting EPAH2.

See article, p. 264

PRMT5 Is Required for Lymphomagenesis Triggered by Multiple Oncogenic Drivers


Précis: PRMT5 cooperates with oncogenic drivers such as cyclin D1 to promote lymphomagenesis via p53 methylation, which alters p53 chromatin occupancy and inhibits proapoptotic p53 target genes.

Combined Inhibition of MAP Kinase and KIT Signaling Synergistically Destabilizes ETV1 and Suppresses GIST Tumor Growth


Précis: Targeted destabilization of the lineage-specific transcription factor ETV1 via dual KIT/MEK inhibition disrupts an ETV1–KIT positive feedback loop and potently inhibits GIST tumor growth.

See commentary, p. 231

Correction

Correction: Comprehensive Genomic Profiling of Pancreatic Acinar Cell Carcinomas Identifies Recurrent RAF Fusions and Frequent Inactivation of DNA Repair Genes

Chromatin-modifying enzymes such as lysine (K)-specific demethylases (KDM) have been implicated in tumorigenesis. Van Rechem and colleagues identified a nonsynonymous coding SNP in KDM4A, which increased its protein turnover and was associated with worse outcome in non–small cell lung cancer. Reduced KDM4A expression or homozygosity for this SNP increased the sensitivity of lung cancer cells to mTOR inhibitors. In a second article, Van Rechem and colleagues found that KDM4A regulated protein synthesis by interacting with and modulating the distribution of translation initiation factors in polysome fractions. In addition, KDM4A depletion or treatment with a JmjC demethylase inhibitor enhanced the suppressive effects of mTOR inhibition on translation initiation. Together, these studies implicate KDM4A as a potential therapeutic target and a possible biomarker for mTOR inhibitor therapy. For details, please see the articles by Van Rechem and colleagues on pages 245 and 255. Cover photo by Johnathan R. Whetstine, of the sculpture Dancing Peptides by Mara Haseltine.