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STK11/LKB1 Mutations and PD-1 Inhibitor Resistance in KRAS-Mutant Adenocarcinoma Lung ............ 822
Précis: In patients with KRAS-mutant lung adenocarcinoma, co-occurring alterations in STK11 conferred primary resistance to PD-1 blockade, suggesting that genomic profiling may guide selection of patients likely to respond.
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Published for American Association for Cancer Research by Wiley.
Precision Targeted Therapy with BLU-667 for RET-Driven Cancers . . . . 836
Précis: BLU-667 is a potent selective RET inhibitor with activity against multiple RET mutations and fusions, and it achieved clinical responses with limited toxicity in four patients with RET-driven tumors.
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PTEN Deficiency and AMPK Activation Promote Nutrient Scavenging and Anabolism in Prostate Cancer Cells . . . . 866
Précis: AMPK-dependent macropinocytosis of necrotic cell debris enhances the growth and survival of PTEN-deficient prostate cancer cells
See commentary, p. 800

CDK6 Antagonizes p53-Induced Responses during Tumorigenesis . . . . 884
Précis: CDK6 antagonizes p53 to promote leukemia cell growth, and CDK6 loss promotes the outgrowth of p53 mutant malignant cell lines, suggesting a potential risk in therapeutic targeting of CDK6.

ON THE COVER
Skoulidis, Goldberg, Greenawalt, and colleagues linked STK11 mutations to PD-1 inhibitor resistance in KRAS-mutant lung cancer. Patients with lung cancer harboring co-occurring STK11 and KRAS alterations had a lower response rate to PD-1/PD-L1 blockade than patients with co-occurring KRAS and TP53 alterations or KRAS mutations alone. STK11 alterations were enriched in PD-L1-negative tumors with an intermediate to high tumor mutation burden. However, STK11 alterations were also associated with primary resistance to PD-1 blockade in patients with PD-L1-positive tumors. STK11 deletion induced de novo resistance to PD-1 inhibition in a mouse model of KRAS-mutant lung adenocarcinoma. These results demonstrate that STK11 alterations confer primary resistance to PD-1/PD-L1 blockade and suggest that genomic profiling may identify patients likely to benefit from PD-1 blockade. For details, please see the article by Skoulidis, Goldberg, Greenawalt, and colleagues on page 822.