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**CANCER DISCOVERY**  
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### Online
- For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.
Autophagy Is Required for Glucose Homeostasis and Lung Tumor Maintenance


Précis: Acute inhibition of autophagy impairs the regulation of glucose metabolism and selectively suppresses the growth of established KRAS-driven lung tumors in mice.

See commentary, p. 873

NSD3–NUT Fusion Oncoprotein in NUT Midline Carcinoma: Implications for a Novel Oncogenic Mechanism


Précis: Impaired differentiation and increased proliferation in NMC requires formation of a NSD3–BRD4–NUT complex that can be targeted by bromodomain inhibitors.

PTEN-Deficient Tumors Depend on AKT2 for Maintenance and Survival

Y.R. Chin, X. Yuan, S.P. Baik, and A. Toker

Précis: Specific depletion of AKT2 but not AKT1 or AKT3 in PTEN-deficient cancer cells results in p21-mediated apoptosis and prostate tumor regression.

EGFR Variant Heterogeneity in Glioblastoma Resolved through Single-Nucleus Sequencing


Précis: Glioblastoma is characterized by subpopulations of cells with heterogeneous EGFR variant expression, which likely cooperate in driving tumor progression and treatment resistance.

See commentary, p. 876

ON THE COVER

Chin and colleagues found that knockdown or pharmacologic inhibition of AKT2 but not AKT1 induced apoptosis in established tumor spheroids derived from PTEN-deficient prostate, breast, and glioblastoma cell lines, indicating that this isoform is essential for PTEN-deficient tumor survival. AKT2 depletion resulted in upregulation of p21 and BAX and downregulation of insulin-like growth factor 1 receptor; knockdown of p21, but not BAX, rescued apoptosis induced by AKT2 depletion, suggesting that p21 is a downstream target of AKT2. Importantly, although AKT1 silencing exhibited a largely cytostatic effect in prostate cancer xenografts, AKT2 depletion increased p21 levels, stimulated apoptosis, and promoted tumor regression. These results indicate that AKT2 is required for the maintenance of PTEN-deficient tumors and highlight the need for preclinical development of AKT2-selective inhibitors. For details, please see the article by Chin and colleagues on page 942.
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