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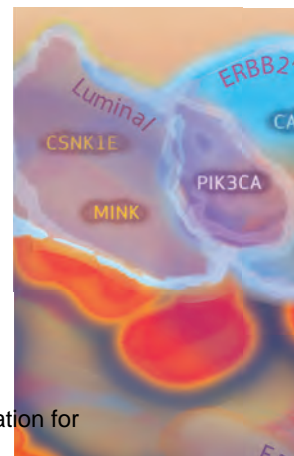
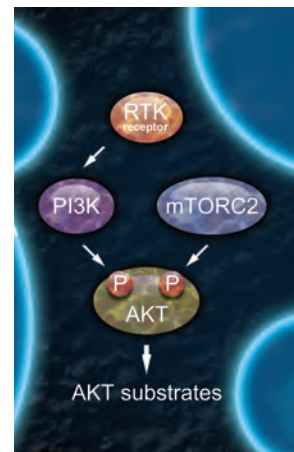
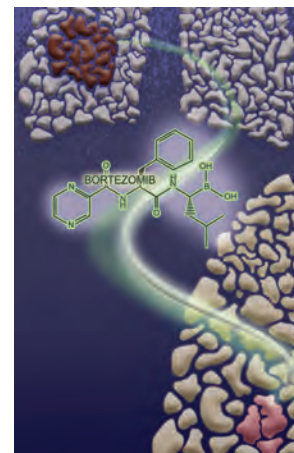
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J. Capdevila and J. Tabernero

RESEARCH ARTICLES Genetic and Functional Studies Implicate *HIF1α* as a 14q Kidney Cancer Suppressor Gene222
C. Shen, R. Beroukhim, S.E. Schumacher, J. Zhou, M. Chang, S. Signoretti, and W.G. Kaelin, Jr

Précis: Genetic and functional studies demonstrate that loss of chromosome 14q is a critical event in the etiology of clear cell renal carcinoma and identify *HIF1α* as a tumor suppressor gene in this disease.





Response and Resistance to NF- κ B Inhibitors in Mouse Models of Lung

Adenocarcinoma236

W. Xue, E. Meylan, T.G. Oliver, D.M. Feldser, M.M. Winslow, R. Bronson, and T. Jacks

Précis: This study provides preclinical evidence that the NF- κ B pathway is a potential therapeutic target in a subset of lung adenocarcinomas that have activation of the NF- κ B pathway.

mTOR Kinase Inhibition Causes Feedback-Dependent Biphasic Regulation of AKT Signaling . . .248

V.S. Rodrik-Outmezguine, S. Chandralapaty, N.C. Pagano, P.I. Poulikakos, M. Scaltriti, E. Moskatel, J. Baselga, S. Guichard, and N. Rosen

Précis: Inhibition of mTOR kinase causes biphasic regulation of AKT signaling involving receptor tyrosine kinases.

Functional Viability Profiles of Breast Cancer260

R. Brough, J.R. Frankum, D. Sims, A. Mackay, A.M. Mendes-Pereira, I. Bajrami, S. Costa-Cabral, R. Rafiq, A.S. Ahmad, M.A. Cerone, R. Natrajan, R. Sharpe, K-K. Shiu, D. Wetterskog, K.J. Dedes, M.B. Lambros, T. Rawjee, S. Linardopoulos, J.S. Reis-Filho, N.C. Turner, C.J. Lord, and A. Ashworth

Précis: Functional RNAi screen exploiting synthetic lethality identifies genes critical for growth and survival of breast cancer cells as well as potential therapeutic targets.

ON THE COVER

Rodrik-Outmezguine and colleagues identify an adaptive mechanism in the AKT signaling pathway. AKT signaling becomes reactivated through feedback-induced phosphorylation of AKT on T308 but not on S473. The addition of RTK inhibitors prevented reactivation, causing cell death and tumor regression *in vivo*, highlighting the possible need for combinatorial approaches to block feedback-regulated pathways. For details, please see the article by Rodrik-Outmezguine and colleagues on page 248.



CANCER DISCOVERY

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