

CANCER DISCOVERY CONTENTS

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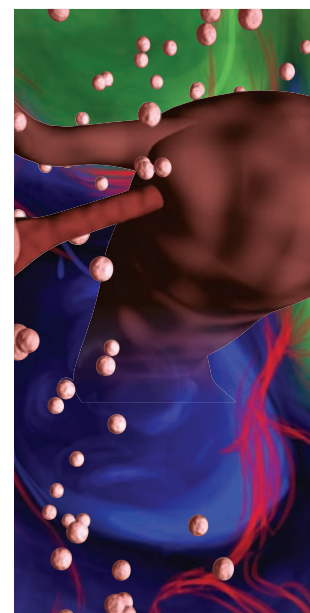
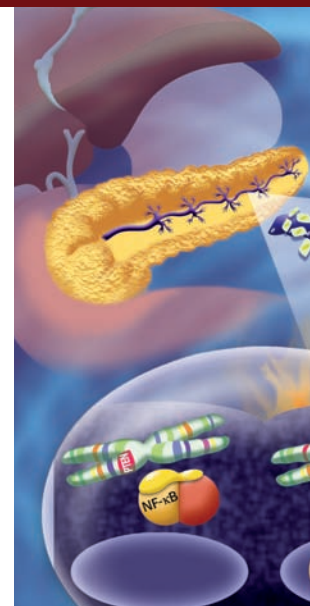
F. A. Karreth, K. K. Frese, G. M. DeNicola, M. Baccarini, and D. A. Tuveson

Précis: C-Raf, but not B-Raf, is required for K-Ras^{G12D}-induced tumorigenesis and should be considered an important therapeutic target.

Temporal Dissection of Tumorigenesis in Primary Cancers 137

S. Durinck, C. Ho, N. J. Wang, W. Liao, L. R. Jakkula, E. A. Collisson, J. Pons, S-W. Chan, E. T. Lam, C. Chu, K. Park, S-W. Hong, J. S. Hur, N. Huh, I. M. Neuhaus, S. S. Yu, R. C. Grekin, T. M. Mauro, J. E. Cleaver, P-Y. Kwok, P. E. LeBoit, G. Getz, K. Cibulskis, J. C. Aster, H. Huang, E. Purdom, J. Li, L. Bolund, S. T. Arron, J. W. Gray, P. T. Spellman, and R. J. Cho

Précis: Next-generation sequencing is used to temporally order the occurrence of genetic aberrations in epithelial cancer.



**RESEARCH
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Ovarian Cancer Spheroids Use Myosin-Generated Force to Clear the Mesothelium.....144



M. P. Iwanicki, R. A. Davidowitz, M. R. Ng, A. Besser, T. Muranen, M. Merritt, G. Danuser, T. Ince, and J. S. Brugge

Précis: Time-lapse video microscopy shows that ovarian cancer spheroids clear the mesothelium via myosin-generated force.

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Précis: PTEN is shown to be a tumor suppressor in human PDAC and controls NF- κ B-dependent transcription via PI3K-AKT signaling.

High Frequency of *PIK3R1* and *PIK3R2* Mutations in Endometrial Cancer Elucidates a Novel Mechanism for Regulation of PTEN Protein Stability170

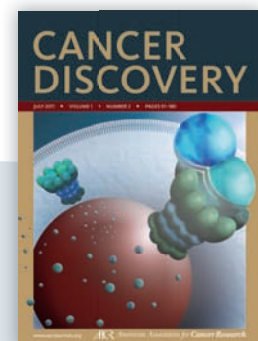


L. W. T. Cheung, B. T. Hennessey, J. Li, S. Yu, A. P. Myers, B. Djordjevic, Y. Lu, K. Stemke-Hale, M. D. Dyer, F. Zhang, Z. Ju, L. C. Cantley, S. E. Scherer, H. Liang, K. H. Lu, R. R. Broaddus, and G. B. Mills

Précis: High frequency of mutations in endometrioid endometrial cancers leads to PI3K pathway activation.

ON THE COVER

Cheung and colleagues report aberrations in the PI3K pathway occur in a majority of endometrioid endometrial cancers, with coordinate mutations of multiple pathway members being more common than predicted by chance. Multiple gain-of-function *PIK3R1* and *PIK3R2* mutations result in the stabilization of PTEN protein with likely contribution from the ubiquitin-proteasome degradative pathway, as depicted by the cover. For details, please see the article by Cheung and colleagues on page 158.



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