

CANCER DISCOVERY

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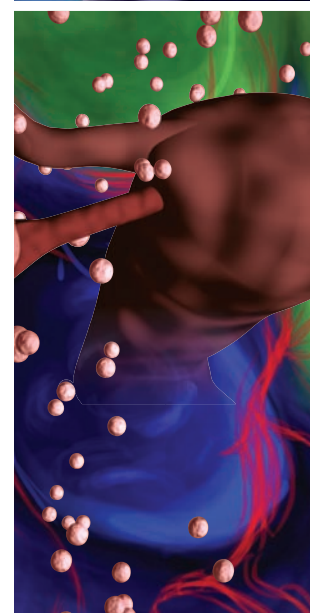
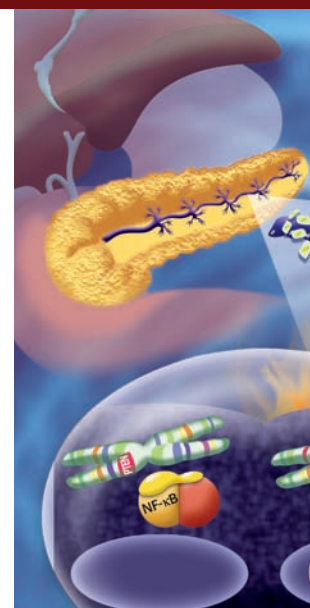
F. A. Karreth, K. K. Frese, G. M. DeNicola, M. Baccarini, and D. A. Tuveson

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

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



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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. Hennessy, 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.

