Prospective

The APL Paradigm and the “Co-Clinical Trial” Project

C. Nardella, A. Lunardi, A. Patnaik, L. C. Cantley, and P. P. Pandolfi

REVIEW

The Drug-Induced Degradation of Oncoproteins: An Unexpected Achilles’ Heel of Cancer Cells?

J. Ablain, R. Nasr, A. Bazarbachi, and H. de Thé

RESEARCH BRIEF

C-Raf Is Required for the Initiation of Lung Cancer by K-RasG12D

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-RasG12D–induced tumorigenesis and should be considered an important therapeutic target.

Temporal Dissection of Tumorigenesis in Primary Cancers


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

PTEN Is a Major Tumor Suppressor in Pancreatic Ductal Adenocarcinoma and Regulates an NF-κB–Cytokine Network ......................... 158


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

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.

High Frequency of PIK3R1 and PIK3R2 Mutations in Endometrial Cancer Elucidates a Novel Mechanism for Regulation of PTEN Protein Stability .......................... 170


Précis: High frequency of mutations in endometriod endometrial cancers leads to PI3K pathway activation.
CANCER DISCOVERY

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