### IN THIS ISSUE

- Highlighted research articles

### NEWS IN BRIEF

- Important news stories affecting the community

### NEWS IN DEPTH

- Drug Discovery Gets an Academic Push

### RESEARCH WATCH

- Selected highlights of recent articles of exceptional significance from the cancer literature

### VIEWS

- In The Spotlight
  - New Insight Puts CRAF in Sight as a Therapeutic Target
  - The First Line of Intra-abdominal Metastatic Attack: Breaching the Mesothelial Cell Layer
  - Kras, Pten, NF-kB, and Inflammation: Dangerous Liaisons
  - New Routes to Old Places: PIK3R1 and PIK3R2 Join PIK3CA and PTEN as Endometrial Cancer Genes

### RESEARCH BRIEF

- C-Raf Is Required for the Initiation of Lung Cancer by K-Ras
- Temporal Dissection of Tumorigenesis in Primary Cancers

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- Prospective
  - The APL Paradigm and the “Co-Clinical Trial” Project
  - The Drug-Induced Degradation of Oncoproteins: An Unexpected Achilles’ Heel of Cancer Cells
  - C-Raf Is Required for the Initiation of Lung Cancer by K-Ras
  - Temporal Dissection of Tumorigenesis in Primary Cancers

### REVIEW

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

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**RESEARCH BRIEF**

- C-Raf Is Required for the Initiation of Lung Cancer by K-Ras
- Temporal Dissection of Tumorigenesis in Primary Cancers

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**Précis:**

- C-Raf, but not B-Raf, is required for K-Ras-induced tumorigenesis and should be considered an important therapeutic target.

- Next-generation sequencing is used to temporally order the occurrence of genetic aberrations in epithelial cancer.
Ovarian Cancer Spheroids Use Myosin-Generated Force to Clear the Mesothelium

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


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

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.

ON THE COVER

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


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