### IN THIS ISSUE

Highlighted research articles 893

### NEWS IN BRIEF

Important news stories affecting the community 896

### RESEARCH WATCH

Selected highlights of recent articles of exceptional significance from the cancer literature 901

### ONLINE

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.

### VIEWS

**In The Spotlight**

- **Cancer Metastasis: Perivascular Macrophages Under Watch** 906
  E. Kadioglu and M. De Palma
  See article, p. 932
- **Targeting a Novel ER/HOXB7 Signaling Loop in Tamoxifen-Resistant Breast Cancer** 909
  M.R. Heideman, A. Frei, and N.E. Hynes
  See article, p. 944
- **Mass Cytometry: A High-Throughput Platform to Visualize the Heterogeneity of Acute Myeloid Leukemia** 912
  P. Do and J.C. Byrd
  See article, p. 988

### MINI REVIEW

Adaptive Immune Resistance: How Cancer Protects from Immune Attack 915
A. Ribas

### RESEARCH ARTICLES

**A Genome-Wide Scan Identifies Variants in NFIB Associated with Metastasis in Patients with Osteosarcoma** 920

**Précis:** The risk variant rs7034162 in NFIB contributes to osteosarcoma metastasis susceptibility.

### Real-Time Imaging Reveals Local, Transient Vascular Permeability, and Tumor Cell Intravasation Stimulated by TIE2hi Macrophage–Derived VEGFA 932

**Précis:** Hyperpermeability of tumor vasculature is dynamic and restricted to the Tumor MicroEnvironment of Metastasis (TMEM).

See commentary, p. 906

### HOXB7 Is an ERα Cofactor in the Activation of HER2 and Multiple ER Target Genes Leading to Endocrine Resistance 944

**Précis:** HOXB7 is upregulated by MYC-mediated suppression of miR-196a and enhances expression of ER target genes in tamoxifen-resistant breast cancer cells.

See commentary, p. 909
Combined EGFR/MEK Inhibition Prevents the Emergence of Resistance in EGFR-Mutant Lung Cancer  ........................................ 960
Précis: Acquired resistance to EGFR inhibitors can be prevented with dual EGFR and MEK inhibition, which results in prolonged ERK1/2 inhibition and increased apoptosis in EGFR-mutant NSCLC.

Synthetic Lethal Approaches Exploiting DNA Damage in Aggressive Myeloma  ................. 972
Précis: Upregulation of MYC in multiple myeloma cells drives DNA damage via replicative stress and ROS induction, and confers sensitivity to ATR inhibitors and small-molecule inducers of ROS.

Mass Cytometric Functional Profiling of Acute Myeloid Leukemia Defines Cell-Cycle and Immunophenotypic Properties That Correlate with Known Responses to Therapy  ................. 988
G.K. Behbehani, N. Samusik, Z.B. Bjornson, W.J. Fantl, B.C. Medeiros, and G.P. Nolan
Précis: High-dimensional analysis of patient-derived AML cells using mass cytometry identifies changes in immunophenotypic patterns and cell-cycle kinetics that are predictive of AML subtype and chemotherapeutic response.
See commentary, p. 912

Tricker, Xu, and colleagues found that combined treatment with the mutant EGFR-selective inhibitor WZ4002 and the MEK inhibitor trametinib delayed the development of acquired resistance in EGFR inhibitor-naïve and EGFR<sup>T790M</sup>-positive lung cancer cells. WZ4002/trametinib treatment prevented ERK1/2 reactivation and increased apoptosis. Combination treatment was also significantly more effective than WZ4002 alone in suppressing tumor regrowth in xenograft models and a genetically engineered mouse model of EGFR<sup>T790M</sup>-mutant lung cancer. Although EGFR and ERK inhibition were maintained in the majority of WZ4002/trametinib-resistant tumor nodules, both AKT and S6 were frequently reactivated, and the addition of an mTOR inhibitor restored WZ4002/trametinib sensitivity in vitro and in vivo. These results highlight the potential clinical utility of initial cotargeting of EGFR and MEK to prevent the emergence of acquired resistance in EGFR-mutant lung cancer. For details, please see the article by Tricker, Xu, and colleagues on page 960.